Prothena Corp plc
Form 424B5
June 23, 2014
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The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell nor do they seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion.

Preliminary Prospectus Supplement dated June 23, 2014.

Prospectus Supplement

(To Prospectus dated June 23, 2014)

Shares

$100,000,000

Ordinary Shares

Prothena Corporation plc is offering $100,000,000 of its ordinary shares.

Our ordinary shares are listed on The NASDAQ Global Select Market under the symbol PRTA. On June 20, 2014, the last reported sale price of our ordinary shares on The NASDAQ Global Select Market was $23.63 per ordinary share.

We are an emerging growth company as that term is defined under the federal securities laws of the United States and, as such, may elect to comply with certain reduced public company reporting requirements for this prospectus supplement and future filings.

Entities managed by Woodford Investment Management LLP have indicated an interest in purchasing approximately $50 million of our ordinary shares in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to these entities and these entities could determine to purchase more, fewer or no shares in this offering. Any ordinary shares sold to these entities will be purchased by the underwriters at the public offering price without the underwriting discount.

Investing in our ordinary shares involves risks that are described in the Risk Factors section beginning on page S-6 of this prospectus supplement.

	Per Share	Total
Public offering price	$	$
Underwriting discount (1)(2)	$	$
Proceeds, before expenses, to Prothena Corporation plc	$	$

(1) See Underwriting in this prospectus supplement for a description of the compensation payable to the underwriters.
(2) No underwriting discount will apply to any ordinary shares sold to entities managed by Woodford Investment Management LLP.

We have granted to the underwriters the right to subscribe for up to an aggregate of $15,000,000 of additional ordinary shares at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the ordinary shares to investors on or about , 2014.

BofA Merrill Lynch **Credit Suisse** **RBC Capital Markets**

Wedbush PacGrow Life Sciences **Ladenburg Thalmann**

The date of this prospectus supplement is , 2014.

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Neither we nor the underwriters have authorized anyone to provide you with information that is different from that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are offering to sell ordinary shares and seeking offers to buy ordinary shares only in jurisdictions where offers and sales are permitted. The information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date on the front of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of our ordinary shares.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of ordinary shares and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated June 23, 2014, provides more general information about our ordinary shares. To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus or the documents incorporated by reference, you should rely on the information in this prospectus supplement. Generally, when we refer to the prospectus, we are referring to this prospectus supplement and the accompanying prospectus combined.

Prothena and our logo are our trademarks and are used in this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus also include

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trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this prospectus supplement and the accompanying prospectus appear without the symbol, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

For investors outside the United States: Neither we nor the underwriters have taken any action that would permit this offering or possession or distribution of this prospectus supplement and the accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons who have come into possession of this prospectus supplement and the accompanying prospectus in a jurisdiction outside the United States are required to inform themselves about and to observe any restrictions relating to this offering and the distribution of this prospectus supplement and the accompanying prospectus.

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PROSPECTUS SUPPLEMENT SUMMARY

The items in the following summary are described in more detail later or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary provides an overview of selected information and does not contain all of the information you should consider before buying our ordinary shares. Therefore, you should read the entire prospectus supplement and the accompanying prospectus carefully (including the documents incorporated by reference herein), especially the Risk Factors section beginning on page S-6 and our consolidated financial statements (which we refer to as our Financial Statements) and the related notes incorporated by reference in this prospectus supplement and the accompanying prospectus, before deciding to invest in our ordinary shares. In this prospectus supplement and the accompanying prospectus, unless the context otherwise requires, references to we, us, our, or Prothena, refer to Prothena Corporation plc.

Overview

We are a clinical stage biotechnology company focused on the discovery, development and commercialization of novel antibodies for the potential treatment of diseases that involve protein misfolding or cell adhesion. We focus on therapeutic monoclonal antibodies directed specifically to disease causing proteins. Our antibody-based product candidates target a number of potential indications including AL and AA forms of amyloidosis (NEOD001), Parkinson s disease and other related synucleinopathies (PRX002) and novel cell adhesion targets involved in inflammatory diseases and cancers (PRX003). Our lead programs consist of two clinical development programs and one late stage preclinical program:

NEOD001 is a monoclonal antibody that specifically targets the amyloid that accumulates in both AL and AA forms of amyloidosis. NEOD001 was granted orphan drug designation for the treatment of AL and AA amyloidosis by the U.S. Food and Drug Administration, or FDA, in 2012 and for the treatment of AL amyloidosis by the European Medicines Agency, or EMA, in 2013. The ongoing multi-center Phase 1 clinical trial is evaluating the safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction. The study is designed to define a maximally tolerated dose and/or recommended dose(s) for Phase 2/3. The study is also evaluating exploratory biomarkers for cardiac, renal and hepatic function. We anticipate initiating a Phase 2/3 trial of NEOD001 in the fourth quarter of 2014.

PRX002 is a monoclonal antibody targeting alpha-synuclein whose efficacy has been tested in various cellular and animal models of synuclein-related disease. Passive immunization with 9E4, the murine version of PRX002, in multiple transgenic mouse models of Parkinson s disease reduced the appearance of synuclein pathology, protected synaptic connections and improved performance by the mice in behavioral testing. PRX002 may slow or reduce the progressive neurodegeneration associated with synuclein misfolding and/or the cell-to-cell transmission of the pathogenic forms of synuclein. In December 2013, we entered into a License, Development, and Commercialization Agreement, or the License Agreement, with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or collectively, Roche, to develop and commercialize, and in the United States, co-develop and potentially co-promote, certain anti-alpha-synuclein antibodies, including PRX002, for the treatment of Parkinson s disease and other related synucleinopathies, which are referred to in this prospectus supplement collectively as Licensed Products. Under the terms of the License Agreement, upon the satisfaction of certain milestones, we may receive up to an aggregate of $600 million in upfront and milestone payments, of which we have received upfront and milestone payments totaling $45.0 million in the first half of 2014. In the United States, we and Roche will share all development and commercialization costs, as well as profits, on a 70/30 basis (70% Roche

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and 30% Prothena), 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. Outside the United States, Roche will have sole responsibility for developing and commercializing PRX002 and will pay us up to double-digit royalties on net sales. We initiated a Phase 1 trial of PRX002 in April 2014.

PRX003 is a monoclonal antibody targeting MCAM (melanoma cell adhesion molecule) for the potential treatment of inflammatory diseases and cancers. We have advanced PRX003 into manufacturing and preclinical safety testing. We anticipate initiating a Phase 1 trial of PRX003 in 2015.

Our strategy is to identify antibody candidates for clinical development and commercialization by applying our extensive expertise in generating novel therapeutic antibodies and working with collaborators having expertise in specific animal models of disease.

We are a public limited company formed under the laws of Ireland. On December 20, 2012, we separated from Elan Corporation Limited (formerly Elan Corporation, plc), or Elan, which subsequently became a wholly owned subsidiary of Perrigo Company plc, or Perrigo. Our ordinary shares trade on The NASDAQ Global Select Market under the symbol PRTA.

Recent Developments

NEOD001

In April 2014, we announced interim findings from the ongoing Phase 1 clinical trial of NEOD001 and presented these interim results at the XIV International Symposium on Amyloidosis, or ISA, conference in Indianapolis, Indiana.

Of the 18 patients enrolled in the study as of March 11, 2014, ten patients (56%) with cardiac involvement had pre-specified baseline levels of the N-terminal prohormone of brain natriuretic peptide, or NT-proBNP, that were ≥ 650 pg/mL (required baseline level for evaluation). In the study, patients with cardiac involvement improve (response) or worsen (progression) based on pre-defined NT-proBNP criteria. NT-proBNP is a biomarker for heart failure that is being used on an exploratory basis in this Phase 1 trial as a marker of AL disease progression or response. The pre-defined NT-proBNP response criteria is a >30% and >300 pg/mL decrease in patients with baseline NT-proBNP ≥650 pg/mL. The pre-defined NT-proBNP progression criteria is a >30% and >300 pg/mL increase in patients with baseline NT-proBNP ≥650 pg/mL. Patients who are not NT-proBNP responders or progressors are considered to be stable.

Evidence of Cardiac Biomarker Activity

Of the ten patients with NT-proBNP screening values of ≥650 pg/mL, nine patients had at least one post-baseline NT-proBNP determination as of the interim cut-off date. Of those nine evaluable patients, eight patients either met the response criteria based on a decrease in NT-proBNP or were considered stable, and the remaining patient met the progression criteria based on an increase of NT-proBNP. Specifically, five of nine (56%) patients had NT-proBNP levels that decreased to a level that met pre-defined response criteria, three of nine (33%) patients had stable NT-proBNP levels, and one of nine (11%) patients had NT-proBNP levels that increased to a level that met pre-defined progression criteria.

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Safety and Tolerability

The interim Phase 1 data demonstrated that NEOD001 appeared to be generally safe and well-tolerated at the doses studied. The most frequently reported adverse events (reported by ≥ 10% patients) as of the data cut-off date were: dyspnea (n=4), fatigue (n=3), cough (n=1), diarrhea (n=2), hyponatremia (n=2), insomnia (n=2), productive cough (n=2) and upper respiratory infection (n=2). No dose limiting toxicities were observed. A total of four patients had discontinued the trial as of the March 11, 2014 data cut-off: two due to organ progression; one due to hematological progression; and one due to withdrawal of consent.

Pharmacokinetics and Immunogenicity

The interim pharmacokinetic data suggested a terminal elimination half-life across all dose levels of approximately 12 days and supported the 28-day dosing interval utilized in the study. Immunogenicity, including anti-NEOD001 response, was not observed in any patient through the interim cut-off date.

PRX002

In April 2014, we initiated a Phase 1 clinical trial of PRX002. The study is a randomized, double-blind, placebo-controlled, single ascending dose study in healthy subjects. It is designed to assess PRX002 for safety, tolerability, pharmacokinetics and immunogenicity. As a result of the initiation of this trial, we received a $15.0 million milestone payment from Roche under the License Agreement, bringing the total amount received to date under the License Agreement to $45.0 million.

Research and Development Pipeline

Lead Programs

Our research and development pipeline includes three lead therapeutic antibody programs that we intend to advance: NEOD001 for the potential treatment of AL and AA amyloidosis; PRX002 for the potential treatment of Parkinson s disease and other related synucleinopathies; and PRX003 for the potential treatment of inflammatory diseases and cancers.

The following table summarizes the status and anticipated upcoming milestones of our research and development pipeline for our lead programs:

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Discovery Programs

Our pipeline also includes several discovery stage programs for which we are testing the efficacy of antibodies in preclinical models of disease. We are also generating additional novel antibodies against other targets involved in protein misfolding or cell adhesion for characterization in vivo and in vitro. If promising, we expect that some of these antibodies will advance to preclinical development.

Implications of Being an Emerging Growth Company

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For further information, please see Risk Factors 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.

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THE OFFERING

Ordinary shares we are offering	$100,000,000 of ordinary shares (or $115,000,000 of ordinary shares if the underwriters exercise in full their option to subscribe for additional shares).
Ordinary shares to be outstanding after the offering	ordinary shares (or ordinary shares if the underwriters exercise in full their option to subscribe for additional shares).
Use of proceeds	We currently intend to use the net proceeds from this offering for the continued research and development of our product candidates, including clinical trials for PRX003 and drug discovery activities, preclinical and clinical trials for potential product candidates targeting misfolded proteins for potentially multiple indications. Net proceeds not used for the development of these product candidates may be used for working capital and other general corporate purposes. Our management will have broad discretion over the use of the net proceeds from this offering. See Use of Proceeds on page S-36 of this Prospectus Supplement.
Risk factors	See Risk Factors beginning on page S-6 and other information included in this prospectus supplement and the accompanying prospectus for a discussion of factors that you should consider carefully before deciding to invest in our ordinary shares.
Symbol on The NASDAQ Global Select Market	PRTA

Entities managed by Woodford Investment Management LLP have indicated an interest in purchasing approximately $50 million of our ordinary shares in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to these entities and these entities could determine to purchase more, fewer or no shares in this offering. Any ordinary shares sold to these entities will be purchased by the underwriters at the public offering price without the underwriting discount.

The number of ordinary shares to be outstanding after this offering is based on 21,904,780 ordinary shares outstanding as of March 31, 2014, and excludes the following:

- 2,433,981 ordinary shares issuable upon the exercise of outstanding options as of March 31, 2014 having a weighted-average exercise price of approximately $12.19 per share; and
- 167,500 ordinary shares reserved for issuance pursuant to future awards under our 2012 Long Term Incentive Plan as of March 31, 2014 (plus an additional 2,900,000 ordinary shares reserved for issuance pursuant to future awards under our Amended and Restated 2012 Long Term Incentive Plan, as approved by our shareholders on May 21, 2014).

Unless otherwise indicated, all information in this prospectus supplement assumes:

- no exercise of options outstanding as of March 31, 2014; and

no exercise of the underwriters option to subscribe for additional ordinary shares.

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RISK FACTORS

Investing in our ordinary shares involves a high degree of risk. You should carefully consider the risks described below, as well as the other information included in and incorporated by reference in this prospectus supplement and the accompanying prospectus, including our Financial Statements and the related notes and Management s Discussion and Analysis of Financial Condition and Results of Operations, included in our periodic reports filed with the Securities and Exchange Commission and incorporated by reference into this prospectus supplement and the accompanying prospectus, before deciding whether to invest in our ordinary shares. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our ordinary shares could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

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

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

We may not generate the cash that is necessary to finance our operations in the foreseeable future. We incurred net losses of $41.0 million, $41.4 million and $29.7 million for the years ended December 31, 2013, 2012 and 2011, respectively. Although we achieved net income of $17.9 million in the first quarter of 2014, primarily as a result of the $30.0 million upfront milestone payment under the License Agreement, we expect to incur substantial losses for the foreseeable future as we:

- conduct our Phase 1 clinical trials for NEOD001 and PRX002 and initiate additional clinical trials, if supported by the results of these Phase 1 trials;
- develop and commercialize our product candidates, including NEOD001, PRX002 and PRX003 and any other antibodies targeting alpha-synuclein pursuant to our License Agreement with Roche;
- 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 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 March 31, 2014, we had cash and cash equivalents of $195.1 million. In addition, we received a $15.0 million clinical milestone payment from Roche in May 2014. 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. 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 1 clinical trials for NEOD001 and PRX002, and our development and commercialization activities, including our portion of similar costs relating to PRX002 in the United States pursuant to our License Agreement with Roche;

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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;

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.

We are not able to provide specific estimates of the timelines or total costs to complete the ongoing Phase 1 clinical trial for NEOD001 or PRX002. Under the License Agreement with Roche, we are responsible for 30% of all development and commercialization costs for PRX002 for the treatment of Parkinson s disease in the United States, and for any future Licensed Products and/or indications that we opt to co-develop in the United States, in each case unless we elect to opt out of profit and loss sharing. 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.

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 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;

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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.

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 on December 20, 2012, which we refer to in this prospectus supplement as the Separation and Distribution. The historical financial information we have included or incorporated by reference in this report may not reflect what our results of operations, financial position 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 may be higher than Elan s cost of capital prior to the Separation and Distribution because Elan s current cost of debt will likely be lower than ours; and

our historical financial information does not reflect changes that we have incurred as a result of the separation of the Prothena 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, or 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, the Prothena 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 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. For additional information about our past financial performance and the basis of presentation of our consolidated Financial Statements, please see Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated Financial Statements and the notes thereto included in the periodic reports filed with the SEC that are incorporated by reference into this prospectus supplement.

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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 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.

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 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/Elan 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, which are at an early stage. Our drug candidates are still in early 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 initiated Phase 1 clinical trials for each of NEOD001 and 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

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trials, and, with respect to approval in the United States, to the satisfaction of 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 1 clinical trials for NEOD001 or 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, or 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;

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- 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 approved effective 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, or 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,

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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, or BLA, or other submission or to obtain regulatory approval in the United States 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, or 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 United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA s Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the

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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 European Union. 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 European Union 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 United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. 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 European Union, 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 United States and Europe, 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 United States, 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 United States 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

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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, or cGMP, requirements and current good clinical practice, or 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 IV 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

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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, and local 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;

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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 U.S. 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 in the context of our 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 United States 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.

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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 United States, 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 United States 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 United States, 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 United States, 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 United States, our potential to generate future revenue outside of the United States 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 United States for the treatment of Parkinson s disease and any future Licensed Products approved for Parkinson s disease in the United States. 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

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additional revenue from potential sales of PRX002 or such products in the United States 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 United States, 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 United States 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:

- 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;

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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.

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There can be no assurance that our drug candidates, if they are approved for sale in the United States 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, or 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

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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 United States, 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, or 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, or 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

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was the first reporting period, and manufacturers were required to report aggregate payment data by March 31, 2014, and will be required to report detailed payment data and submit legal attestation to the accuracy of such data during Phase 2 of the program (which begins in May 2014 and extends for at least 30 days). Thereafter, manufacturers must submit reports by the 90th day of each subsequent calendar year. CMS will commence disclosure of such information on a publicly available website by September 2014;

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

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coming into contact with our products. Clinical trial liability claims may be filed against us for damages suffered by clinical trial subjects or their families. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

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

We currently have clinical trial liability insurance coverage in the aggregate amount of $15.0 million annual coverage limit for our clinical trials, of which at least $5.0 million annual coverage limit is designated for our ongoing Phase 1 clinical trial of NEOD001. 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 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.

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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 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

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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 such 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

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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 United States 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 United States 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, or 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 United States. 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 United States 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, or 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

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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 U.S. Patent and Trademark Office 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 U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review, or other patent office proceedings or litigation, in the United States 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 United States 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

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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

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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 and this Offering

The market price of our 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;

regulatory developments or enforcement in the United States 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;

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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 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 budget 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.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion to use the net proceeds from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. Our management might not apply the net proceeds from this offering in ways that increase the value of your investment. We intend to use the net proceeds from this offering for the continued research and development of our product candidates, including clinical trials for PRX003 and drug discovery activities, preclinical and clinical trials for potential product candidates targeting misfolded proteins for potentially multiple indications. Net proceeds not used for the development of these product candidates may be used for working capital and other general corporate purposes. Until we use the net proceeds to us from this offering, we plan to invest them, and these investments may not yield a favorable rate of return. The failure by our management to invest and apply the net proceeds from this offering effectively could harm our business.

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 March 31, 2014, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plan is 167,500. In addition, in May 2014, our shareholders approved an increase of 2.9 million additional ordinary shares authorized for issuance under our Amended and Restated 2012 Long Term Incentive Plan.

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, or the Exchange Act, 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

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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, or 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 United States. 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.

In April 2012, President Obama signed into law the JOBS Act. 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, or the Securities Act.

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.

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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 U.S. holders of our ordinary shares.

Based on the current market price of our ordinary shares and the value and composition of our assets, we do not believe we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2013. In addition, we do not expect to be a PFIC for U.S. federal income tax purposes for our current taxable year ending on December 31, 2014 or any future taxable year. However, the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you the U.S. Internal Revenue Service, or IRS, will not take a contrary position. A non-U.S. corporation will be considered a PFIC for any taxable year if either (1) at least 75% of its gross income for such year is passive income or (2) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during such year) is attributable to assets that produce or are held for the production of passive income (the asset test). In general, the total value of our assets for purposes of the asset test will be 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). If we are a PFIC for our current taxable year, certain adverse U.S. federal income tax consequences could apply to U.S. persons who acquire our ordinary shares with respect to any excess distribution received from us and any gain from a sale or other disposition of our ordinary shares.

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 United States 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 United States 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 United States.

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, or the Irish Takeover Rules. Under the Irish Takeover Rules, our Board is not permitted to take any action that might frustrate an offer for our shares once our Board has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time

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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 United States.

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

Transfers of our 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 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 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 shares. Please see Certain Irish Tax Consequences Relating to the Holding of our Ordinary Shares in this prospectus supplement.

We do not anticipate paying cash dividends, and accordingly, shareholders must rely on 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 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 shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our 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. Please see Certain Irish Tax Consequences Relating to the Holding of our Ordinary Shares in this prospectus supplement. It is recommended that each shareholder consult his or her own tax advisor as to the tax consequences of holding our shares or receiving dividends from us.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus contain forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as aim, anticipate, assume, believe, contemplate, continue, could, estimate, expect, goal, intend, may, objective, plan, predict, potential, positioned, seek, should, target, will, would, that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our ability to obtain additional financing in this or future offerings;
- our operating losses;
- our ability to successfully complete research and development of our drug candidates and the growth of the markets for those drug candidates;
- our ability to develop and commercialize products that are superior to those of our competitors;
- our collaboration with Roche pursuant to the License Agreement to develop and commercialize PRX002, as well as any future Licensed Products targeting alpha-synuclein;
- expected activities and responsibilities of us and Roche under the License Agreement;
- our potential receipt of revenue under the License Agreement, including milestone and royalty revenue;
- the satisfaction of conditions under the License Agreement required for continued commercialization, and the payment of potential milestone payments, royalties and fulfillment of other Roche obligations under the License Agreement;
- expectations with respect to our intent and ability to carry out plans to promote PRX002 for the treatment of Parkinson s disease in the United States through our co-promotion option under the License Agreement;
- our ability to protect our patents and other intellectual property;
- loss of key employees;
- tax treatment of our separation from Elan, now owned by Perrigo, and subsequent distribution of our ordinary shares;

restrictions on our taking 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;

disruptions in the U.S. and global capital and credit markets;

fluctuations in foreign currency exchange rates;

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extensive government regulation;

the volatility of our share price;

business disruptions caused by information technology failures;

our use of proceeds from this offering; and

the other risks and uncertainties described in Risk Factors.

These forward-looking statements are based on management s current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management s beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this prospectus supplement and the accompanying prospectus may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Risk Factors and elsewhere in or incorporated by reference in this prospectus supplement and the accompanying prospectus. Potential investors are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus supplement and the accompanying prospectus. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus supplement. See Where You Can Find More Information in this prospectus supplement.

MARKET, INDUSTRY AND OTHER DATA

This prospectus supplement and the accompanying prospectus may contain estimates, projections and other information concerning our industry, our business, and the markets for our product candidates, including data regarding the estimated size of those markets, their projected growth rates, the perceptions and preferences of patients and physicians regarding certain therapies and other prescription, prescriber and patient data, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

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USE OF PROCEEDS

We estimate that the net proceeds from the issue by us of the ordinary shares in this offering will be approximately $96.1 million after deducting the underwriting discount and estimated offering expenses payable by us. If the underwriters exercise their option to subscribe for additional shares in full, we estimate that net proceeds will be approximately $110.1 million after deducting the underwriting discount and estimated offering expenses payable by us.

Entities managed by Woodford Investment Management LLP have indicated an interest in purchasing approximately $50 million of our ordinary shares in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to these entities and these entities could determine to purchase more, fewer or no shares in this offering. Any ordinary shares sold to these entities will be purchased by the underwriters at the public offering price without the underwriting discount.

We currently intend to use the net proceeds from this offering for the continued research and development of our product candidates, including clinical trials for PRX003 and drug discovery activities, pre-clinical and clinical trials for potential product candidates targeting misfolded proteins for potentially multiple indications. Net proceeds not used for development of these product candidates may be used for working capital and other general corporate purposes.

Our management will have broad discretion over the use of the net proceeds from this offering. The amounts and timing of our expenditures will depend upon numerous factors, including the results of our clinical trials for NEOD001 and PRX002; the timing and success of preclinical studies or clinical trials we may commence in the future; and the timing of regulatory submissions. The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development and clinical trial efforts; the scope of research and development efforts; regulatory approvals; competition; and our evaluation of strategic opportunities to further the development efforts for our product candidates. We reserve the right to change the use of proceeds as a result of certain contingencies such as competitive developments, clinical trial results, opportunities to acquire technologies or products, any unanticipated cash expenses and other factors. Pending application of these net proceeds, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

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PRICE RANGE OF OUR ORDINARY SHARES AND DIVIDEND POLICY

Our ordinary shares began trading on The NASDAQ Global Market, or NASDAQ, under the symbol PRTA since December 21, 2012 and currently trade on The NASDAQ Global Select Market. The following table sets forth, for the periods indicated, the high and low intraday prices per share of our ordinary shares as reported by NASDAQ.

Year Ended December 31, 2012	**High**	**Low**
Fourth quarter (beginning December 21, 2012)	$ 8.10	$ 6.60

Year Ended December 31, 2013	**High**	**Low**
First quarter	$ 7.50	$ 5.64
Second quarter	14.00	6.49
Third quarter	22.48	12.14
Fourth quarter	30.55	18.93

Year Ending December 31, 2014	**High**	**Low**
First quarter	$ 49.24	$ 24.42
Second quarter (through June 20, 2014)	41.33	18.52

On June 20, 2014, the last sale price of our ordinary shares as reported on The NASDAQ Global Select Market was $23.63 per share. As of March 31, 2014, there were approximately 1,468 holders of record of our ordinary shares. 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 recordholders.

We have never declared or paid cash dividends on our ordinary shares. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our Board.

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CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of March 31, 2014:

- on an actual basis;
- on an as adjusted basis to give effect to the issuance and sale by us of 4,231,908 ordinary shares in this offering at an assumed public offering price of $23.63 per share, the last reported sale price of our ordinary shares on The NASDAQ Global Select Market on June 20, 2014, after deducting the underwriting discount and estimated offering expenses payable by us (of which the underwriting discount will not apply to the approximately $50 million of such ordinary shares that may be purchased by entities managed by Woodford Investment Management LLP).

The following information should be read in conjunction with our consolidated Financial Statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus. For more details on how you can obtain our periodic reports and other information, please see Where You Can Find More Information in this prospectus supplement.

	March 31, 2014	
	Actual	As Adjusted
	(unaudited, in thousands)	
Cash and cash equivalents	$ 195,052	$ 291,177
Shareholders equity:		
Euro deferred shares, 22 nominal value:		
10,000 shares authorized and none issued and outstanding, actual and as adjusted	$	$
Ordinary shares, $0.01 par value:		
100,000,000 shares authorized; 21,904,780 and 26,136,688 shares issued and outstanding, actual and as adjusted, respectively	219	261
Additional paid-in capital	216,281	312,364
Accumulated deficit	(23,489)	(23,489)
Total shareholders equity	193,011	289,136
Total capitalization	$ 193,011	$ 289,136

The outstanding share information in the table above is based on the number of ordinary shares outstanding as of March 31, 2014, and excludes the following:

- 2,433,981 ordinary shares issuable upon the exercise of outstanding options as of March 31, 2014 having a weighted-average exercise price of approximately $12.19 per share; and
- 167,500 ordinary shares reserved for issuance pursuant to future awards under our 2012 Long Term Incentive Plan as of March 31, 2014 (plus an additional 2,900,000 ordinary shares reserved for issuance pursuant to future awards under our Amended and Restated 2012 Long Term Incentive Plan, as approved by our shareholders in May 2014).

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DILUTION

If you invest in our ordinary shares, your interest will be diluted to the extent of the difference between the public offering price per share of our ordinary shares in this offering and the net tangible book value per share of our ordinary shares after this offering. As of March 31, 2014, we had a historical net tangible book value of $193.0 million, or $8.81 per ordinary share. Our net tangible book value represents total tangible assets less total liabilities, all divided by the number of ordinary shares outstanding on March 31, 2014.

After giving effect to the issue of 4,231,908 ordinary shares in this offering at an assumed public offering price of $23.63 per share, the last reported sale price of our ordinary shares on The NASDAQ Global Select Market on June 20, 2014, and after deducting the underwriting discount and estimated offering expenses (of which the underwriting discount will not apply to the approximately $50 million of such ordinary shares that may be purchased by entities managed by Woodford Investment Management LLP), our as adjusted net tangible book value as of March 31, 2014 would have been $289.1 million, or $11.06 per share. This represents an immediate increase in as adjusted net tangible book value of $2.25 per share to existing shareholders and an immediate dilution of $12.57 per share to new investors. The following table illustrates this per share dilution:

Assumed public offering price per share		$ 23.63
Historical net tangible book value per share as of March 31, 2014	$ 8.81	
Increase in as adjusted net tangible book value per share attributable to new investors	2.25	
As adjusted net tangible book value per share after this offering		11.06
Dilution per share to new investors participating in this offering		$ 12.57

If the underwriters fully exercise their option to subscribe for an additional 634,786 shares (assuming we offer and sell an aggregate of 4,866,694 ordinary shares at an assumed public offering price of $23.63 per share, the last reported sale price of our ordinary shares on The NASDAQ Global Select Market on June 20, 2014), as adjusted net tangible book value after this offering would increase to $11.32 per share, and there would be an immediate dilution of $12.31 per share to new investors.

To the extent that outstanding options with an exercise price per share that is less than the as adjusted net tangible book value per share, before giving effect to the issuance and sale of shares in this offering, are exercised, new investors will experience further dilution. If all of our outstanding options described above were exercised, our net tangible book value as of March 31, 2014, before giving effect to the issuance and sale of shares in this offering, would have been $203.8 million, or $8.64 per share, and our as adjusted net tangible book value as of March 31, 2014 after this offering at an assumed public offering price of $23.63 per share, the last reported sale price of our ordinary shares on NASDAQ on June 20, 2014, would have been $299.9 million, or $10.78 per share, causing dilution to new investors of $12.85 per share.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

The number of ordinary shares to be outstanding after this offering is based on the number of shares outstanding as of March 31, 2014, and excludes the following:

- 2,433,981 ordinary shares issuable upon the exercise of outstanding options as of March 31, 2014 having a weighted-average exercise price of approximately $12.19 per share; and

- 167,500 ordinary shares reserved for issuance pursuant to future awards under our 2012 Long Term Incentive Plan as of March 31, 2014 (plus an additional 2,900,000 ordinary shares reserved for issuance pursuant to future awards under our Amended and Restated 2012 Long Term Incentive Plan, as approved by our shareholders in May 2014).

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MATERIAL UNITED STATES FEDERAL INCOME TAX CONSEQUENCES

TO U.S. HOLDERS

The following discussion describes the material U.S. federal income tax consequences to U.S. Holders (as defined below) under present law of an investment in our ordinary shares. The effects of any applicable state or local laws, or other U.S. federal tax laws such as estate and gift tax laws, or the Medicare contribution tax, are not discussed. This summary applies only to investors who hold our ordinary shares as capital assets (generally, property held for investment) and who have the U.S. dollar as their functional currency. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, U.S. Treasury regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the IRS in effect as of the date of this offering. All of the foregoing authorities are subject to change, which change could apply retroactively and could affect the tax consequences described below.

The following discussion does not address all U.S. federal income tax consequences relevant to a holder s particular circumstances or to holders subject to particular rules, including:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our ordinary shares as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities, commodities or currencies;
- partnerships, S corporations, or other entities or arrangements treated as partnerships for U.S. federal income tax purposes;
- tax-exempt organizations or governmental organizations;
- persons who acquired our ordinary shares pursuant to the exercise of any employee share option or otherwise as compensation;
- persons deemed to sell our ordinary shares under the constructive sale provisions of the Code; and
- persons that own or are deemed to own ten percent (10%) or more of our ordinary shares.

U.S. HOLDERS ARE URGED TO CONSULT THEIR TAX ADVISORS ABOUT THE APPLICATION OF THE U.S. FEDERAL TAX RULES TO THEIR PARTICULAR CIRCUMSTANCES AS WELL AS THE U.S. STATE AND LOCAL AND FOREIGN TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR ORDINARY SHARES.

For purposes of this discussion, a U.S. Holder is a beneficial owner of our ordinary shares who is for U.S. federal income tax purposes:

an individual who is a citizen or resident of the United States;

a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) organized under the laws of the United States, any State or the District of Columbia;

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an estate, the income of which is subject to U.S. federal income tax regardless of its source; or

a trust that (1) is subject to the supervision of a U.S. court and the control of one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

If you are a partner in a partnership (or other entity taxable as a partnership for U.S. federal income tax purposes) that holds our ordinary shares, your tax treatment generally will depend on your status and the activities of the partnership. Partnerships holding our ordinary shares and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences applicable to them.

Taxation of Dividends and Other Distributions on our Ordinary Shares

Subject to the PFIC rules discussed below, distributions to you with respect to our ordinary shares will be included in your gross income as a dividend when actually or constructively received to the extent that the distribution is paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). To the extent the amount of the distribution exceeds our current and accumulated earnings and profits, it will be treated first as a tax-free return of your tax basis in the ordinary shares, and to the extent the amount of the distribution exceeds your tax basis, the excess will be taxed as capital gain. We do not intend to calculate our earnings and profits under U.S. federal income tax principles. Therefore, a U.S. Holder should expect a distribution will generally be treated as a dividend even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. The dividends will not be eligible for the dividends-received deduction allowed to corporations in respect of dividends received from other U.S. corporations.

Subject to certain limitations, including minimum holding period requirements, and provided we are not a PFIC in the taxable year in which a dividend is paid or in the preceding taxable year, dividends paid to non-corporate U.S. Holders may be qualified dividend income taxable at a maximum rate of 20%. As discussed below in Passive Foreign Investment Company, we do not believe we will be a PFIC for our current taxable year. You should consult your tax advisor regarding the availability of this preferential tax rate under your particular circumstances.

Dividends will generally constitute foreign source income for foreign tax credit limitation purposes. If the dividends are qualified dividend income (as discussed above), the amount of the dividend taken into account for purposes of calculating the foreign tax credit limitation will be limited to the gross amount of the dividend, multiplied by the reduced rate divided by the highest rate of tax normally applicable to dividends. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. For this purpose, dividends distributed by us with respect to our ordinary shares generally will constitute passive category income but could, in the case of certain U.S. Holders, constitute general category income. The rules with respect to the foreign tax credit are complex and you are urged to consult your tax advisor regarding the availability of the foreign tax credit under your particular circumstances.

Taxation of Disposition of our Ordinary Shares

Subject to the PFIC rules discussed below, you will recognize taxable gain or loss on any sale, exchange or other taxable disposition of an ordinary share equal to the difference between the amount realized (in U.S. dollars) on the disposition of the ordinary share and your tax basis (in U.S. dollars) in the ordinary share. The gain or loss will be capital gain or loss. If you are a non-corporate U.S. Holder, including an individual, who has held the ordinary share for more than one year, you generally will be eligible for reduced tax rates on a long-term capital gain. The deductibility of a capital loss is subject to limitations. Any such gain or loss you recognize generally will be treated as U.S. source income or loss.

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Passive Foreign Investment Company

Based on the current market price of our ordinary shares and the value and composition of our assets, we do not believe we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2013. In addition, we do not expect to be a PFIC for U.S. federal income tax purposes for our current taxable year ending on December 31, 2014 or any future taxable year. However, the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you that the IRS will not take a contrary position. A non-U.S. corporation is considered a PFIC for any taxable year if either:

- at least 75% of its gross income for such taxable year is passive income (the gross income test), or
- at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income (the asset test).

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation in which we own, directly or indirectly, at least 25% (by value) of the stock of such corporation.

A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). Because the value of our assets for purposes of the asset test will generally be determined by reference to the market price of our ordinary shares, our PFIC status will depend in large part on the market price of our ordinary shares, which may fluctuate significantly. As a result, there is a risk that we will be a PFIC if the market price of our ordinary shares decreases materially or we materially increase the amount of cash and other passive assets we hold relative to the amount of non-passive assets we hold.

If we are a PFIC for any year during which you hold our ordinary shares, we generally will continue to be treated as a PFIC with respect to you for all succeeding years during which you hold our ordinary shares. However, if we cease to be a PFIC, you may avoid some of the adverse effects of the PFIC regime by making a deemed sale election with respect to our ordinary shares. If such election is made, you will be deemed to have sold our ordinary shares you hold at their fair market value, and any gain from such deemed sale would be subject to the tax consequences described in the following paragraph. After the deemed sale election, your ordinary shares with respect to which the deemed sale election was made would not be treated as shares in a PFIC and you would not be subject to the rules described below with respect to any excess distribution you receive from us or any gain from an actual sale or other disposition of the ordinary shares. **The rules dealing with deemed sale elections are very complex. You are strongly encouraged to consult your tax advisor as to the possibility and consequences of making a deemed sale election if such election becomes available to you.**

For each taxable year we are treated as a PFIC with respect to you, you will be subject to special tax rules with respect to any excess distribution you receive and any gain you realize from a sale or other disposition (including a pledge) of our ordinary shares, unless you make a mark-to-market election as discussed below. Distributions you receive in a taxable year that are greater than 125% of the average annual distributions you received during the shorter of the three preceding taxable years or your holding period for the ordinary shares will be treated as an excess distribution. Under these special tax rules, if you receive any excess distribution or realize any gain from a sale or other disposition of our ordinary shares:

- the excess distribution or gain will be allocated ratably over your holding period for the ordinary shares,
- the amount allocated to the current taxable year, and any taxable year before the first taxable year in which we were a PFIC, will be treated as ordinary income, and

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the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years before the year of disposition or excess distribution cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of our ordinary shares cannot be treated as capital, even if you hold the ordinary shares as capital assets.

If we are treated as a PFIC with respect to you for any taxable year, to the extent any of our subsidiaries are also PFICs, you will be deemed to own shares in such lower-tier PFICs that are directly or indirectly owned by us in the proportion that the value of the ordinary shares you own bears to the value of all of our ordinary shares, and you may be subject to the rules described in the preceding two paragraphs with respect to the shares of such lower-tier PFICs you would be deemed to own. You should consult your tax advisor regarding the application of the PFIC rules to any of our subsidiaries.

Alternatively, a U.S. Holder of marketable stock (as defined below) in a PFIC may make a mark-to-market election for such stock to elect out of the tax treatment discussed above. If you make a mark-to-market election for our ordinary shares, you will include in income for each year we are a PFIC, (*i.e.*, for each taxable year in which we meet the gross income test or asset test), an amount equal to the excess, if any, of the fair market value of our ordinary shares as of the close of your taxable year over your adjusted basis in such ordinary shares. You are allowed a deduction for the excess, if any, of the adjusted basis of the ordinary shares over their fair market value as of the close of the taxable year. However, deductions are allowable only to the extent of any net mark-to-market gains on the ordinary shares included in your income for prior taxable years. Amounts included in your income under a mark-to-market election, as well as gain on the actual sale or other disposition of the ordinary shares are treated as ordinary income. Ordinary loss treatment also applies to the deductible portion of any mark-to-market loss on the ordinary shares, as well as to any loss realized on the actual sale or disposition of the ordinary shares to the extent the amount of such loss does not exceed the net mark-to-market gains previously included for such ordinary shares. Your basis in the ordinary shares will be adjusted to reflect any such income or loss amounts. If you make a valid mark-to-market election, the tax rules that apply to distributions by corporations which are not PFICs would apply to distributions by us, except the lower applicable tax rate for qualified dividend income would not apply. If we cease to be a PFIC when you have a mark-to-market election in effect, gain or loss realized by you on the sale of our ordinary shares will be a capital gain or loss and taxed in the manner described above under Taxation of Dispositions of our Ordinary Shares.

The mark-to-market election is available only for marketable stock, which is stock that is traded in other than *de minimis* quantities on at least 15 days during each calendar quarter (regularly traded) on a qualified exchange or other market, as defined in applicable U.S. Treasury regulations. We expect our ordinary shares will continue to be listed on the NASDAQ and, accordingly, provided the ordinary shares are regularly traded, if you are a holder of ordinary shares, the mark-to-market election would be available to you if we are a PFIC. If any of our subsidiaries are or become PFICs, the mark-to-market election will not be available with respect to the shares of such subsidiaries that are treated as owned by you. Consequently, you could be subject to the PFIC rules with respect to income of the lower-tier PFICs the value of which already had been taken into account indirectly via mark-to-market adjustments.

In certain circumstances, a U.S. Holder of stock in a PFIC can make a qualified electing fund election to mitigate some of the adverse tax consequences of holding stock in a PFIC by including in income its share of the corporation s income on a current basis. However, we do not currently intend to prepare or provide the information that would enable you to make a qualified electing fund election.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require.

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YOU ARE STRONGLY URGED TO CONSULT YOUR TAX ADVISOR REGARDING THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN our ORDINARY SHARES.

Information Reporting and Backup Withholding

Dividend payments with respect to our ordinary shares and proceeds from the sale, exchange or redemption of ordinary shares may be subject to information reporting to the IRS and possible U.S. backup withholding. Backup withholding will not apply, however, to a U.S. Holder who furnishes a correct taxpayer identification number and makes any other required certification or who is otherwise exempt from backup withholding. U.S. Holders who are required to establish their exempt status generally must provide such certification on IRS Form W-9. U.S. Holders should consult their tax advisors regarding the application of the U.S. information reporting and backup withholding rules.

Backup withholding is not an additional tax. Amounts withheld as backup withholding may be credited against your U.S. federal income tax liability, and you may obtain a refund of any excess amounts withheld under the backup withholding rules by filing the appropriate claim for refund with the IRS and furnishing any required information.

Additional Reporting Requirements

Certain U.S. Holders who are individuals are required to report information relating to an interest in our ordinary shares, subject to certain exceptions (including an exception for ordinary shares held in accounts maintained by certain financial institutions). U.S. Holders should consult their tax advisors regarding the effect, if any, of these rules on their ownership and disposition of our ordinary shares.

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CERTAIN IRISH TAX CONSEQUENCES RELATING TO THE HOLDING OF OUR ORDINARY SHARES

The information set out in these paragraphs is intended as a brief and general guide only based on current legislation and the current published practice of the Revenue Commissioners of Ireland. Legislative, administrative or judicial changes may modify the tax consequences described below. The statements do not constitute tax advice and are intended only as a general guide. This information relates only to the certain limited aspects of the Irish taxation treatment for the holders of our ordinary shares. It is intended to apply only to persons who are absolute beneficial holders of our ordinary shares and who hold them as investments (and not as securities to be realized in the course of a trade). The information set out below may not apply to certain holders of our ordinary shares such as dealers in securities, insurance companies and those holders who have (or are deemed to have) acquired their ordinary shares by virtue of an office or employment. Such persons may be subject to special rules. This summary is not exhaustive and shareholders should consult their own tax advisers as to the tax consequences in Ireland, or other relevant jurisdictions where we operate, including the acquisition, ownership and disposition of ordinary shares.

Stamp Duty

Irish stamp duty may be payable in respect of transfers of our ordinary shares at the rate of 1% of the higher of the price paid or the market value of the shares acquired.

Shares Held Through DTC

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 (currently at the rate of 1% of the price paid or the market value of the shares acquired, if higher) payable by the buyer.

A shareholder who holds our ordinary shares outside of DTC may transfer those shares into DTC (or vice versa) without giving rise to Irish stamp duty provided there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and, at the time of the transfer into DTC (or out of DTC), there is no sale of the shares to a third party being contemplated by a beneficial owner. 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.

Payment of Stamp Duty

A written instrument of transfer is required under Irish law in order for a transfer of the legal ownership of shares to be registered on our official share register. Such instruments of transfer may be subject to Irish stamp duty, which must be paid prior to the official share register being updated. A holder of ordinary shares who holds shares through DTC is not the legal owner of such shares (instead, the depository (for example, Cede & Co., as nominee for DTC) is holder of record of such shares). Accordingly, a transfer of shares from a person who holds such shares through DTC to a person who also holds such shares through DTC will not be registered in our official share register, i.e., the nominee of the depository will remain the record holder of such shares.

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To the extent that stamp duty is due but has not been paid, we may, in our absolute discretion, pay (or cause one of our subsidiaries to pay) the outstanding stamp duty in respect of a transfer of shares. Our Articles of Association provide that, in the event of any such payment, we (i) may seek reimbursement from the transferee, (ii) may set-off the amount of the stamp duty against future dividends payable to the transferee, and (iii) will have a lien against the ordinary shares on which we (or one of our subsidiaries) have paid stamp duty.

Irish Tax on Capital Gains

Disposal of Prothena ordinary shares.

A liability to Irish tax on capital gains on a disposal of our ordinary shares depends on the individual circumstances of each shareholder.

(i) Non-Irish resident / ordinarily resident shareholders:

Shareholders should not be subject to Irish tax on capital gains on a disposal of our ordinary shares if such holders are neither resident nor ordinarily resident in Ireland and do not hold such shares in connection with a trade carried on by such holder in Ireland through a branch or agency.

(ii) Irish resident shareholders:

Shareholders who are resident or ordinarily resident in Ireland for tax purposes, or corporate shareholders who hold their shares in connection with a trade carried on by such holder in Ireland through a branch or agency may be subject to Irish tax on capital gains at the rate of 33% if they dispose of our ordinary shares. Shareholders falling into this category should consult their own tax advisers as to the tax consequences of such a disposal.

Dividends

We do not currently intend to pay dividends to our shareholders. A payment of a dividend by an Irish resident entity is subject to dividend withholding tax at the current rate of 20% (subject to applicable exemptions).

Capital Acquisitions Tax

Irish capital acquisitions tax, or CAT, is comprised 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.

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UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated, Credit Suisse Securities (USA) LLC and RBC Capital Markets, LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to issue to the underwriters, and each of the underwriters has agreed, severally and not jointly, to subscribe from us the number of ordinary shares set forth opposite its name below.

Underwriter	Number of Ordinary Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Credit Suisse Securities (USA) LLC	
RBC Capital Markets, LLC	
Wedbush Securities Inc.	
Ladenburg Thalmann & Co. Inc.	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the ordinary shares sold under the underwriting agreement if any of these ordinary shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the ordinary shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the ordinary shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer s certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the ordinary shares to the public at the public offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of $ per ordinary share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

Entities managed by Woodford Investment Management LLP have indicated an interest in purchasing approximately $50 million of our ordinary shares in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to these entities and these entities could determine to purchase more, fewer or no shares in this offering.

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The following table shows the public offering price, underwriting discount and proceeds before expenses to us. Any ordinary shares sold to entities managed by Woodford Investment Management LLP will be purchased by the underwriters at the public offering price without the underwriting discount. The information assumes either no exercise or full exercise by the underwriters of their option to subscribe for additional ordinary shares.

	Per Ordinary Share	Without Option	With Option
Public Offering Price	$	$	$
Underwriting Discount(1)	$	$	$
Proceeds, Before Expense	$	$	$

(1) No underwriting discount will apply to any ordinary shares sold to entities managed by Woodford Investment Management LLP.

Our portion of the expenses of the offering are estimated at $0.4 million, which includes an amount not to exceed $20,000 that we have agreed to reimburse the underwriters for certain FINRA-related expenses incurred by them in connection with this offering.

Option to Subscribe for Additional Ordinary Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus supplement, to subscribe for up to an aggregate of $15,000,000 of additional ordinary shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to subscribe for a number of additional ordinary shares proportionate to that underwriter s initial amount reflected in the above table.

No Sales of Similar Securities

We and our executive officers and directors have agreed not to sell or transfer any ordinary shares, or securities convertible into or exchangeable or exercisable for ordinary shares, for 90 days after the date of this prospectus supplement without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Credit Suisse Securities (USA) LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

offer, pledge, sell or contract to sell any shares;

sell any option or contract to purchase any shares;

purchase any option or contract to sell any shares;

grant any option, right or warrant for the sale of any shares;

otherwise dispose of or transfer any shares;

request or demand that we file a registration statement related to the shares; or

enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of any shares, whether any such swap or transaction is to be settled by delivery of shares or

other securities, in cash or otherwise.

This lock-up provision applies to ordinary shares and to securities convertible into or exchangeable or exercisable for ordinary shares. It also applies to shares owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

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The NASDAQ Global Select Market Listing

The ordinary shares are listed on The NASDAQ Global Select Market under the symbol PRTA.

Price Stabilization, Short Positions

Until the distribution of the ordinary shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our ordinary shares. However, the representatives may engage in transactions that stabilize the price of the ordinary shares, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our ordinary shares in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of ordinary shares than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters option to subscribe for additional ordinary shares described above. The underwriters may close out any covered short position by either exercising their option to subscribe for additional ordinary shares or purchasing ordinary shares in the open market. In determining the source of ordinary shares to close out the covered short position, the underwriters will consider, among other things, the price of ordinary shares available for purchase in the open market as compared to the price at which they may purchase ordinary shares through the option granted to them. Naked short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing ordinary shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our ordinary shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of ordinary shares made by the underwriters in the open market prior to the completion of the offering.

Similar to other purchase transactions, the underwriters purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our ordinary shares or preventing or retarding a decline in the market price of our ordinary shares. As a result, the price of our ordinary shares will be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on The NASDAQ Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our ordinary shares. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our

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affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a Relevant Member State), no offer of ordinary shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of ordinary shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any ordinary shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any ordinary shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the ordinary shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any ordinary shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus supplement has been prepared on the basis that any offer of ordinary shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of ordinary shares. Accordingly any person making or intending to make an offer in that Relevant Member State of ordinary shares which are the subject of the offering contemplated in this prospectus supplement may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of ordinary shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression an offer to the public in relation to any ordinary shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe for the ordinary shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

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Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are qualified investors (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The ordinary shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the ordinary shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the ordinary shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of ordinary shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of ordinary shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of ordinary shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus supplement relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus supplement is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The ordinary shares to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the ordinary shares offered should conduct their own due diligence on the ordinary shares. If you do not understand the contents of this prospectus supplement you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, or ASIC, in relation to the offering. This prospectus supplement does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or the Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the ordinary shares may only be made to persons, or the Exempt Investors, who are sophisticated investors (within the meaning of section 708(8) of the Corporations Act), professional

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investors (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the ordinary shares without disclosure to investors under Chapter 6D of the Corporations Act.

The ordinary shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring ordinary shares must observe such Australian on-sale restrictions.

This prospectus supplement contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus supplement is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, Japanese Person shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus supplement and the accompanying prospectus have not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement, the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of ordinary shares may not be circulated or distributed, nor may the ordinary shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

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Where the ordinary shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire ordinary share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the ordinary shares pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Ordinary shares and Debentures) Regulations 2005 of Singapore.

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LEGAL MATTERS

A&L Goodbody, Dublin, Ireland will pass upon certain legal matters relating to the issuance of our ordinary shares offered hereby. Latham & Watkins LLP is acting as special U.S. counsel for us. Cooley LLP is acting as counsel for the underwriters in connection with this offering.

EXPERTS

The consolidated financial statements of Prothena Corporation plc and subsidiaries as of December 31, 2013 and 2012, and for each of the years in the two-year period ended December 31, 2013, have been incorporated by reference herein, and in the registration statement of which this prospectus supplement and the accompanying prospectus are a part, in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The consolidated financial statements of Prothena Corporation plc formerly referred to as the carve-out financial statements of the Prothena Business (formerly, the Neotope Business), for the year ended December 31, 2011, have been incorporated by reference herein, and in the registration statement of which this prospectus supplement and the accompanying prospectus are a part, in reliance upon the report of KPMG, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. You may also read and copy any document we file at the SEC s Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at (800) 732-0330 for further information on the Public Reference Room. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge in the Investor Relations section of our website, which is located at http://ir.prothena.com. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not part of this prospectus supplement.

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INCORPORATION BY REFERENCE

The SEC s rules allow us to incorporate by reference information into this prospectus supplement and the accompanying prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus supplement, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that have previously been filed with the SEC:

- Our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the SEC on March 7, 2014 as amended by Amendment No. 1 on Form 10-K/A, filed with the SEC on June 6, 2014.
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2013 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on March 31, 2014.
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, filed with the SEC on May 5, 2014.
- Our Current Reports on Form 8-K filed with the SEC on January 27, 2014 (solely with respect to Item 8.01), January 29, 2014, March 3, 2014, March 18, 2014 and May 22, 2014.
- The description of our ordinary shares contained in our Registration Statement on Form 10, dated December 17, 2012 and filed with the SEC on December 17, 2012, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and the accompanying prospectus and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Prothena Corporation plc

c/o Prothena Biosciences Inc

650 Gateway Boulevard

South San Francisco, CA 94080

(650) 837-8550

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus supplement and the accompanying prospectus.

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PROSPECTUS

Prothena Corporation plc

$115,000,000

Ordinary Shares

We may offer and issue up to $115,000,000 of our ordinary shares from time to time in one or more offerings. This prospectus provides you with a general description of our ordinary shares.

Each time we offer and issue ordinary shares, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the ordinary shares. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in our ordinary shares.

We may offer and issue the ordinary shares described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any ordinary shares, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus titled About this Prospectus and Plan of Distribution for more information. No ordinary shares may be issued without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such ordinary shares.

Investing in our ordinary shares involves risks. See the Risk Factors on page 7 of this prospectus and any similar section contained in the applicable prospectus supplement concerning factors you should consider before investing in our ordinary shares.

Our ordinary shares are listed on The NASDAQ Global Select Market under the symbol PRTA. On June 20, 2014, the last reported sale price of our ordinary shares on The NASDAQ Global Select Market was $23.63 per ordinary share.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is June 23, 2014.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, using a shelf registration process. By using a shelf registration statement, we may issue ordinary shares from time to time and in one or more offerings as described in this prospectus. Each time that we offer and issue ordinary shares, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and issued and the specific terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you should rely on the prospectus supplement. Before subscribing for any ordinary shares, you should carefully read both this prospectus and the applicable prospectus supplement, together with the additional information described under the heading Where You Can Find More Information; Incorporation by Reference.

We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to issue these securities in any jurisdiction where the offer or issue is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate as of the date on its respective cover, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates.

When we refer to Prothena, we, our, us and the Company in this prospectus, we mean Prothena Corporation plc and its consolidated subsidia unless otherwise specified. When we refer to you, we mean the holders and potential subscribers of our ordinary shares.

Prothena and our logo are our trademarks and are used in this prospectus. This prospectus also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this prospectus appear without the symbol, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

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WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Section of the SEC at prescribed rates. Further information on the operation of the SEC s Public Reference Room in Washington, D.C. can be obtained by calling the SEC at (800) 732-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is *http://www.sec.gov*.

Our web site address is http://www.prothena.com. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC s Public Reference Room in Washington, D.C. or through the SEC s website, as provided above.

Incorporation by Reference

The SEC s rules allow us to incorporate by reference information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

Our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the SEC on March 7, 2014, as amended by Amendment No. 1 on Form 10-K/A, filed with the SEC on June 6, 2014.

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2013 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on March 31, 2014.

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, filed with the SEC on May 5, 2014.

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Our Current Reports on Form 8-K filed with the SEC on January 27, 2014 (solely with respect to Item 8.01), January 29, 2014, March 3, 2014, March 18, 2014 and May 22, 2014.

The description of our ordinary shares contained in our Registration Statement on Form 10, dated and filed with the SEC on December 17, 2012, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Prothena Corporation plc

c/o Prothena Biosciences Inc

650 Gateway Boulevard

South San Francisco, California 94080

(650) 837-8550

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus and any accompanying prospectus supplement.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as aim, anticipate, assume, believe, contemplate, continue, could, due, estimate, expect, goa objective, plan, predict, potential, positioned, seek, should, target, will, would, and other similar expressions that are predictio future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our ability to obtain additional financing in future offerings;
- our operating losses;
- our ability to successfully complete research and development of our drug candidates and the growth of the markets for those drug candidates;
- our ability to develop and commercialize products that are superior to those of our competitors;
- our collaboration with F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc., or collectively Roche, pursuant to the License, Development, and Commercialization Agreement, or the License Agreement, to develop and commercialize PRX002, as well as any future licensed products targeting alpha-synuclein;
- expected activities and responsibilities of us and Roche under the License Agreement;
- our potential receipt of revenue under the License Agreement, including milestone and royalty revenue;
- the satisfaction of conditions under the License Agreement required for continued commercialization, and the payment of potential milestone payments, royalties and fulfillment of other Roche obligations under the License Agreement;
- expectations with respect to our intent and ability to carry out plans to promote PRX002 for the treatment of Parkinson s disease in the United States through our co-promotion option under the License Agreement;
- our ability to protect our patents and other intellectual property;
- loss of key employees;
- restrictions on our taking certain actions due to tax rules and covenants with Elan Corporation Limited;

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;

disruptions in the U.S. and global capital and credit markets;

fluctuations in foreign currency exchange rates;

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extensive government regulation;

the volatility of our share price;

business disruptions caused by information technology failures; and

the other risks and uncertainties described in Risk Factors herein.

These forward-looking statements are based on management s current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management s beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this prospectus may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Risk Factors and elsewhere in or incorporated by reference in this prospectus. Potential investors are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See Where You Can Find More Information; Incorporation By Reference.

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THE COMPANY

We are a clinical stage biotechnology company focused on the discovery, development and commercialization of novel antibodies for the potential treatment of diseases that involve protein misfolding or cell adhesion.

We are a public limited company formed under the laws of Ireland. We separated from Elan Corporation Limited (formerly Elan Corporation, plc), or Elan, which subsequently became a wholly owned subsidiary of Perrigo Company plc, or Perrigo, on December 20, 2012.

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 separation and distribution we 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. After the separation from Elan, and the related distribution of our ordinary shares to Elan s shareholders (which we refer to as 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 principal executive offices are located at Alexandra House, The Sweepstakes, Ballsbridge, Dublin 4, Ireland, and our telephone number is 011-353-1-902-3519. Our website address is http://www.prothena.com. The information contained in, or that can be accessed through, our website is not part of this prospectus.

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RISK FACTORS

Investment in our ordinary shares offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference into this prospectus from our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K that we have filed or that we file after the date of this prospectus, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement before acquiring any ordinary shares. The occurrence of any of these risks might cause you to lose all or part of your investment.

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USE OF PROCEEDS

We intend to use the net proceeds from the issue of ordinary shares as set forth in the applicable prospectus supplement.

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DESCRIPTION OF SHARE CAPITAL

The following description of our share capital is not complete and may not contain all the information you should consider before investing in our share capital. This description is summarized from, and qualified in its entirety by reference to, our Memorandum and Articles of Association, which has been publicly filed with the SEC. See Where You Can Find More Information; Incorporation by Reference.

The following description of our ordinary shares and Euro Deferred Shares is a summary. This summary does not purport to be complete and is qualified in its entirety by reference to the Irish Companies Acts 1963-2013, or the Companies Acts, and the complete text of our Memorandum and Articles of Association. You should read those laws and documents carefully.

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

Capital Structure

Issued Share Capital

As March 31, 2014, our issued share capital was 21,904,780 ordinary shares. We have no Euro Deferred Shares in issue. Our ordinary shares are listed on The NASDAQ Global Select Market, or NASDAQ, under the symbol PRTA.

Authorized Share Capital

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

Our Articles of Association authorize our board of directors, or our Board, to issue new ordinary shares and Euro Deferred Shares for cash without shareholder approval for a period of five years from the date of adoption of such Articles of Association, which adoption was effective prior to the completion of the Separation and Distribution.

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

Irish law does not recognize fractional shares held of record. Accordingly, our Articles of Association do not provide for the issuance of fractional shares of the Company, and the official Irish share register of the Company will not reflect any fractional shares. Whenever as a result of an issuance, alteration, reorganisation,

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consolidation, division, or subdivision of the share capital of the Company would result in any shareholder becoming entitled to fractions of a share, no such fractions shall be issued or delivered to any shareholder. All such fractions of a share will be aggregated into whole shares and sold in the open market at prevailing market prices and the aggregate cash proceeds from such sale (net of tax, commissions, costs and other expenses) shall be distributed on a pro rata basis, rounding down to the nearest cent, to each shareholder who would otherwise have been entitled to receive fractions of a share.

Preemption Rights, Share Warrants and Share Options

Under Irish law, certain statutory preemption rights apply automatically in favor of shareholders where shares are to be issued for cash. However, we have opted out of these preemption rights in our Articles of Association as permitted under Irish law. Because Irish law requires this opt-out to be renewed every five years by a resolution approved by not less than 75% of the votes cast at a general meeting of our shareholders (referred to under Irish law as a special resolution), our Articles of Association provide that this opt-out must be so renewed. If the opt-out is not renewed, shares issued for cash must be offered to existing shareholders of the Company on a *pro rata* basis to their existing shareholding before the shares may be issued to any new shareholders. The statutory preemption rights do not apply (i) where shares are issued for non-cash consideration (such as in a share-for-share acquisition), (ii) to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or (iii) where shares are issued pursuant to an employee share option or similar equity plan.

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

Dividends

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

The determination as to whether or not we have sufficient distributable reserves to fund a dividend must be made by reference to the relevant accounts of the Company. 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).

Our Articles of Association authorize the Board to declare dividends without shareholder approval to the extent they appear justified by profits lawfully available for distribution. Our Board may also recommend a dividend to be approved and declared by the shareholders at a general meeting. Our Board may direct that the

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payment be made by distribution of assets, shares or cash, and no dividend issued may exceed the amount recommended by the directors. Dividends may be declared and paid in the form of cash or non-cash assets and may be paid in dollars or any other currency.

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

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

Share Repurchases, Redemptions and Conversions

Overview

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

Repurchases and Redemptions by Prothena

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

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

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

Purchases by Subsidiaries of Prothena

Under Irish law, an Irish or non-Irish subsidiary of the Company may purchase our shares by way of an: (i) overseas market purchase; or (ii) off-market purchase. For one of our subsidiaries to make overseas market

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purchases of our ordinary shares, our shareholders must provide general authorization for such purchase by way of ordinary resolution. However, as long as this general authority has been granted, no specific shareholder authority for a particular overseas market purchase by a subsidiary of our ordinary shares is required. For a purchase by one of our subsidiaries off-market, the proposed purchase contract must be authorized by special resolution of our shareholders before the contract is entered into. The person whose ordinary shares are to be bought back cannot vote in favor of the special resolution and, for at least 21 days prior to the special resolution being passed, the purchase contract must be on display or must be available for inspection by our shareholders at our registered office.

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

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

Lien on Shares, Calls on Shares and Forfeiture of Shares

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

Consolidation and Division; Subdivision

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

Reduction of Share Capital

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

Annual Meetings of Shareholders

Under Irish company law, we are required to hold annual general meetings at intervals of no more than 15 months from the previous annual general meeting, provided that an annual general meeting is held in each calendar year following the first annual general meeting and no more than nine months after our fiscal year-end. Any of our annual general meetings may be held outside Ireland if a resolution so authorizing has been passed at the preceding annual general meeting.

Notice of an annual general meeting must be given to all of our shareholders and to our auditors. Our Articles of Association provide for a minimum notice period of 21 days notice, which is the minimum permitted by the Irish Companies Acts.

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The only matters which must, as a matter of Irish company law, be transacted at an annual general meeting are the presentation of the annual accounts, balance sheet and reports of the directors and auditors, the appointment of new auditors and the fixing of the auditor s remuneration (or delegation of same). If no resolution is made in respect of the reappointment of an existing auditor at an annual general meeting, the existing auditor will be deemed to have continued in office.

Extraordinary General Meetings of Shareholders

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

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

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

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

Quorum for General Meetings

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

Voting

Our Articles of Association provide that our Board or chairman may determine the manner in which the poll is to be taken and the manner in which the votes are to be counted.

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

In accordance with our Articles of Association, we may from time to time be authorized by ordinary resolution to issue preferred shares. These preferred shares may have such voting rights as may be specified in

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the terms of such preferred shares (e.g., they may carry more votes per share than ordinary shares or may entitle their holders to a class vote on such matters as may be specified in the terms of the preferred shares). Treasury shares or our shares that are held by our subsidiaries are not entitled to be voted at general meetings of shareholders.

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

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