Prothena Corp plc
Form 10-K
March 29, 2013
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2012

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to .

Commission file 001-35676

Prothena Corporation plc

(Exact name of registrant as specified in its charter)

Ireland	**43-1256213**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
650 Gateway Boulevard South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number, including area code: **(650) 837-8550**

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Ordinary Shares, par value $0.01 per share	**The NASDAQ Global Market**

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ¨ No ¨

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule12b-2 of the Exchange Act.:

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company x

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

The number of shares of common stock outstanding as of February 28, 2013 was 17,679,182.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive Proxy Statement for its 2013 Annual Stockholders Meeting are incorporated by reference into Part III of this Annual Report on Form 10-K, to be filed within 120 days of the registrant s fiscal year ended December 31, 2012.

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PROTHENA CORPORATION plc

Form 10K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2012

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

In this Annual Report, except as otherwise indicated or unless the context otherwise requires, all references to we, our, us, Prothena or the Company refer to Prothena Corporation plc, an Irish public limited company, together with its consolidated subsidiaries. References in this Annual Report to Elan refer to Elan Corporation, plc and its consolidated subsidiaries (other than, for all periods following the separation and distribution, Prothena). All references to we, our, us, Prothena or the Company in the context of historical results refer to the Prothena Busin (as defined herein). Except as otherwise indicated or unless the context otherwise requires, the information included in this Annual Report, including the combined financial statements of Prothena, which are comprised of the assets and liabilities of the Prothena Business, assumes the completion of all the transactions referred to in this Annual Report in connection with the separation of the Prothena Business from Elan (including the issuance of Prothena ordinary shares to Elan immediately following the separation and distribution).

This Annual Report on Form 10-K and the documents incorporated herein by reference contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the safe harbor created by those sections. These statements relate to future events or our future financial performance. Forward-looking statements may include words such as may, will, should, expect, plan, intend, anticipate, believe, estimate, pr continue or other wording indicating future results or expectations. Forward-looking statements are subject to risks and uncertainties, and actual events or results may differ materially. Factors that could cause our actual results to differ materially include, but are not limited to, those discussed under Risk Factors in this report. We also face risks and uncertainties relating to our business including:

- our ability to obtain additional financing;
- our history of operating losses;
- tax treatment of our separation from Elan and subsequent distribution of our ordinary shares;
- restrictions on our taking certain actions due to tax rules and covenants with Elan;
- 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 before competitors that are superior to the alternatives developed by such competitors;
- our ability to protect our patents and other intellectual property;
- loss of key employees;
- the impact of our separation from Elan and risks relating to our ability to operate effectively as a stand-alone, publicly traded company, including, without limitation:
- our ability to achieve benefits from our separation;

changes in our cost structure, management, financing and business operations;

growth in costs and expenses;

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;

the failure to comply with anti-kickback and false claims laws in the United States;

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extensive government regulation;

the volatility of our share price;

general changes in U.S. generally accepted accounting principles and International Financial Reporting Standards as adopted by the European Union; and

business disruptions caused by information technology failures; and

the other risks and uncertainties described in Item 1A, Risk Factors.

We undertake no obligation to revise or update any forward-looking statements to reflect any event or circumstance that arises after the date of this report, or to conform such statements to actual results or changes in our expectations, except as required by law.

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated Financial Statements and the Notes thereto appearing elsewhere in this Annual Report on Form 10-K. In addition to the other information in this Annual Report on Form 10-K, investors should carefully consider the following discussion and the information under Risk Factors when evaluating us and our business.

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PART I

Item 1. Business

Overview

We are a biotechnology company focused on the discovery and development of novel antibodies for the potential treatment of a broad range of diseases that involve protein misfolding or cell adhesion. We focus on the discovery and development of potential therapeutic monoclonal antibodies directed specifically to disease causing proteins. These potential therapies have a broad range of indications including AL and AA forms of amyloidosis, Parkinson s disease and related synucleinopathies, and novel cell adhesion targets involved in inflammatory disease and metastatic cancers. We plan to initiate Phase 1 clinical trials in these indications during the first half of 2013, 2014 and 2015, respectively. Our strategy is to apply our extensive expertise in generating novel therapeutic antibodies and work with collaborators having expertise in specific animal models of disease, to identify antibody candidates for clinical development.

We were incorporated in Ireland as a private limited company under the name Neotope Corporation Limited on September 26, 2012. We subsequently re-registered as a public limited company and changed the name of the company to Neotope Corporation plc . On November 1, 2012, our shareholders resolved to change the name of the company to Prothena Corporation plc , and this was approved by the Irish Registrar of Companies on November 7, 2012.

Prothena s business consists of a substantial portion of Elan Corporation, plc s (Elan) former drug discovery business platform, including Neotope Biosciences Limited and Onclave Therapeutics Limited, each former wholly-owned subsidiaries of Elan (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 stockholders (which we refer to in this report as the separation and distribution), our ordinary shares began trading on The NASDAQ Global Market under the symbol PRTA on December 21, 2012.

In connection with the separation and distribution, Elan invested cash in us in an amount that, together with the 18% of our outstanding ordinary shares (as calculated immediately following the consummation of such subscription) that a wholly-owned subsidiary of Elan acquired immediately following the separation and distribution, equaled $125.0 million.

Our Approach

We focus on the discovery and development of potential therapeutic monoclonal antibodies directed specifically to disease causing proteins. These potential therapies have a broad range of indications including AL (primary) and AA (secondary) forms of amyloidosis, Parkinson s disease and related synucleinopathies, and novel cell adhesion targets involved in inflammatory disease and metastatic cancers. Our strategy is to apply our extensive expertise in generating novel therapeutic antibodies and work with collaborators having expertise in specific animal models of disease, to identify antibody candidates for clinical development.

An epitope is the molecular target recognized by an antibody. A neo-epitope is a site on a protein that becomes accessible only after modification, such as from cleavage or by misfolding into an abnormal shape. The neo-epitopes we target may occur as part of a disease-associated pathological process. We are developing novel, specific monoclonal antibodies against neo-epitope targets for the potential treatment of patients having a disease associated with the neo-epitope.

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Targeting Neo-epitopes of Misfolded Proteins Associated with Disease

In addition to antibodies directed to neo-epitope targets, we are developing antibodies directed to other targets. For example, we have generated antibodies against novel cell adhesion targets expressed on certain pathogenic Th17 immune cells and tumor cells. One specific cell adhesion protein, called melanoma cell adhesion molecule, or MCAM, interacts with another protein called laminin near blood vessel walls which allows circulating tumor cells and a critical subset of T cells to leave the bloodstream and enter into tissues, sometimes initiating pathogenic processes that result in disease. Antibodies that interfere with the cell adhesion process may be useful for treating a range of inflammatory disease and metastatic cancers.

Targeting Cell Adhesion Involved in Disease Processes

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Research and Development Pipeline

Our research and development pipeline includes three lead therapeutic antibody programs that we will aggressively advance: NEOD001 for the treatment of AL and AA Amyloidosis; PRX002 (*formerly* NEOD002) for the treatment of Parkinson s disease; and PRX003 for the potential treatment of inflammatory disease and metastatic cancers.

Our pipeline also includes two late discovery stage programs for which we are testing efficacy of antibodies in preclinical models of disease: tau antibodies for potential treatment of Alzheimer s disease and antibodies for the potential treatment of type 2 diabetes. We are also generating additional novel antibodies against other targets involved in protein misfolding and cell adhesion for characterization in vivo and in vitro. If promising, these antibodies will advance to preclinical development.

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

Our Lead Programs

NEOD001 for amyloidosis

We are developing NEOD001, a monoclonal antibody targeting AL and AA amyloid for the potential treatment of amyloidosis.

Systemic amyloidoses are a complex group of diseases caused by tissue deposition of misfolded proteins that result in progressive organ damage. The most common type, AL amyloidosis or primary amyloidosis, involves a hematological disorder caused by plasma cells that produce misfolded AL protein resulting in deposits of abnormal AL protein (amyloid), in the tissues and organs of individuals with AL amyloidosis. Although little data are available on amyloidosis populations, AL amyloidosis is a rare disorder with an estimated incidence of 8.9 in 1,000,000 patient years. Only 1,200 to 3,200 new cases of AL amyloidosis are reported each year in the United States. Both the causes and origins of AL amyloidosis remain poorly understood.

Current treatments of patients with AL amyloidosis are organ transplant or treatments aimed at reducing or eliminating the bone marrow disorder, i.e. the plasma cells that are responsible for producing the AL protein, thereby limiting production of amyloid. There are no currently approved treatments for AL amyloidosis that directly target potentially toxic forms of the AL protein.

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A different form of systemic amyloidosis, AA amyloidosis or secondary amyloidosis, occurs secondarily as a result of other illnesses, such as chronic inflammatory diseases (for example, rheumatoid arthritis and ankylosing spondylitis) or chronic infections (for example, tuberculosis or osteomyelitis). In secondary amyloidosis, the depositing amyloid protein is amyloid A protein. Amyloid A protein is a cleaved fragment from the acute phase protein serum amyloid A that is produced in abundance by the liver as a result of chronic inflammation. The treatment of secondary amyloidosis is directed at treating the underlying illness, typically with broad acting anti-inflammatory agents such as tumor necrosis factor, or TNF, inhibitors. It is estimated that there are 8,000 patients in the United States and Europe suffering from AA amyloidosis.

NEOD001 is a monoclonal antibody that specifically targets the amyloid that accumulates in both AL and AA forms of amyloidosis. The antibody was designed to not react with normal serum amyloid and only with the aberrant cleaved form of the protein (amyloid A). This approach has the potential to be a first-in-class agent for this orphan disease with a significant unmet medical need. Together with scientists at the University of Tennessee performing under a Sponsored Research Agreement pursuant to which such scientists perform research at our direction and pursuant to project plans we establish, Prothena scientists have published a number of papers characterizing the mouse version of this antibody. NEOD001 was granted orphan drug designation by the FDA in 2012 and by the European Medicines Agency in 2013. An Investigational New Drug application, or IND, for NEOD001 in systemic amyloidosis (AL and AA forms of amyloidosis) was filed and accepted by the FDA in 2012. We plan to initiate a Phase 1 clinical trial for NEOD001 in this indication during the first half of 2013. The primary objectives of the phase 1 trial are to evaluate safety and tolerability of NEOD001 and determine a recommended dose for testing NEOD001 in phase 2 trials. We anticipate that a phase 2 trial of NEOD001 could be initiated in 2014 assuming a phase 2 recommended dose is identified prior to that date.

PRX002 (formerly NEOD002) for Parkinson s disease

We are developing PRX002, a monoclonal antibody targeting synuclein for the potential treatment of Parkinson s disease and other synucleinopathies. Together with scientists at the University of California, San Diego performing under a Laboratory Services Agreement pursuant to which such scientists perform research at our direction and pursuant to project plans we establish, Prothena scientists have published a number of scientific papers describing effects of these antibodies in preclinical models resembling Parkinson s disease.

Alpha-synuclein is a protein that is a prominent component of Lewy bodies and neurites which are pathological hallmarks of Parkinson s disease, dementia with Lewy bodies multiple system atrophy and certain other neurological disorders, collectively known as synucleinopathies. While the normal function of synuclein is not well understood, the protein normally occurs in an unstructured soluble form. In synucleinopathies, the synuclein protein can misfold and aggregate to form insoluble fibrils that contribute to the pathology of the disease.

Parkinson s disease is a degenerative disorder of the central nervous system. The motor symptoms of Parkinson s disease result from the death of dopamine-generating cells in the substantia nigra, a region of the midbrain.

Early in the course of the disease, the most obvious symptoms are movement-related and include shaking, rigidity, slowness of movement and difficulty with walking and gait. Later, cognitive and behavioral problems may arise, with dementia commonly occurring in the advanced stages of the disease. Other symptoms include sensory, sleep and emotional problems. Parkinson s disease is more common in the elderly, with most cases occurring after the age of 50.

Parkinson s disease is the second most common neurodegenerative disorder after Alzheimer s disease. In the United States, at least 500,000 people are believed to suffer from Parkinson s disease, and about 50,000 new cases are reported annually. Current treatments for Parkinson s disease are effective at managing the early motor symptoms of the disease, mainly through the use of levodopa and dopamine agonists. As the disease progresses

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and dopaminergic neurons continue to be lost, these drugs eventually become ineffective at treating the symptoms. The goal of our approach is to slow down the progressive neurodegenerative consequences of disease, a current unmet need.

There is genetic evidence for a causal role of synuclein in Parkinson s disease. In rare cases of familial forms of Parkinson s disease, there are mutations in the synuclein gene, or duplication and triplications of the gene that may cause synuclein protein to form amyloid-like fibrils that contribute to the disease. There is also increasing evidence that pathogenic forms of synuclein can be propagated and transmitted from neuron to neuron. Recent studies in cellular and animal models suggest that the spread of synuclein-associated neurodegeneration can be disrupted by targeting the pathogenic synuclein.

We have generated proprietary antibodies targeting alpha-synuclein that may slow or reduce the neurodegeneration associated with synuclein misfolding and/or transmission. We have tested the efficacy of these antibodies in various cellular and animal models of synuclein-related disease. We have identified a lead clinical candidate, PRX002, that has advanced into manufacturing and is advancing into preclinical safety testing and anticipate that we will file an IND and initiate a phase 1 trial of PRX002 for Parkinson s disease in 2014.

PRX003 for inflammatory disease and metastatic cancer

We are developing PRX003, a monoclonal antibody targeting MCAM (melanoma cell adhesion molecule) for the potential treatment of inflammatory disease and metastatic cancer.

MCAM is a cell adhesion molecule that allows certain cells travelling in the blood stream to leave the circulation and enter tissues. For example, MCAM is expressed on pathogenic Th-17 expressing immune cells that underlie inflammatory disease and on tumor cells involved in metastatic cancer. MCAM functions like VELCRO hook-and-loop fasteners, allowing these cells to stick to the blood vessel wall and migrate into tissues to initiate their pathogenic process.

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

Anti-MCAM antibodies may be useful for treating a variety of inflammatory disease such as rheumatoid arthritis, psoriasis and multiple sclerosis. Inflammatory disease arises from an inappropriate immune response of the body against substances and tissues normally present in the body. In other words, the immune system mistakes some part of the body as a pathogen and attacks its own cells. A substantial portion of the population suffers from these diseases, which are often chronic, debilitating, and life-threatening. There are more than eighty illnesses caused by autoimmunity. It has been estimated that inflammatory disease are among the ten leading causes of death among women in all age groups up to 65 years. Current treatment for many inflammatory disease typically entails use of broad acting immunosuppressive agents that weaken the body s ability to fight infection. Only 3-5% of CD4+ T-cells in the circulation express MCAM, yet these cells appear to be disproportionately involved in propagation of inflammatory disease. Hence, anti-MCAM based therapy may provide a more specific way to target the disease -causing immune cells while not interfering with normal function of the immune system.

MCAM antibodies may also be useful for treating metastatic cancers, including melanoma. Melanoma is a malignant tumor of melanocytes, a potentially dangerous form of skin cancer. It was estimated that doctors in the United States would diagnose about 76,250 new cases of melanoma in 2012, with approximately 9,000 melanoma-related deaths that are usually related to metastatic spread of the tumors. Normal melanocytes do not express MCAM, but expression is turned on and continues to increase as the cells become more malignant. Treatment with anti-MCAM antibodies may help patients with melanoma by inhibiting the growth and spread of the tumor.

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We have generated monoclonal antibodies that selectively block MCAM-mediated cell adhesion. Our antibodies are currently being tested in animal models of inflammatory disease and metastatic cancer. Based on early results from these studies, we have identified a lead clinical candidate, PRX003, and intend to advance this antibody into manufacturing and preclinical safety testing. We anticipate that we will file an IND and initiate a phase 1 trial of PRX003 in 2015.

Our Discovery Programs

Tau antibodies for Alzheimer s disease

We are developing antibodies targeting tau for the potential treatment of Alzheimer s disease and other tauopathies.

Tau proteins are proteins that stabilize microtubules. They are abundant in neurons of the central nervous system and are less common elsewhere in the body. When tau proteins are defective, they often misfold and aggregate to form neurofibrillary tangles. Tau sequestered in neurofibrillary tangles no longer has the ability to stabilize microtubules properly and is thought to be linked to the progressive neurodegeneration characteristic of several neurological diseases known as tauopathies. Tauopathies are a class of neurodegenerative diseases associated with the pathological aggregation of tau protein in the human brain. The best-known of these illnesses is Alzheimer s disease, wherein tau protein is deposited within neurons.

Alzheimer s disease is a degenerative brain disease that slowly destroys memory and thinking skills. It can begin with simple forgetfulness, but may rapidly progress into more advanced symptoms, including confusion, profound memory loss, language disturbances, personality and behavior changes, impaired judgment and dementia. Alzheimer s disease primarily affects older people, and in most cases, readily apparent symptoms appear after age 60. It is estimated that more than 5 million Americans and more than 35 million people worldwide, at the age of 60 years or older, suffer from some form of dementia. Although some patients may live up to 20 years after being diagnosed with Alzheimer s disease, the average life expectancy after diagnosis is eight to ten years. No current therapy alters the progressive and eventually fatal neurodegenerative consequences of these conditions.

Recent experimental data from multiple laboratories show that pathogenic forms of tau can be propagated and spread between neurons. It has further been demonstrated that administration of tau antibodies in animal models with tauopathies can potentially interrupt tau propagation and the resulting neurodegenerative effects of this process.

We have generated and tested in vivo a variety of proprietary tau antibodies. We are currently selecting optimal candidates for their ability to block propagation and toxicity associated with misfolded forms in animal models of tauopathies. These studies will help us to identify a potential clinical candidate to advance into manufacturing and preclinical safety testing and we anticipate that, if successful, we will file an IND with a tau clinical candidate in 2015.

Antibodies for Type 2 diabetes

We are developing antibodies to protect against loss of insulin producing beta cells of the pancreas for the potential treatment of type 2 diabetes.

Type 2 diabetes is a metabolic disorder characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. Type 2 diabetes makes up about 90% of cases of diabetes, and obesity is thought to be the primary cause of type 2 diabetes in people who are genetically predisposed to the disease. Rates of diabetes have increased markedly over the last 50 years in parallel with obesity. Type 2 diabetes is a global health problem affecting more than 300 million people worldwide. Long-term complications from high blood sugar can include heart disease, strokes, diabetic retinopathy where eyesight is affected, kidney failure which may require dialysis, and poor circulation of limbs leading to amputations.

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Type 2 diabetes is initially managed by increasing exercise and dietary modification. If blood glucose levels are not adequately lowered by these measures, medications may be needed. In type 2 diabetes, patients become increasingly unable to adequately regulate blood glucose levels and current therapies such as metformin and insulin only target this hyperglycemia. In many cases, the progressive loss of insulin producing beta cells of the pancreas leads to dependence upon injected insulin to manage blood glucose levels. Current therapies do not target the fundamental mechanism by which these beta cells are lost in disease.

We have generated unique antibodies and are currently testing the hypothesis that treatment with these antibodies may reduce the progressive increase in glucose levels in animal models of type 2 diabetes. If successful, these studies will help us identify a potential clinical candidate to advance into manufacturing and preclinical safety testing and we anticipate that, if successful, we will file an IND with a type 2 diabetes clinical candidate in 2015.

Our Strategy

We will advance novel and proprietary therapeutic antibodies discovered by our scientists internally. Our goal is to be a leading biotechnology company focused on discovery and development of novel antibodies for the potential treatment of a broad range of diseases that involve protein misfolding or cell adhesion. Key elements of our strategy to achieve this goal are:

Continue to discover potential therapeutic antibodies directed against novel targets involved in protein misfolding and cell adhesion. We will continue to leverage our core scientific expertise and proprietary technology to develop innovative antibody-based therapeutics for the potential treatment of a range of diseases. Once we formulate a novel hypothesis or approach to a known target, we generate antibodies against that target. Specific and selective antibodies are characterized in vitro, then used to test the initial hypothesis in vivo using animal models of disease. We typically rely on the use of animal models that have been extensively developed by external laboratories, as we have already done with three of our programs: AL amyloidosis, Parkinson s disease and tau for Alzheimer s disease. We plan to maintain a broad and diverse pipeline of antibodies with multiple potential indications.

Quickly translate our research discoveries into clinical development. Once we establish in vivo proof of concept for our antibody candidates, we use animal models to identify potential clinical candidates to rapidly advance to manufacturing and preclinical testing. We have contracted with Boehringer Ingelheim for cell line development and antibody drug substance production. In 2012, we filed an Investigational Drug Application with the FDA for NEOD001 in AL and AA amyloidosis and we plan to initiate a Phase 1 clinical trial of NEOD001 in amyloidosis patients during the first half of 2013.

Establish early clinical proof of concept with our therapeutic antibodies. We will leverage our insight of pathology in diseases involving protein misfolding and cell adhesion to employ biomarker endpoints as a way to detect signals of clinical efficacy early in the clinical development process. We may elect to start clinical testing of our antibodies in smaller indications having more well-established endpoints in order to demonstrate proof of concept as a basis for further investment in clinical trials, potentially in larger indications, by us or potential partners.

Strategically collaborate or out-license select programs. We intend to seek to collaborate or license certain potentially therapeutic antibody products to biotechnology or pharmaceutical companies for preclinical and clinical development and commercialization. For certain product opportunities, we may choose to proceed with further clinical development independently in order to create long term value. We intend to seek strategic alliances in which we would provide our research and development services for our collaborators as part of our plan to generate revenue.

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Highly leverage external talent and resources.

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

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

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

Regulation

We anticipate that if we commercialize any products, the U.S. market will be our most important market. For this reason, the factors discussed below, in Government Regulation, Product Approval and Orphan Drugs place emphasis on requirements in the United States.

Government Regulation

The pharmaceutical industry is subject to significant regulation by international, national, state and local governmental regulatory agencies. Pharmaceutical product registration is primarily concerned with the safety, efficacy and quality of new drugs and devices and, in some countries, their pricing. A product must generally undergo extensive clinical trials before it can be approved for marketing. The process of developing a new pharmaceutical product, from idea to commercialization, can take in excess of 10 years.

Governmental authorities, including the FDA and comparable regulatory authorities in other countries, regulate the design, development, testing, manufacturing and marketing of pharmaceutical products. Non-compliance with applicable requirements can result in fines and other judicially imposed sanctions, including product seizures, import restrictions, injunctive actions and criminal prosecutions of both companies and individuals. In addition, administrative remedies can involve requests to recall violative products; the refusal of the government to enter into supply contracts; or the refusal to approve pending product approval applications for drugs, biological products or medical devices until manufacturing or other alleged deficiencies are brought into compliance. The FDA also has the authority to cause the withdrawal of approval of a marketed product or to impose labeling restrictions.

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

Product Approval

Preclinical tests assess the potential safety and efficacy of a product candidate in animal models. The results of these studies must be submitted to the FDA as part of an Investigational New Drug Application before human testing may proceed.

The clinical trial process can take three to ten years or more to complete, and there can be no assurance that the data collected will demonstrate that the product is safe or effective or, in the case of a biologic product, pure and potent, or will provide sufficient data to support FDA approval of the product. The FDA may place clinical

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trials on hold at any point in this process if, among other reasons, it concludes that clinical subjects are being exposed to an unacceptable health risk. Trials may also be terminated by institutional review boards, which must review and approve all research involving human subjects. Side effects or adverse events that are reported during clinical trials can delay, impede or prevent marketing authorization.

The results of the preclinical and clinical testing, along with information regarding the manufacturing of the product and proposed product labeling, are evaluated and, if determined appropriate, submitted to the FDA through a license application such as a New Drug Application, or NDA, or a Biologics License Application, or BLA. In certain cases, an Abbreviated New Drug Application, or ANDA, can be filed in lieu of filing an NDA.

There can be no marketing in the United States of any drug, biologic or device for which a marketing application is required until the application is approved by the FDA. Until an application is actually approved, there can be no assurance that the information requested and submitted will be considered adequate by the FDA. Additionally, any significant change in the approved product or in how it is manufactured, including changes in formulation or the site of manufacture, generally require prior FDA approval. The packaging and labeling of all products developed by us are also subject to FDA approval and ongoing regulation.

Whether or not FDA approval has been obtained, approval of a pharmaceutical product by comparable regulatory authorities in other countries outside the United States must be obtained prior to the marketing of the product in those countries. The approval procedure varies from country to country. It can involve additional testing and the time required can differ from that required for FDA approval. Although there are procedures for unified filings for EU countries, in general, most other countries have their own procedures and requirements.

Once a product has been approved, significant legal and regulatory requirements apply in order to market a product. In the United States, these include, among other things, requirements related to adverse event and other reporting, product advertising and promotion, and ongoing adherence to cGMP requirements, as well as the need to submit appropriate new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process.

The FDA also enforces the requirements of the Prescription Drug Marketing Act, which, among other things, imposes various requirements in connection with the distribution of product samples to physicians. Sales, marketing and scientific/educational grant programs must comply with the Medicare-Medicaid Anti-Fraud and Abuse Act, as amended, the False Claims Act, as amended, and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended. We are also subject to Section 6002 of the Affordable Care Act, or ACA, commonly known as the Physician Payment Sunshine Act, or Sunshine Act, which regulates disclosure of payments to healthcare professionals and providers.

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

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the

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FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan.

Patents and Intellectual Property Rights

We aggressively strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining domestic and international patents intended to cover our products and compositions, their methods of use and processes for their manufacture and any other inventions that may be commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business. Our competitive position depends on our ability to obtain patents on our technologies and our potential products, to defend our patents, to protect our trade secrets and to operate without infringing valid and enforceable patents or trade secrets of others. We seek licenses from others as appropriate to enhance or maintain our competitive position.

We own or hold licenses to a number of issued patents and US pending patent applications, as well as foreign patents and pending Patent Corporation Treaty applications and foreign counterparts.

In connection with our program targeting AL and AA amyloid for the potential treatment of amyloidosis, we own US Patent No. 7,928,203, which is a composition of matter patent and expires in 2029 and US Patent No. 8,268,973, which is a composition of matter patent and expires in 2028. We also have ownership rights in US Patent No. 8,124,081, which is a method of treatment patent and expires in 2020. In addition, we jointly own with the University of Tennessee patent applications pending in the United States, Australia, Brazil, China, Colombia, Eurasia, Europe, Hong Kong, Indonesia, Israel, India, Japan, South Korea, Mexico, Norway, New Zealand, Philippines, Singapore and South Africa, and have exclusively licensed the University of Tennessee s joint ownership interest in these patent applications. Under our exclusive, sublicensable, worldwide license agreement with the University of Tennessee entered into on December 8, 2008, we paid to the University of Tennessee an annual maintenance fee of $10,000 on each of the first two anniversaries of execution of the license agreement, and have paid, and are required to continue to pay, $25,000 on each anniversary thereafter. In addition, we have paid a license issue fee of $10,000, and we are required to pay to the University of Tennessee an amount equal to 1% of net sales of any product covered by any applicable patent, plus certain additional royalties in the event that all or a portion of the license is sublicensed. To date, we have not paid or incurred any royalties to the University of Tennessee under our license agreement. The license agreement will continue in effect on a country-by-country basis for the longer of (i) a period of twenty years from the date of execution of the license agreement, or (ii) in each country in which a valid claim for any licensed patent or patent application exists, expiration of such valid claim. The University of Tennessee may terminate the agreement prior to the end of its term if we are adjudicated by a court of competent jurisdiction to be insolvent, if we are dissolved or are declared bankrupt, upon our failure to make payment under the agreement within 120 days of notice of such failure or upon our material breach of the agreement, which breach has not been cured within sixty days of written notice of such breach. We may terminate the agreement prior to the end of its term upon three months written notice to the University of Tennessee or upon material breach of the agreement by the University of Tennessee, which breach has not been cured within sixty days of written notice of such breach.

We also hold exclusive, royalty-free sublicenses from affiliates of Elan under US and foreign patent rights owned by Janssen Alzheimer Immunotherapy relating to immunotherapeutic approaches targeting misfolding proteins other than amyloid beta peptide. In connection with our program targeting synuclein for the potential treatment of Parkinson s disease and other synucleinopathies, we own or hold an exclusive, royalty-free license from affiliates of Elan to US Patent No. 7,910,333, which is a composition of matter patent and expires in 2024,

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and we own or hold non-exclusive royalty-free licenses from affiliates of Elan under patent rights relating to research tools such as animal models and assay technology in support of our programs relating to synucleinopathies and Alzheimer s disease. In addition, we jointly own with the University of California San Diego US Patent Nos. 7,919,088, 8,092,801 and 8,147,833, which are method of treatment patents and expire in 2025, 2029 and 2027, respectively.

We also own patent applications relating to AL and AA, synuclein, MCAM and various discovery programs that are pending in the United States and other countries, which, if issued, would have expiration dates in the range of 2020 through 2032, excluding any available patent term adjustment.

Competition

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

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

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

Product Supply

While supplies of raw materials and clinical supplies of our main product candidate are generally available in quantities adequate to meet the needs of our business, we are dependent on Boehringer Ingelheim to manufacture our clinical supplies of NEOD001. An inability to obtain product supply could have a material adverse effect on our business, financial condition and results of operations.

Research and Development

Our research and development expenses totaled $34.1 million, $24.2 million and $9.8 million in 2012, 2011 and 2010, respectively. For more information, see Management s Discussion and Analysis of Financial Condition and Results of Operations.

We are performing certain research and development services for Elan and we intend to pursue opportunities to perform research and development services for unrelated parties with whom we are otherwise collaborating, using compensation arrangements that are consistent with industry arrangements between unrelated parties. We also may earn income through licensing agreements and other types of transactions.

Employees

As of December 31, 2012, we had 30 employees, of whom approximately 23 were engaged in research and development activities and the remainder working in general and administrative areas.

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Information about Segment and Geographic Revenue

Information about segment and geographic revenue is set forth in Note 2 of the Notes to Consolidated Financial Statements under Item 8 of this Annual Report on Form 10-K.

Available information

Our registration statement on Form 10 and our current reports on Form 8-K, and all amendments to those reports, filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge on our website at www.prothena.com as soon as reasonably practicable after we file such reports with the Securities and Exchange Commission, or the SEC. Information contained in, or accessible through, our website is not incorporated by reference into and does not form a part of this report.

Our periodic and current reports, registration statements, proxy and information statements and other information are available for inspection and copying at the SEC s Public Reference Room at 100 F Street, NE, Washington, DC 20549 or may be obtained by calling the SEC at 1-800-SEC-0330.The SEC also maintains a website containing such information available free of charge to the public at http://www.sec.gov.

Item 1A. Risk Factors

You should carefully consider the risks described below, together with all of the other information included in this Annual Report on Form 10-K, in considering our business and prospects. Set forth below and elsewhere in this report and in other documents we file with the SEC are descriptions of the risks and uncertainties that could cause our actual results to differ materially from the results contemplated by the forward-looking statements contained in this report. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Each of these risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock.

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

We have not generated any significant third party external revenue to date, and we anticipate that we will incur losses for the foreseeable future and we may never achieve or sustain profitability.

We may not generate the cash that is necessary to finance our operations in the foreseeable future. We have not generated any significant third party external revenues to date. We have incurred losses of $41.4 million, $29.7 million and $12.5 million for the years ended December 31, 2012, 2011 and 2010, respectively. We expect to continue to incur substantial losses for the foreseeable future as we:

- conduct our planned Phase 1 clinical trial for NEOD001 and initiate additional clinical trials, if supported by the results of the Phase 1 trial;
- complete preclinical development of other product candidates and initiate clinical trials, if supported by positive preclinical data;
- 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; and
- add operational, financial and management information systems and other personnel.

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

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

As of December 31, 2012, we had cash and cash equivalents of approximately $124.9 million. Although we expect that our existing cash and cash equivalents will be sufficient to support us through 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:

- the timing of initiation, progress, results and costs of our clinical trials;
- the results of our research and preclinical studies;
- the costs of clinical manufacturing and of establishing commercial manufacturing arrangements;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims;
- the costs and timing of capital asset purchases;
- our ability to establish research collaborations and strategic collaborations and 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 this expectation 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. Our future capital requirements will depend on numerous factors, including, the timing of initiation, progress, results and costs of our clinical trials; the results of our research and preclinical studies; the costs of clinical manufacturing and of establishing commercial manufacturing arrangements; the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims; the costs and timing of capital asset purchases; our ability to establish research collaborations and strategic collaborations and 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.

In order to develop and obtain regulatory approval for our potential products we will need to raise substantial additional funds through public or private equity offerings, debt financings, strategic alliances, joint ventures and licensing 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. If adequate funds are not available on a timely basis, we may be required to:

- terminate or delay clinical trials or other development for one or more of our drug candidates;

delay arrangements for activities that may be necessary to commercialize our drug candidates; or

curtail or eliminate our drug research and development programs that are designed to identify new drug candidates or cease operations.