

PROTHENA CORP PLC

FORM 10-Q (Quarterly Report)

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

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2017

Or

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

Commission file number: 001-35676

PROTHENA CORPORATION PUBLIC LIMITED COMPANY

(Exact name of registrant as specified in its charter)

Ireland

(State or other jurisdiction of
incorporation or organization)

98-1111119

(I.R.S. Employer
Identification Number)

**Adelphi Plaza
Upper George's Street
Dún Laoghaire
Co. Dublin, A96 T927, Ireland**

(Address of principal executive offices including Zip Code)

Registrant's telephone number, including area code: 011-353-1-236-2500

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

Indicate by check mark whether the registrant has submitted electronically 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 whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

| | | | |
|-------------------------|--|---------------------------|--------------------------|
| Large accelerated filer | <input checked="" type="checkbox"/> | Accelerated filer | <input type="checkbox"/> |
| Non-accelerated filer | <input type="checkbox"/> (Do not check if a smaller reporting company) | Smaller reporting company | <input type="checkbox"/> |
| | | Emerging growth company | <input type="checkbox"/> |

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards† provided pursuant to Section 13(a) of the Exchange Act.

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

The number of ordinary shares outstanding as of April 21, 2017 was 38,020,181 .

PROTHENA CORPORATION plc
Form 10-Q – QUARTERLY REPORT
For the Quarter Ended March 31, 2017

TABLE OF CONTENTS

| | Page |
|--|-------------|
| PART I. FINANCIAL INFORMATION | 1 |
| Item 1. Financial Statements (unaudited) | 1 |
| Condensed Consolidated Balance Sheets as of March 31, 2017 and December 31, 2016 | 1 |
| Condensed Consolidated Statements of Operations for the three months ended March 31, 2017 and 2016 | 2 |
| Condensed Consolidated Statements of Cash Flows for the three months ended March 31, 2017 and 2016 | 3 |
| Notes to Condensed Consolidated Financial Statements | 4 |
| Item 2. Management’s Discussion and Analysis of Financial Condition and Results of Operations | 15 |
| Item 3. Quantitative and Qualitative Disclosures About Market Risk | 21 |
| Item 4. Controls and Procedures | 21 |
| PART II. OTHER INFORMATION | 22 |
| Item 1. Legal Proceedings | 22 |
| Item 1A. Risk Factors | 22 |
| Item 2. Unregistered Sales of Equity Securities and Use of Proceeds | 44 |
| Item 3. Defaults Upon Senior Securities | 44 |
| Item 4. Mine Safety Disclosures | 44 |
| Item 5. Other Information | 44 |
| Item 6. Exhibits | 44 |
| SIGNATURES | 45 |
| EXHIBIT INDEX | 46 |

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

| | March 31, 2017 | December 31, 2016 |
|---|-------------------|----------------------|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$ 506,550 | \$ 386,923 |
| Receivable from Roche | 271 | 178 |
| Prepaid expenses and other current assets | 7,383 | 4,261 |
| Total current assets | 514,204 | 391,362 |
| Non-current assets: | | |
| Property and equipment, net | 56,084 | 56,452 |
| Deferred tax assets | 5,176 | 5,913 |
| Restricted cash | 4,056 | 4,056 |
| Other non-current assets | 2,430 | 2,193 |
| Total non-current assets | 67,746 | 68,614 |
| Total assets | \$ 581,950 | \$ 459,976 |
| Liabilities and Shareholders' Equity | | |
| Current liabilities: | | |
| Accounts payable | \$ 6,254 | \$ 13,069 |
| Accrued research and development | 21,710 | 19,073 |
| Income taxes payable, current | 385 | 378 |
| Other current liabilities | 5,331 | 8,555 |
| Total current liabilities | 33,680 | 41,075 |
| Non-current liabilities: | | |
| Income taxes payable, non-current | — | 98 |
| Deferred rent | 287 | 2,080 |
| Build-to-suit lease obligation, non-current | 51,735 | 51,320 |
| Total non-current liabilities | 52,022 | 53,498 |
| Total liabilities | 85,702 | 94,573 |
| Commitments and contingencies (Note 7) | | |
| Shareholders' equity: | | |
| Euro deferred shares, €22 nominal value: | — | — |
| Authorized shares — 10,000 at March 31, 2017 and December 31, 2016 | | |
| Issued and outstanding shares — none at March 31, 2017 and December 31, 2016 | | |
| Ordinary shares, \$0.01 par value: | 380 | 348 |
| Authorized shares — 100,000,000 at March 31, 2017 and December 31, 2016 | | |
| Issued and outstanding shares — 37,957,649 and 34,752,116 at March 31, 2017 and December 31, 2016, respectively | | |
| Additional paid-in capital | 820,365 | 654,266 |
| Accumulated deficit | (324,497) | (289,211) |
| Total shareholders' equity | 496,248 | 365,403 |
| Total liabilities and shareholders' equity | \$ 581,950 | \$ 459,976 |

See accompanying Notes to Condensed Consolidated Financial Statements.

Prothena Corporation plc and Subsidiaries
Condensed Consolidated Statements of Operations
(in thousands, except per share data)
(unaudited)

| | Three Months Ended March 31, | |
|---|---|-------------|
| | 2017 | 2016 |
| Collaboration revenue | \$ 259 | \$ 265 |
| Total revenue | 259 | 265 |
| Operating expenses: | | |
| Research and development | 25,698 | 20,493 |
| General and administrative | 10,832 | 7,182 |
| Total operating expenses | 36,530 | 27,675 |
| Loss from operations | (36,271) | (27,410) |
| Other income (expense): | | |
| Interest income, net | (364) | 277 |
| Other expense, net | (410) | (207) |
| Total other income (expense) | (774) | 70 |
| Loss before income taxes | (37,045) | (27,340) |
| Provision for (benefit from) income taxes | (1,661) | 181 |
| Net loss | \$ (35,384) | \$ (27,521) |
| Basic and diluted net loss per share | \$ (0.99) | \$ (0.81) |
| Shares used to compute basic and diluted net loss per share | 35,758 | 34,026 |

See accompanying Notes to Condensed Consolidated Financial Statements.

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

| | Three Months Ended | |
|--|---------------------------|-------------------|
| | March 31, | |
| | 2017 | 2016 |
| Operating activities | | |
| Net loss | \$ (35,384) | \$ (27,521) |
| Adjustments to reconcile net loss to cash used in operating activities: | | |
| Depreciation and amortization | 759 | 251 |
| Share-based compensation | 5,602 | 3,724 |
| Deferred income taxes | 737 | (445) |
| Interest expense under build-to-suit lease obligation | 916 | — |
| Gain from early lease retirement | (2,096) | — |
| Changes in operating assets and liabilities: | | |
| Receivable from Roche | (93) | (494) |
| Prepaid and other assets | (5,452) | (1,181) |
| Accounts payable, accruals and other liabilities | (2,831) | 609 |
| Net cash used in operating activities | <u>(37,842)</u> | <u>(25,057)</u> |
| Investing activities | | |
| Purchases of property and equipment | (2,499) | (238) |
| Proceeds from disposal of fixed assets | 100 | — |
| Net cash used in investing activities | <u>(2,399)</u> | <u>(238)</u> |
| Financing activities | | |
| Proceeds from issuance of ordinary shares in public offering, net | 150,421 | 128,785 |
| Proceeds from issuance of ordinary shares upon exercise of stock options | 9,948 | 176 |
| Reduction of build-to-suit lease obligation | (501) | — |
| Net cash provided by financing activities | <u>159,868</u> | <u>128,961</u> |
| Net increase in cash, cash equivalents and restricted cash | 119,627 | 103,666 |
| Cash, cash equivalents and restricted cash, beginning of the year | 390,979 | 370,586 |
| Cash, cash equivalents and restricted cash, end of the period | <u>\$ 510,606</u> | <u>\$ 474,252</u> |
| Supplemental disclosures of cash flow information | | |
| Cash paid for income taxes, net of refunds | <u>\$ —</u> | <u>\$ (383)</u> |
| Supplemental disclosures of non-cash investing and financing activities | | |
| Acquisition of property and equipment included in accounts payable and accrued liabilities | <u>\$ 88</u> | <u>\$ 260</u> |
| Receivable from option exercises | <u>\$ 311</u> | <u>\$ —</u> |
| Offering costs included in accounts payable and accrued liabilities | <u>\$ 107</u> | <u>\$ 8</u> |

See accompanying Notes to Condensed Consolidated Financial Statements.

Notes to the Condensed Consolidated Financial Statements
(unaudited)

1. Organization

Description of Business

Prothena Corporation plc and its subsidiaries (“Prothena” or the “Company”) is a global, late-stage clinical biotechnology company establishing fully-integrated research, development and commercial capabilities. Fueled by its deep scientific understanding built over decades of research in protein misfolding and cell adhesion - the root causes of many serious or currently untreatable amyloid and inflammatory diseases - Prothena seeks to fundamentally change the course of progressive diseases associated with this biology.

The Company's pipeline of antibody-based product candidates target a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002/RG7935), inflammatory diseases including psoriasis and psoriatic arthritis (PRX003) and ATTR amyloidosis (PRX004). The Company continues discovery of additional novel therapeutic candidates where its deep scientific understanding of disease pathology can be leveraged.

The Company is a public limited company formed under the laws of Ireland. The Company separated from Elan Corporation, plc (“Elan”) on December 20, 2012. After the separation from Elan, and the related distribution of the Company's ordinary shares to Elan's shareholders, the Company's ordinary shares commenced trading on The Nasdaq Global Market under the symbol “PRTA” on December 21, 2012 and currently trade on The Nasdaq Global Select Market.

Liquidity and Business Risks

As of March 31, 2017, the Company had an accumulated deficit of \$324.5 million and cash and cash equivalents of \$506.6 million.

In March 2017, the Company sold an aggregate of 2,700,000 ordinary shares for net proceeds of approximately \$150.3 million, after deducting the underwriting discount and estimated offering expenses, in an underwritten public offering.

Based on the Company's business plans, management believes that the Company's cash and cash equivalents at March 31, 2017 are sufficient to meet its obligations for at least the next twelve months. To operate beyond such period, or if the Company elects to increase its spending on development programs significantly above current long-term plans or enters into potential licenses and or other acquisitions of complementary technologies, products or companies, the Company may need additional capital. The Company expects to continue to finance future cash needs that exceed its cash from operating activities primarily through its current cash and cash equivalents, its collaboration with Roche, and to the extent necessary, through proceeds from public or private equity or debt financings, loans and other collaborative agreements with corporate partners or other arrangements.

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

2. Summary of Significant Accounting Policies

Basis of Preparation and Presentation of Financial Information

These accompanying Unaudited Interim Condensed Consolidated Financial Statements have been prepared in accordance with the accounting principles generally accepted in the U.S. (“GAAP”) and with the instructions for Form 10-Q and Regulation S-X statements. Accordingly, they do not include all of the information and notes required for complete financial statements. These interim Condensed Consolidated Financial Statements should be read in conjunction with the Consolidated Financial Statements and Notes thereto contained in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission (the “SEC”) on February 27, 2017 (the “2016 Form 10-K”). These Unaudited Interim Condensed Consolidated Financial Statements are presented in U.S. dollars, which is the functional currency of the Company and its consolidated subsidiaries. These Unaudited Interim Condensed Consolidated Financial Statements include the accounts of the Company and its consolidated subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Unaudited Interim Financial Information

The accompanying Unaudited Interim Condensed Consolidated Financial Statements and related disclosures are unaudited, have been prepared on the same basis as the annual consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for a fair presentation of the results of operations for the periods presented. The year-end condensed consolidated balance sheet data was derived from audited financial statements, however certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted. The condensed consolidated results of operations for any interim period are not necessarily indicative of the results to be expected for the full year or for any other future year or interim period.

Certain amounts in the condensed consolidated financial statements have been reclassified to conform to the current year presentation.

Use of Estimates

The preparation of the Condensed Consolidated Financial Statements in conformity with GAAP requires management to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures. On an ongoing basis, management evaluates its estimates, including critical accounting policies or estimates related to revenue recognition, share-based compensation and research and development expenses. The Company bases its estimates on historical experience and on various other market specific and other relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Because of the uncertainties inherent in such estimates, actual results may differ materially from these estimates.

Significant Accounting Policies

There were no significant changes to the accounting policies during the three months ended March 31, 2017, from the significant accounting policies described in Note 2 of the "Notes to Consolidated Financial Statements" in the 2016 Form 10-K, with the exception of those noted below.

Share-based Compensation

To determine the fair value of share-based payment awards, the Company uses the Black-Scholes option-pricing model. The determination of fair value using the Black-Scholes option-pricing model is affected by the Company's share price as well as assumptions regarding a number of complex and subjective variables. Share-based compensation expense is recognized on a straight-line basis over the requisite service period for each award. Further, share-based compensation expense recognized in the Condensed Consolidated Statements of Operations is based on awards expected to vest and therefore the amount of expense has been reduced for estimated forfeitures. If actual forfeitures differ from estimates at the time of grant they will be revised in subsequent periods. The Company bases its assumptions on historical data when available or when not available, on a peer group of companies. If factors change and different assumptions are employed in determining the fair value of share-based awards, the share-based compensation expense recorded in future periods may differ significantly from what was recorded in the current period (see Note 10 for further information).

The Company will record any excess tax benefits or deficiencies from its equity awards in its Condensed Consolidated Statements of Operations in the reporting periods in which stock options are exercised.

Segment and Concentration of Risks

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

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash and cash equivalents and accounts receivable. The Company places its cash equivalents with high credit quality financial institutions and by policy, limits the amount of credit exposure with any one financial institution. Deposits held with banks may exceed the amount of insurance provided on such deposits. The Company has not experienced any losses on its deposits of cash and cash equivalents and its credit risk exposure is up to the extent recorded on the Company's Condensed Consolidated Balance Sheet.

Receivable from Roche as of March 31, 2017 and December 31, 2016 are amounts due from Roche entities located in the U.S. and Switzerland under the License Agreement that became effective January 22, 2014. Revenue recorded in the Statements of Operations consists of reimbursement from Roche for research and development services. Credit risk exposure is up to the extent recorded on the Company's Condensed Consolidated Balance Sheet.

As of March 31, 2017, \$55.4 million of the Company's long-lived assets were held in the U.S. and \$0.7 million were in Ireland. As of December 31, 2016, \$55.7 million of the Company's long-lived assets were held in the U.S. and \$0.8 million were in Ireland.

The Company does not own or operate facilities for the manufacture, packaging, labeling, storage, testing or distribution of preclinical or clinical supplies of any of its drug candidates, including for commercial supplies if the Company obtains regulatory approval to market any of its drug candidates. The Company instead contracts with and relies on third-parties to manufacture, package, label, store, test and distribute all pre-clinical development and clinical supplies of our drug candidates, and it plans to continue to do so for the foreseeable future, including for commercial supplies if the Company obtains regulatory approval to market any of its drug candidates. The Company also relies on third-party consultants to assist in managing these third-parties and assist with its manufacturing strategy.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update 2014-09 (ASU 2014-09), Revenue from Contracts with Customers. ASU 2014-09 supersedes the revenue recognition requirements in Revenue Recognition (Topic 605). The new standard requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. To achieve that core principle, an entity must identify the contract(s) with a customer, identify the performance obligations in the contract, determine the transaction price, allocate the transaction price to the performance obligations in the contract, and recognize revenue when (or as) the entity satisfies the performance obligation. ASU 2014-09 is effective for annual reporting periods beginning after December 15, 2017, including interim periods within that reporting period, which for the Company is January 1, 2018. Early adoption is permitted after January 1, 2017. The standard allows for two transition methods - retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of initially applying the standard recognized at the date of initial adoption. The Company expects to adopt the requirements of the new standard effective January 1, 2018 using the retrospective with the cumulative effect transition method. In March 2016, the FASB issued ASU No. 2016-08 Revenue from Contracts with Customers: Principal vs. Agent Considerations, to help provide interpretive clarifications on the new guidance for ASC Topic 606. In April 2016, the FASB issued ASU No. 2016-10 Revenue from Contracts with Customers: Identifying Performance Obligations and Licensing to clarify the guidance for identifying performance obligations and accounting for licenses of intellectual property. In May 2016, the FASB issued ASU No. 2016-12 Revenue from Contracts with Customers: Narrow-Scope Improvements; and Practical Expedients, to improve the guidance on collectibility, noncash consideration, and completed contracts at transition. In December 2016, the FASB issued ASU No. 2016-20 Revenue from Contracts with Customers: Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers. The Company continues to evaluate the impact that the adoption of these standards will have on its consolidated financial statements in connection with the Roche License Agreement.

In February 2016, the FASB issued Accounting Standards Update 2016-02 (ASU 2016-02), Leases (ASC Topic 842), which will require lessees to recognize assets and liabilities for leases with lease terms of more than 12 months. Consistent with current GAAP, the recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee primarily will depend on its classification as a finance or operating lease. However, unlike current GAAP, which requires only capital leases to be recognized on the balance sheet, the new guidance will require both types of leases to be recognized on the balance sheet. ASU 2016-02 is effective for annual periods beginning after December 15, 2018, and interim periods within those years. Early adoption is permitted for all entities. The standard requires that entities use a modified retrospective approach for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Entities have the option to use certain relief. Full retrospective application is prohibited. Note 7 Commitments and Contingencies provides details on the Company's current lease arrangements. The Company is evaluating the provisions of ASC Topic 842 to determine the impact the adoption of ASU 2016-02 will have on its consolidated financial statements; however, the Company anticipates recognition of additional assets and corresponding liabilities related to leases on its consolidated balance sheets.

In March 2016, the FASB issued Accounting Standards Update 2016-09 (ASU 2016-09), Improvements to Employee Share-Based Payment Accounting, which modifies certain aspects of the accounting for share-based payment transactions, including income taxes, classification of awards and classification in the statement of cash flows. Through December 31, 2016, excess tax benefits or deficiencies from the Company's equity awards were recorded as additional paid-in capital in its Consolidated Balance Sheets. Upon adoption, the Company will record any excess tax benefits or deficiencies from its equity awards in its Condensed Consolidated Statements of Operations in the reporting periods in which stock options are exercised. This guidance also requires excess tax benefits and deficiencies to be presented as an operating activity on the statement of cash flows and allows an entity to make an accounting policy election to either estimate expected forfeitures or to account for them as they occur. The ASU is effective for reporting periods beginning after December 15, 2016, with early adoption permitted. The Company adopted this ASU on January 1, 2017.

Pursuant to the adoption of ASU 2016-09, tax attributes previously tracked off balance sheet have been recorded as deferred tax assets, offset by a valuation allowance. In addition, the Company has reversed its non-current tax liability of \$98,000 with the offsetting entry recorded to retained earnings pursuant to the adoption of this ASU. Further, the year-to-date excess benefits have been recorded as a discrete benefit to the tax provision. For the three months ended March 31, 2017, the Company recorded excess tax benefits of \$1.9 million as part of its income tax provision in the Condensed Consolidated Statements of Operations. The Company's income tax expense will continue to be impacted by fluctuations in stock price between the grant dates and the exercise dates of its option awards. The presentation requirements for cash flows related to excess tax benefits will be applied retrospectively; as such, prior years have been restated. Lastly, the Company elected to continue to estimate the number of forfeitures related to share-based payments, rather than account for forfeitures as they occur.

In August 2016, the FASB issued Accounting Standards Update 2016-15 (ASU 2016-15), Statement of Cash Flows - Classification of Certain Cash Receipts and Cash Payments, which clarifies existing guidance related to accounting for cash receipts and cash payments and classification of statement of cash flow. This guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017, and early adoption is permitted. The Company is evaluating the impact the adoption of ASU 2016-15 will have on its consolidated financial statements.

3. Fair Value Measurements

The Company measures certain financial assets and liabilities at fair value on a recurring basis, including cash equivalents. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or a liability. A three-tier fair value hierarchy is established as a basis for considering such assumptions and for inputs used in the valuation methodologies in measuring fair value:

Level 1 — Observable inputs such as quoted prices (unadjusted) for identical assets or liabilities in active markets.

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

Level 3 — Unobservable inputs that are supported by little or no market activities, which would require the Company to develop its own assumptions.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The carrying amounts of certain financial instruments, such as cash equivalents, accounts receivable, accounts payable and accrued liabilities, approximate fair value due to their relatively short maturities, and low market interest rates, if applicable.

Based on the fair value hierarchy, the Company classifies its cash equivalents within Level 1. This is because the Company values its cash equivalents using quoted market prices. The Company's Level 1 securities consist of \$428.7 million and \$307.3 million in money market funds included in cash and cash equivalents at March 31, 2017 and December 31, 2016, respectively.

4. Composition of Certain Balance Sheet Items

Property and Equipment, net

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

| | <u>March 31, 2017</u> | <u>December 31, 2016</u> |
|---|-----------------------|--------------------------|
| Machinery and equipment | \$ 8,802 | \$ 9,629 |
| Leasehold improvements | 580 | 2,769 |
| Purchased computer software | 531 | 363 |
| Build-to-suit property | 51,760 | 51,359 |
| | <u>61,673</u> | <u>64,120</u> |
| Less: accumulated depreciation and amortization | (5,589) | (7,668) |
| Property and equipment, net | <u>\$ 56,084</u> | <u>\$ 56,452</u> |

Depreciation expense was \$0.8 million and \$0.3 million for the three months ended March 31, 2017 and 2016 , respectively.

Other Current Liabilities

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

| | <u>March 31, 2017</u> | <u>December 31, 2016</u> |
|------------------------------|-----------------------|--------------------------|
| Payroll and related expenses | \$ 3,835 | \$ 6,629 |
| Professional services | 411 | 435 |
| Deferred rent | 49 | 363 |
| Other | 1,036 | 1,128 |
| Other current liabilities | <u>\$ 5,331</u> | <u>\$ 8,555</u> |

5. Net Income (loss) Per Ordinary Share

Basic net income (loss) per ordinary share is calculated by dividing net income (loss) by the weighted-average number of ordinary shares outstanding during the period. Shares used in diluted net income per ordinary share would include the dilutive effect of ordinary shares potentially issuable upon the exercise of stock options outstanding. However, potentially issuable ordinary shares are not used in computing diluted net loss per ordinary share as their effect would be anti-dilutive due to the loss recorded during the three months ended March 31, 2017 and 2016 , and therefore diluted net loss per share is equal to basic net loss per share.

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

| | <u>Three Months Ended March 31,</u> | |
|--|---|--------------------|
| | <u>2017</u> | <u>2016</u> |
| Numerator: | | |
| Net loss | <u>\$ (35,384)</u> | <u>\$ (27,521)</u> |
| Denominator: | | |
| Weighted-average ordinary shares outstanding | <u>35,758</u> | <u>34,026</u> |
| Net loss per share: | | |
| Basic and diluted net loss per share | <u>\$ (0.99)</u> | <u>\$ (0.81)</u> |

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

| | <u>Three Months Ended March 31,</u> | |
|---|---|--------------|
| | <u>2017</u> | <u>2016</u> |
| Stock options to purchase ordinary shares | <u>4,395</u> | <u>4,097</u> |

6. Build-to-Suit Lease

In March 2016 , the Company entered into a noncancelable operating sublease (the "Lease") to lease 128,751 square feet of office and laboratory space in South San Francisco, California (the "Current SSF Facility"). Subsequently, in April 2016, the Company took possession of the Current SSF Facility. The Lease includes a free rent period and escalating rent payments and has a term that expires on December 31, 2023 , unless terminated earlier. The Company's obligation to pay rent commenced on August 1, 2016. The Company is obligated to make lease payments totaling approximately \$39.2 million over the lease term. The Lease further provides that the Company is obligated to pay to the sublandlord and master landlord certain costs, including taxes and operating expenses. Expected future lease payments under the build-to-suit lease as of Mach 31, 2017 are included in Note 7, "Commitments and Contingencies."

In connection with this Lease, the Company received a tenant improvement allowance of \$14.2 million from the sublandlord and the master landlord, for the costs associated with the design, development and construction of tenant improvements for the Current SSF Facility. The Company is obligated to fund all costs incurred in excess of the tenant improvement allowance. The scope of the tenant improvements did not qualify as “normal tenant improvements” under the lease accounting guidance. Accordingly, for accounting purposes, the Company is the deemed owner of the building during the construction period and the Company capitalized \$36.5 million within property and equipment, net, including \$1.2 million for capitalized interest and recognized a corresponding build-to-suit obligation in other non-current liabilities in the Condensed Consolidated Balance Sheets as of March 31, 2017 . The Company has also recognized structural and non-structural tenant improvements totaling \$15.3 million as of March 31, 2017 as an addition to the build-to-suit lease property for amounts incurred by the Company during the construction period, of which \$14.2 million were reimbursed by the landlord during the year ended December 31, 2016 through the tenant improvement allowance. The Company increased its financing obligation for the additional building costs reimbursements received from the landlord during the construction period. In addition, for the three months ended March 31, 2017 , the Company recorded rent expense associated with the ground lease of \$0.1 million in the Condensed Consolidated Statements of Operations. Total interest, which represents the cost of financing obligation under the Lease agreement, was \$0.9 million for the three months ended March 31, 2017 , of which \$0.9 million was recognized within the Condensed Consolidated Statement of Operations.

During the fourth quarter of 2016, construction on the build-to-suit lease property was substantially completed and the build-to-suit lease property was placed in service. As such, the Company evaluated the Lease to determine whether it had met the requirements for sale-leaseback accounting, including evaluating whether all risks of ownership have been transferred back to the landlord, as evidenced by a lack of continuing involvement in the build-to-suit lease property. The Company determined that the construction project did not qualify for sale-leaseback accounting and will instead be accounted for as a financing lease, given the Company’s expected continuing involvement after the conclusion of the construction period. The build-to-suit lease property remains on the Company’s Condensed Consolidated Balance Sheets as of March 31, 2017 at its historical cost of \$51.8 million and is being depreciated over its estimated useful life. As of March 31, 2017 , the total amount of the build-to-suit lease obligation was \$51.7 million , which is classified as a non-current liability on the Condensed Consolidated Balance Sheets. The Company expects to derecognize the build-to-suit lease property and financing lease obligation at the end of the lease term.

The Company obtained a standby letter of credit in April 2016 in the initial amount of \$4.1 million , which may be drawn down by the sublandlord in the event the Company fails to fully and faithfully perform all of its obligations under the Lease and to compensate the sublandlord for all losses and damages the sublandlord may suffer as a result of the occurrence of any default on the part of Company not cured within the applicable cure period. This standby letter of credit is collateralized by a certificate of deposit of the same amount which is classified as restricted cash. As of March 31, 2017 , none of the standby letter of credit amount has been used.

7. Commitments and Contingencies

Lease Commitments

The Company recognizes rent expense for its operating leases on a straight-line basis over the noncancelable lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contain escalation clauses, rent abatements, and/or concessions, such as rent holidays and landlord or tenant incentives or allowances, the Company applies them in the determination of straight-line rent expense over the lease term. The Company records the tenant improvement allowance for operating leases as deferred rent and associated expenditures as leasehold improvements that are being amortized over the shorter of their estimated useful life or the term of the lease. Rent expense was \$0.3 million and \$0.5 million for the three months ended March 31, 2017 and 2016 , respectively.

Dublin

In August 2015 , the Company entered into an agreement to lease 6,258 square feet of office space in Dublin, Ireland. This lease has a term of 10 years from commencement and provides for an option to terminate the lease at the end of the fifth year of the term. It is also subject to a rent review every five years. As a result of this noncancelable operating lease, the Company is obligated to make lease payments totaling approximately €2.0 million , or \$2.2 million as converted using exchange rate as of March 31, 2017 , over the term of the lease, assuming current lease payments. Of this obligation, approximately \$1.9 million remains outstanding as of March 31, 2017 .

Future minimum payments under the above-described noncancelable operating lease as of March 31, 2017 , are as follows (in thousands):

| Year Ended December 31, | Operating Lease |
|--------------------------------|------------------------|
| 2017 (9 months) | \$ 166 |
| 2018 | 221 |
| 2019 | 221 |
| 2020 | 221 |
| 2021 | 221 |
| Thereafter | 811 |
| Total | \$ 1,861 |

Former SSF Facility

The Company has previously leased 50,400 square feet of office and research and development space located South San Francisco, California (the "Former SSF Facility"), which had an annual rent payment of approximately \$2.1 million. In addition, the Company had subleased a portion of its Former SSF Facility with a third party.

In January 2017, in accordance with an Assignment Agreement, the Company assigned to Merck Sharp & Dohme Corp. ("Merck") the Company's lease on the Former SSF Facility. As a result of the assignment, the Company recognized a gain of approximately \$2.4 million on early lease retirement resulting from the recognition of the remaining deferred rent liability. The Company's operating lease commitments was reduced by approximately \$8.4 million over the original lease term and the Company will not receive the future minimum payments from its Sublease of \$0.3 million as a result of the Assignment.

Under the Assignment Agreement, Merck paid the Company the amount of \$500,000 as consideration for the assignment of the Company's interest as tenant in the lease and the amount of \$100,000 as consideration for the Company's transfer to Merck of certain furniture, fixtures and equipment located at the Former SSF Facility. The Company vacated the Former SSF Facility in December 2016 when it moved to the Current SSF Facility.

Current SSF Facility

In March 2016, the Company entered into a noncancelable operating sublease of the Current SSF Facility which expires in December 31, 2023. The Company is considered the "accounting owner" of the Current SSF Facility as a build-to-suit property and has recorded a build-to-suit lease obligation on its condensed consolidated balance sheet. Additional information regarding the build-to-suit lease is included in Note 6. "Build-To-Suit Lease." Future minimum payments under build-to-suit lease obligation as of March 31, 2017, are as follows (in thousands):

| Year Ended December 31, | Expected Cash Payments Under Build-To-Suit Lease Obligation |
|--------------------------------|--|
| 2017 (9 months) | \$ 2,645 |
| 2018 | 4,915 |
| 2019 | 5,803 |
| 2020 | 5,979 |
| 2021 | 6,165 |
| Thereafter | 12,885 |
| Total | \$ 38,392 |

Indemnity Obligations

The Company has entered into indemnification agreements with its current, and former, directors and officers and certain key employees. These agreements contain provisions that may require the Company, among other things, to indemnify such persons against certain liabilities that may arise because of their status or service and advance their expenses incurred as a result of any indemnifiable proceedings brought against them. The obligations of the Company pursuant to the indemnification agreements continue during such time as the indemnified person serves the Company and continues thereafter until such time as a claim can be brought. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited; however, the Company has a director and officer liability insurance policy that limits its exposure and enables the Company to recover a portion of any future amounts paid. As a result of its insurance policy coverage, the Company

believes the estimated fair value of these indemnification agreements is minimal. Accordingly, the Company had no liabilities recorded for these agreements as of March 31, 2017 and 2016 .

Other Commitments

In the normal course of business, the Company enters into various firm purchase commitments primarily related to research and development activities. As of March 31, 2017 , the Company had non-cancelable purchase commitments to suppliers for \$20.8 million of which \$11.5 million is included in accrued current liabilities, and contractual obligations under license agreements of \$1.6 million of which \$0.2 million is included in accrued current liabilities. The following is a summary of the Company's non-cancelable purchase commitments and contractual obligations as of March 31, 2017 (in thousands):

| | Total | 2017 | 2018 | 2019 | 2020 | 2021 | Thereafter |
|---|------------------|------------------|---------------|---------------|---------------|---------------|-------------------|
| Purchase Obligations ⁽¹⁾ | \$ 20,757 | \$ 20,554 | \$ 112 | \$ 59 | \$ 32 | \$ — | \$ — |
| Contractual obligations under license agreements ⁽²⁾ | 1,605 | 285 | 130 | 130 | 100 | 100 | 860 |
| Total | \$ 22,362 | \$ 20,839 | \$ 242 | \$ 189 | \$ 132 | \$ 100 | \$ 860 |

⁽¹⁾ Excludes binding minimum purchase commitments under the Letter Agreement with Boehringer Ingelheim Biopharmaceuticals GmbH entered into on April 5, 2017, effective March 31, 2017.

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

8. Roche License Agreement

Overview

In December 2013 , the Company entered into the License Agreement with Roche to develop and commercialize certain antibodies that target α -synuclein, including PRX002. The License Agreement was evaluated under ASC 605-25, "Multiple Element Arrangements". Under this License agreement, the Company recognizes research reimbursement as collaboration revenue as earned. The Company recognized \$0.3 million as collaboration revenue for research reimbursement from Roche for the three months ended March 31, 2017 , as compared to \$0.3 million for the three months ended March 31, 2016 . Cost sharing payments to Roche are recorded as R&D expenses. The Company recognized \$1.3 million in R&D expenses for payments made to Roche during the three months ended March 31, 2017 , as compared to \$0.5 million for the three months ended March 31, 2016 . Reimbursement for development costs from Roche during the three months ended March 31, 2017 was \$0.8 million , as compared to \$1.2 million for the three months ended March 31, 2016 ,which was recognized as an offset to R&D expenses.

Under the License Agreement, the Company is eligible to receive milestone payments upon the achievement of development, regulatory and various first commercial sales milestones. Milestone payments are evaluated under ASU No. 2010-17, "Milestone Method of Revenue Recognition". Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company recognizes payments related to the achievement of this milestone when the milestone is achieved.

The clinical and regulatory milestones under the License Agreement after the point at which the Company could opt-out are not considered to be substantive due to the fact that active participation in the development activities that generate the milestones is not required by the License Agreement, and the Company can opt-out of these activities. There are no refund or claw-back provisions and the milestones are uncertain of occurrence even after the Company has opted out. Based on this determination, these milestones will be recognized similar to the commercial milestone, which will be accounted for as contingent revenue payments with revenue recognized upon achievement of the milestone assuming all revenue recognition criteria are met. The Company did not achieve any of the clinical and regulatory milestones under the License Agreement during the three months ended March 31, 2017 and 2016 .

9. Shareholders' Equity

Ordinary Shares

As of March 31, 2017, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of \$0.01 per ordinary share and 37,957,649 ordinary shares issued and outstanding. Each ordinary share is entitled to one vote and, on a pro rata basis, to dividends when declared and the remaining assets of the Company in the event of a winding up.

Euro Deferred Shares

As of March 31, 2017, the Company had 10,000 Euro Deferred Shares authorized for issuance with a nominal value of €22 per share. No Euro Deferred Shares are outstanding at March 31, 2017. The rights and restrictions attaching to the Euro Deferred Shares rank *pari passu* with the ordinary shares and are treated as a single class in all respects.

January 2016 Offering

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

March 2017 Offering

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

10. Share-Based Compensation

Amended and Restated 2012 Long Term Incentive Plan ("LTIP")

Employees and consultants of the Company, its subsidiaries and affiliates, as well as members of the Board, are eligible to receive equity awards under the LTIP. The LTIP provides for the grant of stock options, including incentive stock options and nonqualified stock options, stock appreciation rights ("SARS"), restricted shares, restricted share units ("RSUs"), cash or stock-based performance awards and other share-based awards to eligible individuals. Options under the LTIP may be granted for periods up to ten years. All options issued to date have had a ten year life.

The Company granted 854,800 and 1,008,475 share options during the three months ended March 31, 2017 and 2016, respectively, under the LTIP. The Company's option awards generally vest over four years. The aggregate number of ordinary shares authorized for issuance under the LTIP is 7,400,000 ordinary shares, and as of March 31, 2017, 1,448,871 ordinary shares remain available for grant and options to purchase 4,394,741 ordinary shares granted from the LTIP were outstanding with a weighted-average exercise price of approximately \$33.21 per share.

Share-based Compensation Expense

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

As share-based compensation expense recognized in the Condensed Consolidated Financial Statements is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. Forfeitures are estimated at the time of grant and revised,

if necessary, in subsequent periods if actual forfeitures differ from estimates. Forfeitures were estimated based on estimated future turnover and historical experience.

Share-based compensation expense will continue to have an adverse impact on the Company's results of operations, although it will have no impact on its overall financial position. The amount of unearned share-based compensation currently estimated to be expensed from now through the year 2020 related to unvested share-based payment awards at March 31, 2017 is \$66.0 million. The weighted-average period over which the unearned share-based compensation is expected to be recognized is 2.96 years. If there are any modifications or cancellations of the underlying unvested securities, the Company may be required to accelerate and/or increase any remaining unearned share-based compensation expense. Future share-based compensation expense and unearned share-based compensation will increase to the extent that the Company grants additional equity awards.

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

| | Three Months Ended March 31, | |
|--|---|-----------------|
| | 2017 | 2016 |
| Research and development | \$ 2,308 | \$ 1,419 |
| General and administrative | 3,294 | 2,305 |
| Total share-based compensation expense | <u>\$ 5,602</u> | <u>\$ 3,724</u> |

For the three months ended March 31, 2017 and 2016, the Company recognized tax benefit from share-based awards of \$0.9 million and \$0.6 million, respectively.

The fair value of the options granted to employees and non-employee directors during the three months ended March 31, 2017 and 2016 was estimated as of the grant date using the Black-Scholes option-pricing model assuming the weighted-average assumptions listed in the following table:

| | Three Months Ended March 31, | |
|--|---|-------------|
| | 2017 | 2016 |
| Expected volatility | 73.1% | 74.8% |
| Risk-free interest rate | 2.1% | 1.4% |
| Expected dividend yield | —% | —% |
| Expected life (in years) | 6.0 | 6.0 |
| Weighted average grant date fair value | \$35.30 | \$22.94 |

The fair value of employee stock options is being amortized on a straight-line basis over the requisite service period for each award. Each of the inputs discussed above is subjective and generally requires significant management judgment to determine.

The following table summarizes the Company's stock option activity during the three months ended March 31, 2017:

| | Options | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (years) | Aggregate Intrinsic Value (in thousands) |
|---|-----------|--|---|---|
| Outstanding at December 31, 2016 | 4,064,207 | \$ 27.19 | 6.79 | \$ 92,640 |
| Granted | 854,800 | 54.15 | | |
| Exercised | (505,533) | 20.21 | | |
| Canceled | (18,733) | 35.14 | | |
| Outstanding at March 31, 2017 | 4,394,741 | \$ 33.21 | 7.72 | \$ 100,435 |
| Vested and expected to vest at March 31, 2017 | 4,286,605 | \$ 32.85 | 7.68 | \$ 99,472 |
| Vested at March 31, 2017 | 1,964,108 | \$ 19.27 | 6.02 | \$ 72,086 |

During the three months ended March 31, 2017 and 2016, the total intrinsic value of options exercised was \$17.0 million and \$0.3 million, determined as of the date of exercise.

11. Income Taxes

The major taxing jurisdictions for the Company are Ireland and the U.S. The Company recorded an income tax benefit of \$1.7 million for three months ended March 31, 2017 as compared to an income tax expense of \$181,000 for the three months ended March 31, 2016. The provision for income taxes differs from the statutory tax rate of 12.5% applicable to Ireland primarily due to Irish net operating losses for which a tax provision benefit is not recognized, U.S. income taxed at different rates, and excess tax benefits of stock options. The income tax provision reflects the estimate of the effective tax rate expected to be applicable for the full year and the Company re-evaluates this estimate each quarter based on its forecasted tax expense for the full year. Jurisdictions with a projected loss for the year where no tax benefit can be recognized are excluded from the estimated annual effective tax rate.

The Company adopted this ASU on January 1, 2017. Pursuant to the adoption of ASU 2016-09, tax attributes previously tracked off balance sheet have been recorded as deferred tax assets, offset by a valuation allowance. In addition, the Company has reversed its non-current tax liability of \$98,000, with the offsetting entry recorded to retained earnings pursuant to the adoption of this ASU. Further, the year-to-date excess benefits have been recorded as a discrete benefit to the tax provision. For the three months ended March 31, 2017, the Company recorded excess tax benefits of \$1.9 million as part of its income tax provision in the Condensed Consolidated Statements of Operations. The Company's income tax expense will continue to be impacted by fluctuations in stock price between the grant dates and the exercise dates of its option awards.

The Company's deferred tax assets are composed primarily of its Irish subsidiaries' net operating loss carryovers, state net operating loss carryforwards available to reduce future taxable income of the Company's U.S. subsidiary, federal and California research and development credit carryforward, shared-based compensation and other temporary differences. The Company maintains a valuation allowance against certain U.S. federal and state and Irish deferred tax assets. Each reporting period, the Company evaluates the need for a valuation allowance on its deferred tax assets by jurisdiction.

No provision for income tax in Ireland has been recognized on undistributed earnings of the Company's U.S. subsidiary because the Company considers such earnings to be indefinitely reinvested.

12. Related Parties

Carol D. Karp commenced employment with the Company as its Chief Regulatory Officer on December 14, 2016. Prior to that, Ms. Karp provided consulting services to the Company under a written Consulting Agreement which was effective April 1, 2016. That Consulting Agreement terminated as of December 13, 2016, before Ms. Karp joined the Company. There were no consulting fees paid to Ms. Karp for the three months ended March 31, 2017 and 2016.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Quarterly Report on Form 10-Q, including this Management's Discussion and Analysis of Financial Condition and Results of Operations, contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. These statements relate to, among other things, our strategy; the possible clinical benefits of NEOD001, PRX002 and PRX003; a contemplated Phase 2 study for PRX002 and a possible Phase 2 study for PRX003; the contemplated clinical development of PRX004; research and development ("R&D") and general and administrative ("G&A") expenses in 2017; and the sufficiency of our cash and cash equivalents and our future capital requirements. Forward-looking statements may include words such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would," and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. Forward-looking statements are subject to risks and uncertainties, and actual events or results may differ materially. Factors that could cause our actual results to differ materially include, but are not limited to, the risks and uncertainties listed below as well as those discussed under "Risk Factors" in this Form 10-Q.

- our ability to obtain additional financing in future offerings;
- our operating losses;
- our ability to successfully complete research and development of our drug candidates;
- our ability to develop, manufacture and commercialize products;
- our collaboration with Roche pursuant to the License Agreement;
- our ability to protect our patents and other intellectual property;
- our ability to hire and retain key employees;
- tax treatment of our separation from Elan and subsequent distribution of our ordinary shares;
- our ability to maintain financial flexibility and sufficient cash, cash equivalents, and investments and other assets capable of being monetized to meet our liquidity requirements;
- potential disruptions in the U.S. and global capital and credit markets;
- government regulation of our industry;
- the volatility of our ordinary share price;
- business disruptions; and
- the other risks and uncertainties described in the "Risk Factors" section of this Form 10-Q.

We undertake no obligation to revise or update any forward-looking statements to reflect any event or circumstance that arises after the date of this report.

This discussion should be read in conjunction with the Condensed Consolidated Financial Statements and Notes presented in this Quarterly Report on Form 10-Q and the Condensed Consolidated Financial Statements and Notes contained in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on February 27, 2017 (the "2016 Form 10-K").

Overview

Prothena Corporation plc is a global, late-stage clinical biotechnology company establishing fully-integrated research, development and commercial capabilities. Fueled by its deep scientific understanding built over decades of research in protein misfolding and cell adhesion - the root causes of many serious or currently untreatable amyloid and inflammatory diseases - Prothena seeks to fundamentally change the course of progressive diseases associated with this biology.

Our pipeline of antibody-based product candidates target a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002/RG7935), inflammatory diseases including psoriasis and psoriatic arthritis (PRX003) and ATTR amyloidosis (PRX004). The Company continues discovery of additional novel therapeutic candidates where our deep scientific understanding of disease pathology can be leveraged.

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

shareholders, 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.

Recent Developments

NEOD001 for the Potential Treatment of AL Amyloidosis

NEOD001 is an investigational monoclonal antibody that targets circulating misfolded soluble light chain and deposited insoluble amyloid for the potential treatment of AL amyloidosis.

In March 2017, we completed enrollment in the Phase 2b PRONTO study evaluating NEOD001 in previously treated patients with AL amyloidosis and persistent cardiac dysfunction. Based on the high level of patient interest, the study is over-enrolled with 129 patients randomized. The PRONTO study, a global, double-blind, placebo-controlled, registration-directed study with a primary endpoint of best response over 12 months of the cardiac functional biomarker NT-proBNP, defined by the consensus criteria of NT-proBNP change. Secondary endpoints include biomarker, quality of life and functional measures.

By mid-May we expect to complete enrollment in our Phase 3 VITAL Amyloidosis Study evaluating NEOD001 in newly diagnosed, treatment naïve patients with AL amyloidosis and cardiac dysfunction. The original target enrollment of 236 patients has been met, and patients who are currently in screening have an opportunity to complete this process and based on their eligibility will be randomized into the study. The study will therefore be over-enrolled, with the last patient randomized in the coming weeks. The VITAL study is a global, double-blind, placebo-controlled, registration study with an event-based composite primary endpoint of all-cause mortality or cardiac hospitalizations as qualifying events. Secondary endpoints include biomarker, quality of life and functional measures.

PRX002 /RG7935 for the Potential Treatment of Parkinson's Disease and other synucleinopathies

PRX002/RG7935 is an investigational monoclonal antibody targeting alpha-synuclein designed to slow the progressive neurodegeneration associated with synuclein misfolding and/or the cell-to-cell transmission of the pathogenic forms of synuclein in Parkinson's disease and other synucleinopathies. PRX002, also known as RG7935, is the focus of a worldwide collaboration between Prothena and Roche.

In April 2017, at a late-breaking therapeutic strategies session at the 13th International Conference on Alzheimer's and Parkinson's Diseases (AD/PD), Dr. Joseph Jankovic of Baylor College of Medicine presented clinical data from the 80-patient Phase 1b multiple ascending dose study of PRX002/RG7935 in patients with Parkinson's disease. All doses levels of PRX002/RG7935 had an acceptable safety and tolerability profile, meeting the primary objective of the study. Central nervous system (CNS) penetration was demonstrated by a dose-dependent increase in PRX002/RG7935 levels in the cerebrospinal fluid ("CSF") and mean concentration of PRX002/RG7935 in CSF of 0.3 percent relative to serum across all dose levels. In addition, rapid, dose- and time-dependent mean reduction of free serum alpha-synuclein levels to 97 percent ($p < 0.0001$) after a single dose further validated target engagement. These data support advancing PRX002/RG7935 into a Phase 2 study.

March 2017 Offering

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

Critical Accounting Policies and Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our condensed consolidated financial statements, which have been prepared in accordance with the accounting principles generally accepted in the U.S. ("GAAP"). The preparation of these condensed consolidated financial statements requires us to make estimates and assumptions for the reported amounts of assets, liabilities, revenues, expenses and related disclosures.

There were no significant changes to our critical accounting policies and estimates during the three months ended March 31, 2017 from the critical accounting policies and estimates disclosed in Management's Discussion and Analysis of Financial Condition and Results of Operations in our 2016 Form 10-K.

Recent Accounting Pronouncements

Except as described in Note 2 to the Condensed Consolidated Financial Statements under the heading "Recent Accounting Pronouncements", there have been no new accounting pronouncements or changes to accounting pronouncements during the three months ended March 31, 2017, as compared to the recent accounting pronouncements described in our 2016 Form 10-K, that are of significance or potential significance to us.

Results of Operations

Comparison of Three Months Ended March 31, 2017 and 2016

Revenue

| | Three Months Ended March 31, | | Percentage Change |
|-------------------------------|---|-------------|------------------------------|
| | 2017 | 2016 | |
| (Dollars in thousands) | | | |
| Collaboration revenue | \$ 259 | \$ 265 | (2)% |
| Total revenue | \$ 259 | \$ 265 | (2)% |

Total revenue was \$0.3 million and \$0.3 million for the three months ended March 31, 2017 and 2016, respectively.

Collaboration revenue includes reimbursements under our License Agreement with Roche, which became effective January 2014. See Note 8 to the Condensed Consolidated Financial Statements regarding "Roche License Agreement" for more information.

Collaboration revenue for the three months ended March 31, 2017 and 2016 consisted of reimbursement for research services of \$0.3 million and \$0.3 million, respectively.

Operating Expenses

| | Three Months Ended March 31, | | Percentage Change |
|-------------------------------|---|-------------|------------------------------|
| | 2017 | 2016 | |
| (Dollars in thousands) | | | |
| Research and development | \$ 25,698 | \$ 20,493 | 25% |
| General and administrative | 10,832 | 7,182 | 51% |
| Total operating expenses | \$ 36,530 | \$ 27,675 | 32% |

Total operating expenses consist of research and development ("R&D") expenses and general and administrative ("G&A") expenses. Our operating expenses for the three months ended March 31, 2017 and 2016 were \$36.5 million and \$27.7 million, respectively.

Our R&D expenses primarily consist of personnel costs and related expenses, including share-based compensation, external costs associated with preclinical activities and drug development related to our drug programs, including NEOD001, PRX002, PRX003, PRX004 and our discovery programs. Pursuant to our License Agreement with Roche, we make payments to Roche for our share of the development expenses incurred by Roche related to PRX002 program, which is included in our R&D expense. We also recorded reimbursements from Roche for development as an offset to R&D expense.

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

Research and Development Expenses

Our R&D expenses increased by \$5.2 million , or 25% , for the three months ended March 31, 2017 compared to the same period in the prior year. The increase for the three months ended March 31, 2017 compared to the same period in the prior year was primarily due to higher personnel costs (including share-based compensation expenses) and an increase in external expenses related to product manufacturing related to NEOD001 and to a lesser extent PRX003 and higher clinical trial costs associated primarily with the NEOD001 program.

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

The following table sets forth the R&D expenses for our major programs (specifically, any program with successful first dosing in a Phase 1 clinical trial, which were NEOD001, PRX002 and PRX003) and other R&D expenses for the three months ended March 31, 2017 and 2016 , and the cumulative amounts to date (in thousands):

| | Three Months Ended March 31, | | Cumulative to Date |
|--------------------------|---------------------------------|------------------|-----------------------|
| | 2017 | 2016 | |
| NEOD001 ⁽¹⁾ | \$ 18,220 | \$ 13,236 | \$ 168,936 |
| PRX002 ⁽²⁾ | 1,978 | 1,395 | 46,314 |
| PRX003 ⁽³⁾ | 2,615 | 2,430 | 52,055 |
| Other R&D ⁽⁴⁾ | 2,885 | 3,432 | |
| | <u>\$ 25,698</u> | <u>\$ 20,493</u> | |

- (1) Cumulative R&D costs to date for NEOD001 include the costs incurred from the date when the program has been separately tracked in preclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount.
- (2) Cumulative R&D costs to date for PRX002 and related antibodies include the costs incurred from the date when the program has been separately tracked in preclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount. PRX002 cost include payments to Roche for our share of the development expenses incurred by Roche related to PRX002 programs and is net of reimbursements from Roche for development and supply services recorded as an offset to R&D expense. For the three months ended March 31, 2017 and 2016 , \$0.8 million and \$1.2 million , respectively, were recorded as an offset to R&D expenses.
- (3) Cumulative R&D costs to date for PRX003 include the costs incurred from the date when the program has been separately tracked in preclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount.
- (4) Other R&D is comprised of preclinical development and discovery programs that have not progressed to first patient dosing in a Phase 1 clinical trial.

We expect our R&D expenses to increase in 2017 primarily due to increased spending for the NEOD001 program in connection with the ongoing Phase 3 VITAL clinical study and the Phase 2b PRONTO clinical study.

General and Administrative Expenses

Our G&A expenses increased by \$3.7 million , or 51% , for the three months ended March 31, 2017 , compared to the same period in the prior year, primarily due to higher personnel costs, including share-based compensation expenses and higher consulting and other expenses partially offset by a gain recognized from the assignment of our former SSF Facility lease.

We expect our G&A expenses to continue to increase in 2017 in support of our anticipated R&D growth and due to increases in personnel, legal and expenses associated with commercial planning activities.

Other Income (Expense)

| | Three Months Ended March 31, | | Percentage Change |
|--------------------------------|---------------------------------|--------|----------------------|
| | 2017 | 2016 | |
| (Dollars in thousands) | | | |
| Interest income (expense), net | \$ (364) | \$ 277 | (231)% |
| Other expense, net | (410) | (207) | 98 % |
| Total Other Income (Expense) | \$ (774) | \$ 70 | (1,206)% |

Interest income, net decreased by \$641,000 , or 231% , for the three months ended March 31, 2017 , compared to the same period in the prior year, primarily due to higher interest expense associated with our built-to-suit property offset in part by higher interest income associated with higher balances in our cash and money market accounts. Other expense, net for the three months ended March 31, 2017 and 2016 were primarily due to foreign exchange losses from transactions with vendors denominated in Euros.

Provision for (benefit from) Income Taxes

| | Three Months Ended March 31, | | Percentage Change |
|---|---------------------------------|--------|----------------------|
| | 2017 | 2016 | |
| (Dollars in thousands) | | | |
| Provision for (benefit from) income taxes | \$ (1,661) | \$ 181 | (1,018)% |

The tax provisions (benefits) were \$(1.7) million and \$0.2 million for the three months ended March 31, 2017 and 2016 , respectively. The tax provisions for all periods presented reflect U.S. federal taxes associated with recurring profits attributable to intercompany services that our U.S. subsidiary performs for the Company. No tax benefit has been recorded related to tax losses recognized in Ireland and any deferred tax assets for those losses are offset by a valuation allowance.

For the three months ended March 31, 2017 , we recorded excess tax benefits of \$1.9 million as part of our income tax provision related to the adoption of ASU 2016-09, Improvements to Employee Share-Based Payment Accounting. Our income tax expense will continue to be impacted by fluctuations in stock price between the grant dates and the exercise dates of our option awards.

The provision for income taxes decreased by \$1.8 million for the three months ended March 31, 2017 , compared to the same period in the prior year, due to the excess tax benefit recorded in the three months ended March 31, 2017 offset by higher profits generated from our U.S. subsidiary.

Liquidity and Capital Resources

Overview

| | March 31, | December 31, |
|----------------------------|------------|--------------|
| | 2017 | 2016 |
| Working capital | \$ 480,524 | \$ 350,287 |
| Cash and cash equivalents | 506,550 | 386,923 |
| Total assets | 581,950 | 459,976 |
| Total liabilities | 85,702 | 94,573 |
| Total shareholders' equity | 496,248 | 365,403 |

Working capital was \$480.5 million as of March 31, 2017 , an increase of \$130.2 million from working capital of \$350.3 million as of December 31, 2016 . This increase in working capital during the three months ended March 31, 2017 was principally attributable to a higher net cash and cash equivalents balance resulting from the net proceeds of \$150.3 million from our public offering in March 2017, partially offset by use of \$36.5 million for operating expenses (adjusted to exclude non-cash charges).

As of March 31, 2017, we had \$506.6 million in cash and cash equivalents. Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in the future in order to continue the research and development of our drug candidates and preparation for commercialization. As of March 31, 2017, \$61.3 million of our outstanding cash and cash equivalents related to U.S. operations that are considered permanently reinvested. We do not intend to repatriate these funds. However, if these funds were repatriated back to Ireland we would incur a withholding tax from the dividend distribution.

We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development of our product candidates. Our future capital requirements will depend on numerous factors, including, without limitation, the timing of initiation, progress, results and costs of our clinical trials; the results of our research and preclinical studies; the costs of clinical manufacturing and of establishing commercial manufacturing arrangements; the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; the costs and timing of capital asset purchases; our ability to establish research collaborations, strategic collaborations, licensing or other arrangements; the costs to satisfy our obligations under current and potential future collaborations; and the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates. Pursuant to the License Agreement with Roche, in the U.S., we and Roche share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to us, for PRX002 in the Parkinson's disease indication, as well as any other Licensed Products and/or indications for which we opt in to co-develop and co-fund. In order to develop and obtain regulatory approval for our potential products we will need to raise substantial additional funds. We expect to raise any such additional funds through public or private equity or debt financings, collaborative agreements with corporate partners or other arrangements. We cannot assume that such additional financings will be available on acceptable terms, if at all, and such financings may only be available on terms dilutive to our shareholders.

Cash Flows for the Three Months Ended March 31, 2017 and 2016

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

| | Three Months Ended March 31, | |
|---|---|-------------------|
| | 2017 | 2016 |
| Net cash used in operating activities | \$ (37,842) | \$ (25,057) |
| Net cash used in investing activities | (2,399) | (238) |
| Net cash provided by financing activities | 159,868 | 128,961 |
| Net increase in cash and cash equivalents | <u>\$ 119,627</u> | <u>\$ 103,666</u> |

Cash Used in Operating Activities

Net cash used in operating activities was \$37.8 million for the three months ended March 31, 2017, primarily due to use of \$36.5 million for operating expenses (adjusted to exclude non-cash charges), an increase in prepaid expenses and other current assets and a decrease in accounts payable.

Net cash used in operating activities was \$25.1 million for the three months ended March 31, 2016, primarily due to use of \$27.7 million for operating expenses (adjusted to exclude non-cash charges).

Cash Used in Investing Activities

Net cash used in investing activities was \$2.4 million and \$0.2 million for the three months ended March 31, 2017 and 2016, respectively. Net cash used in investing activities for the three months ended March 31, 2017 primarily related to \$2.5 million of purchases of property and equipment.

Net cash used in investing activities was \$0.2 million for the three months ended March 31, 2016, consisting of purchases of property and equipment.

Cash Provided by Financing Activities

Net cash provided by financing activities was \$159.9 million for the three months ended March 31, 2017, primarily from the net proceeds from our March 2017 public offering and \$9.9 million from issuances of ordinary shares upon exercise of stock options.

Net cash provided by financing activities was \$129.0 million for the three months ended March 31, 2016, primarily from the net proceeds from our January 2016 public offering.

Off-Balance Sheet Arrangements

At March 31, 2017, we were not a party to any off-balance sheet arrangements that have, or are reasonably likely to have, a current or future effect on our financial condition, changes in financial condition, revenue or expenses, results of operations, liquidity, capital expenditures or capital resources.

Contractual Obligations

Our main contractual obligations as of March 31, 2017 consisted of minimum cash payments under a build-to-suit lease obligation of \$38.4 million, operating leases of \$1.9 million, purchase obligations of \$41.7 million (of which \$11.5 million is included in accrued current liabilities) and contractual obligations under license agreements of \$1.6 million (of which \$0.2 million is included in accrued current liabilities). Purchase obligations consist of non-cancelable purchase commitments to suppliers. Operating leases represent our future minimum rental commitments under our non-cancelable operating leases.

In August 2015, we entered into an agreement to lease 6,258 square feet of office space in Dublin, Ireland. This lease has a term of 10 years from commencement and provides for an option to terminate the lease at the end of the fifth year of the term. It is also subject to a rent review every five years. As a result of this noncancelable operating lease, we are obligated to make lease payments totaling approximately €2.0 million, or \$2.2 million as converted using an exchange rate as of March 31, 2017, over the term of the lease, assuming current lease payments. Of this obligation, approximately \$1.9 million remains outstanding as of March 31, 2017.

In March 2016, we entered into a noncancelable operating sublease to lease 128,751 square feet of office and laboratory space in South San Francisco, California. We are obligated to make lease payments totaling approximately \$39.2 million over the lease term. Of this obligation, approximately \$38.4 million remains outstanding as of March 31, 2017.

The following is a summary of our contractual obligations as of March 31, 2017 (in thousands):

| | Total | 2017 | 2018 | 2019 | 2020 | 2021 | Thereafter |
|---|------------------|------------------|------------------|------------------|-----------------|-----------------|------------------|
| Operating leases ⁽¹⁾ | \$ 1,861 | \$ 166 | \$ 221 | \$ 221 | \$ 221 | \$ 221 | \$ 811 |
| Minimum cash payments under build-to-suit lease obligation ⁽¹⁾ | 38,392 | 2,645 | 4,915 | 5,803 | 5,979 | 6,165 | 12,885 |
| Purchase obligations ⁽²⁾ | 41,693 | 20,554 | 6,521 | 14,586 | 32 | — | — |
| Contractual obligations under license agreements ⁽³⁾ | 1,605 | 285 | 130 | 130 | 100 | 100 | 860 |
| Total | \$ 83,551 | \$ 23,650 | \$ 11,787 | \$ 20,740 | \$ 6,332 | \$ 6,486 | \$ 14,556 |

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

⁽²⁾ Includes binding purchase commitments under the Letter Agreement entered into with Boehringer Ingelheim Biopharmaceuticals GmbH on April 5, 2017.

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

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Foreign Currency Risk

Our business is primarily conducted in U.S. dollars except for our agreements with contract manufacturers for clinical supplies which are denominated in Euros. We recorded a loss on foreign currency exchange rate differences of approximately \$410,000 and \$205,000 during the three months ended March 31, 2017 and 2016, respectively. At this time, we do not believe that our foreign exchange risk is material. However, if we continue or increase our business activities that require the use of foreign currencies, we may incur losses if the Euro and other such currencies strengthen against the U.S. dollar.

Interest Rate Risk

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

In the future, we anticipate that our exposure to interest rate risk will primarily be related to our investment portfolio. We intend to invest any surplus funds in accordance with a policy approved by our board of directors which will specify the categories, allocations, and ratings of securities we may consider for investment. The primary objectives of our investment policy are to preserve principal and maintain proper liquidity to meet our operating requirements. Our investment policy also specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment.

Credit Risk

Our receivable from Roche as of March 31, 2017 and December 31, 2016 are amounts due from Roche entities located in the U.S. and Switzerland under the

Financial instruments that potentially subject us to concentration of credit risk consist of cash and cash equivalents and accounts receivable. We place our cash and cash equivalents with high credit quality financial institutions and pursuant to our investment policy, we limit the amount of credit exposure with any one financial institution. Deposits held with banks may exceed the amount of insurance provided on such deposits. We have not experienced any losses on our deposits of cash and cash equivalents.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer ("CEO") and chief financial officer ("CFO") evaluated the effectiveness of our disclosure controls and procedures pursuant to Rule 13a-15 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as of the end of the period covered by this Form 10-Q. Based on this evaluation, our CEO and CFO concluded that, as of March 31, 2017, our disclosure controls and procedures are designed and are effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our CEO and CFO, as appropriate, to allow timely decisions regarding required disclosure.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during our fiscal quarter ended March 31, 2017 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management necessarily applies its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

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

ITEM 1A. RISK FACTORS

Investing in our ordinary shares involves a high degree of risk. Our Annual Report on Form 10-K for 2016 (filed with the SEC on February 27, 2017) includes a detailed discussion of our business and the risks to our business. You should carefully read that Form 10-K. You should also read and carefully consider the risks described below and the other information in this Quarterly Report on Form 10-Q. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and/or 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 \$160.1 million, \$80.6 million and \$7.2 million for the years ended December 31, 2016, 2015 and 2014, respectively. We expect to continue to incur substantial losses for the foreseeable future as we:

- conduct our Phase 3, Phase 2b and open label extension ("OLE") clinical trials for NEOD001, conduct our Phase 1b clinical trial for PRX003 and initiate additional clinical trials for these and other programs;
- develop and commercialize our product candidates, including NEOD001, PRX002/RG7935, PRX003 and PRX004;
- complete preclinical development of other product candidates and initiate clinical trials, if supported by positive preclinical data; and
- pursue our early stage research and seek to identify additional drug candidates and potentially acquire rights from third parties to drug candidates through licenses, acquisitions or other means.

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

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

As of March 31, 2017, we had cash and cash equivalents of \$506.6 million. Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in the future in order to continue the research and development, and eventually commercialization, of our drug candidates. Our future capital requirements will depend on many factors that are currently unknown to us, including, without limitation:

- the timing of initiation, progress, results and costs of our clinical trials, including our Phase 3, Phase 2b and OLE clinical trials for NEOD001, the contemplated Phase 2 clinical trial for PRX002/RG7935, our Phase 1b clinical trial for PRX003 and our contemplated Phase 1 clinical trial for PRX004;
- the timing, initiation, progress, results and costs of these and our other research, development and commercialization activities;
- the results of our research and preclinical studies;
- the costs of clinical manufacturing and of establishing commercial manufacturing arrangements and other commercialization needs;

- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- our ability to establish research collaborations, strategic collaborations, licensing or other arrangements;
- the costs to satisfy our obligations under potential future collaborations; and
- the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates.

We have based our expectations relating to liquidity and capital resources on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development and commercialization of our current product candidates.

In the pharmaceutical industry, the research and development process is lengthy and involves a high degree of risk and uncertainty. This process is conducted in various stages and, during each stage, there is a substantial risk that product candidates in our research and development pipeline will experience difficulties, delays or failures. This makes it difficult to estimate the total costs to complete our ongoing clinical trials and to estimate anticipated completion dates with any degree of accuracy, which raises concerns that attempts to quantify costs and provide estimates of timing may be misleading by implying a greater degree of certainty than actually exists.

In order to develop and obtain regulatory approval for our product candidates we will need to raise substantial additional funds. We expect to raise any such additional funds through public or private equity or debt financings, collaborative agreements with corporate partners or other arrangements. We cannot assure you that additional funds will be available when we need them on terms that are acceptable to us, or at all. General market conditions may make it very difficult for us to seek or obtain financing from the capital markets. If we raise additional funds by issuing equity securities, substantial dilution to existing shareholders would result. If we raise additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business. We may be required to relinquish rights to our technologies or drug candidates or grant licenses on terms that are not favorable to us in order to raise additional funds through strategic alliances, joint ventures or licensing arrangements.

If adequate funds are not available on a timely basis, we may be required to:

- terminate or delay clinical trials or other development for one or more of our drug candidates;
- delay arrangements for activities that may be necessary to commercialize our drug candidates;
- curtail or eliminate our drug research and development programs that are designed to identify new drug candidates; or
- cease operations.

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

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

In June 2016, a majority of voters in the United Kingdom (the "UK") elected in a national referendum to withdraw from the European Union (the "EU"). The referendum was advisory, and the terms of any withdrawal are subject to a negotiation period that could last at least two years after the government of the UK formally initiates a withdrawal process. Nevertheless, the referendum has created significant uncertainty about the future relationship between the UK and the EU, including with respect to the laws and regulations that will apply as the UK determines which EU laws to replace or replicate in the event of a withdrawal. The referendum has also given rise to calls for the governments of other EU member states to consider withdrawal. These developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict access to capital, which could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our ordinary shares.

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

We are highly dependent on key personnel, including Dr. Gene G. Kinney, our President and Chief Executive Officer. There can be no assurance that we will be able to retain Dr. Kinney or any of our key personnel. The loss of the services of Dr. Kinney or any other person on whom we are highly dependent might impede the achievement of our research, development and commercial objectives.

Recruiting and retaining qualified scientific and other personnel are critical to our growth and future success. Competition for qualified personnel in our industry is intense. We may not be able to attract and retain these personnel on acceptable terms given that competition. Failure to recruit and retain qualified personnel could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

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

Prior to our separation from Elan on December 20, 2012, our financial results previously were included within the condensed consolidated results of Elan. Therefore, certain historical financial information we have included or incorporated by reference in this report, to the extent it includes information for periods prior to our separation from Elan, might not reflect what our financial condition, results of operations and cash flows would have been had we been an independent, publicly traded company during those 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 our separation from Elan, the cost of capital for our business has been and may continue to be higher than Elan's cost of capital prior to the separation because Elan's cost of debt was lower than ours has been and will likely continue to be; and
- our historical financial information does not reflect changes that we have incurred as a result of the separation from Elan, including changes in the cost structure, personnel needs, financing and operations of the contributed business as a result of the separation from Elan and from reduced economies of scale.

We are also responsible for the additional costs associated with being an independent, public company, including costs related to corporate governance and compliance with the rules of The Nasdaq Stock Market ("Nasdaq") and the SEC. In addition, we incur costs and expenses, including professional fees, to comply with Irish corporate and tax laws and financial reporting requirements and costs and expenses incurred in connection with holding the meetings of our board of directors in Ireland. Prior to our separation from Elan, our business was operated by Elan as part of its broader corporate organization, rather than as an independent company. Elan or one of its affiliates performed various corporate functions for us, including, but 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 for periods prior to our separation from Elan 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, certain financial information in this report might not be indicative of our future performance as an independent company.

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

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

sale of all of its shares of Prothena, Perrigo may be less willing to collaborate with us in connection with the agreements to which we and Elan are a party and other matters.

We may be adversely affected by earthquakes or other natural disasters

We have a key facility and operations in the San Francisco Bay Area of Northern California, which in the past has experienced severe earthquakes. If an earthquake, other natural disaster or similar event were to occur and prevent us from using all or a significant portion of those operations or local critical infrastructure, or that otherwise disrupts our operations, it could be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We have disaster recovery and business continuity plans, but they may prove to be inadequate in the event of a natural disaster or similar event. We may incur substantial expenses if our disaster recovery and business continuity plans prove to be inadequate. We do not carry earthquake insurance. Furthermore, third parties upon which we are materially dependent upon may be vulnerable to natural disasters or similar events. Accordingly, such a natural disaster or similar event could have an adverse effect on our business, financial condition or results of operations.

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

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

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

Although we have ongoing Phase 3, Phase 2b and OLE clinical trials for NEOD001, contemplate a Phase 2 clinical trial for PRX002/RG7935, have an ongoing Phase 1b clinical trial for PRX003 and contemplate a Phase 1 clinical trial for PRX004, there is no assurance that this work will support further development of these drug candidates. In addition, we currently do not, and may never, have any other drug candidates in clinical trials and we have not identified drug candidates for many of our research programs.

Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate with substantial evidence gathered in adequate and well-controlled clinical trials, and, with respect to approval in the U.S., to the satisfaction of the U.S. Food and Drug Administration (the "FDA") or, with respect to approval in other countries, similar regulatory authorities in those countries, that the drug candidate is safe and effective for use for that target indication. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. Despite our efforts, our drug candidates may not:

- offer improvement over existing, comparable products;
- be proven safe and effective in clinical trials; or
- meet applicable regulatory standards.

Positive results in preclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and promising results from early clinical trials of a drug candidate may not be replicated in later clinical trials. Interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage development. Accordingly, the results from completed preclinical studies and clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage trials or studies. Our preclinical studies or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or to discontinue clinical trials altogether.

Furthermore, we have not marketed, distributed or sold any products. Our success will, in addition to the factors discussed above, depend on the successful commercialization of our drug candidates, which may require:

- obtaining and maintaining commercial manufacturing arrangements with third-party manufacturers;
- collaborating with pharmaceutical companies or contract sales organizations to market and sell any approved drug; or

- acceptance of any approved drug in the medical community and by patients and third-party payors.

Many of these factors are beyond our control. We do not expect any of our drug candidates to be commercially available for several years and some or all may never become commercially available. Accordingly, we may never generate revenues through the sale of products.

If clinical trials of our drug candidates are prolonged, delayed, suspended or terminated, we may be unable to commercialize our drug candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.

We cannot predict whether we will encounter problems with our Phase 3, Phase 2b or OLE clinical trials for NEOD001, the contemplated Phase 2 clinical trial for PRX002/RG7935, our Phase 1b clinical trial for PRX003 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 other regulatory authority regarding the scope or design of our clinical trials;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards ("IRBs") or other reviewing entities at clinical sites selected for participation in our clinical trials;
- insufficient supply or deficient quality of our drug candidates or other materials necessary to conduct our clinical trials;
- delays in obtaining regulatory agency agreement for the conduct of our clinical trials;
- lower than anticipated enrollment and retention rate of subjects in clinical trials for a variety of reasons, including size of patient population, nature of trial protocol, the availability of other treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- serious and unexpected drug-related side effects experienced by patients in clinical trials; or
- failure of our third-party contractors and collaborators to meet their contractual obligations to us in a timely manner.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a trial, or a data safety monitoring board ("DSMB") overseeing the clinical trial at issue, or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- varying interpretation of data by the FDA or other regulatory authorities;
- requirement by the FDA or other regulatory authorities to perform additional studies;
- failure to achieve primary or secondary endpoints or other failure to demonstrate efficacy;
- unforeseen safety issues; or
- lack of adequate funding to continue the clinical trial.

Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to regulatory authorities and IRBs for reexamination, which may impact the cost, timing or successful completion of a clinical trial.

We do not know whether our clinical trials will be conducted as planned, will need to be restructured or will be completed on schedule, if at all. Delays in our clinical trials will result in increased development costs for our drug candidates. In addition, if we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for our drug candidates may be delayed or harmed and our ability to generate product revenues will be delayed or jeopardized. Furthermore,

many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a drug candidate.

The regulatory approval processes of the FDA and comparable 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 regulatory authorities is inherently unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any drug candidate and it is possible that none of our existing drug candidates or any drug candidates we may seek to develop in the future will ever obtain regulatory approval.

Our drug candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable 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 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 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 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 Biologic License Application ("BLA") or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- the FDA or comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; or
- the approval policies or regulations of the FDA or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our drug candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

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

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

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

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

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

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

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

Both before and after regulatory approval to market a particular drug candidate, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and record keeping related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practice ("cGMP") requirements and current good clinical practice ("cGCP") requirements for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with the regulatory requirements of the FDA and other applicable U.S. and other 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 regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. Even if any of our drug candidates receives marketing approval, as greater numbers of patients use a drug following its approval, an increase in the incidence of side effects or the incidence of other post-approval problems that were not seen or anticipated during pre-approval clinical trials could result in a number of potentially significant negative consequences, including:

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

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

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

Some of our research and development activities involve the controlled storage, use, and disposal of hazardous materials. We are subject to U.S. federal, state, local and other countries' and jurisdictions' laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that our safety procedures for the handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials, and we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Because we believe that our laboratory and materials handling policies and practices sufficiently mitigate the likelihood of materials liability or third-party claims, we currently carry no insurance covering such claims. An accident could damage, or force us to shut down, our operations.

Risks Related to the Commercialization of Our Drug Candidates

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

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

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

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

The success of PRX002/RG7935 in the United States is dependent upon the strength and performance of our collaboration with Roche. If we fail to maintain our existing collaboration with Roche, such termination would likely have a material adverse effect on our ability to develop and commercialize PRX002/RG7935 and our business. Furthermore, if we opt out of profit and loss sharing with Roche, our revenues from PRX002/RG7935 will be reduced.

The success of sales of PRX002/RG7935 in the U.S. will be dependent on the ability of Roche to successfully develop in collaboration with us, and launch and commercialize PRX002/RG7935, if approved by the FDA, pursuant to the License Agreement we entered into in December 2013. Our collaboration with Roche is complex, particularly with respect to future U.S. commercialization of PRX002/RG7935, with respect to financial provisions, allocations of responsibilities, cost estimates and the respective rights of the parties in decision making. Accordingly, significant aspects of the development and commercialization of PRX002/RG7935 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/RG7935 in the U.S. In addition, Roche may under some circumstances independently develop products that compete with PRX002/RG7935, or Roche may decide to not commit sufficient resources to the development, commercialization, marketing and distribution of PRX002/RG7935. If we are not able to collaborate effectively with Roche on plans and efforts to develop and commercialize PRX002/RG7935, 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/RG7935 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/RG7935 could be substantially harmed as we will be required to develop, commercialize and build our own sales and marketing organization or enter into another strategic collaboration in order to develop and commercialize PRX002/RG7935 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/RG7935, including the timing of launch and potential pricing, will have a significant impact on the ultimate success of PRX002/RG7935 in the U.S., and the success of the overall commercial arrangement with Roche. If launch of commercial sales of PRX002/RG7935 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/RG7935 sales and marketing efforts may result in lower revenue and thus lower profits with respect to the U.S. The outcome of Roche's commercialization efforts in the U.S. could also have a negative effect on investors' perception of potential sales of PRX002/RG7935 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/RG7935 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/RG7935 will be reduced.

Our right to co-develop PRX002/RG7935 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/RG7935 and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease.

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

Our ability to receive any significant revenue from PRX002/RG7935 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/RG7935 as diligently as we would like. We could also become involved in disputes with Roche, which could lead to delays in or termination of development or commercialization activities and time-consuming and expensive litigation or arbitration. If Roche terminates or breaches the License Agreement, or otherwise decides not to complete its obligations in a timely manner, the chances of successfully developing, commercializing or marketing PRX002/RG7935 would be materially and adversely affected.

Outside of the United States, we are solely dependent on the efforts and commitments of Roche, either directly or through third parties, to further develop and commercialize PRX002/RG7935. If Roche's efforts are unsuccessful, our ability to generate future product sales from PRX002/RG7935 outside the United States would be significantly reduced.

Under our License Agreement, outside of the U.S., Roche has responsibility for developing and commercializing PRX002/RG7935 and any future Licensed Products targeting α -synuclein. As a consequence, any progress and commercial success outside of the U.S. is dependent solely on Roche's efforts and commitment to the program. For example, Roche may delay, reduce or terminate development efforts relating to PRX002/RG7935 outside of the U.S., or under some circumstances independently develop products that compete with PRX002/RG7935, or decide not to commit sufficient resources to the commercialization, marketing and distribution of PRX002/RG7935.

In the event that Roche does not diligently develop and commercialize PRX002/RG7935, 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/RG7935, including inside the U.S., and we may choose not to terminate as we may not be able to find another partner and any new collaboration likely will not provide comparable financial terms to those in our arrangement with Roche. In the event of our termination, this may require us to develop and commercialize PRX002/RG7935 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/RG7935 outside of the U.S., our potential to generate future revenue outside of the U.S. would be significantly reduced.

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

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

We have entered into the License Agreement with Roche for the development of PRX002/RG7935 and may develop our own sales force and marketing infrastructure to co-promote PRX002/RG7935 in the U.S. for the treatment of Parkinson's disease and any future Licensed Products approved for Parkinson's disease in the U.S. If we exercise our co-promotion option and are unable to develop our own sales force and marketing infrastructure to effectively commercialize PRX002/RG7935 or other Licensed Products, our ability to generate additional revenue from potential sales of PRX002/RG7935 or such products in the U.S. may be

harmful. In addition, our right to co-promote PRX002/RG7935 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 U.S. and non-U.S. markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party 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 countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, and negatively impact our ability to generate revenue from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

U.S. and other governments continue to propose and pass legislation designed to reduce the cost of healthcare. In the U.S., we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the U.S. will continue to put pressure on pharmaceutical product pricing. For example, in 2010, the U.S. Patient Protection and Affordable Care Act, as amended by the U.S. Health Care and Education Reconciliation Act (collectively, the "Healthcare Reform Law"), was enacted. The Healthcare Reform Law substantially 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;
- an increase in the minimum rebates a manufacturer must pay under the U.S. Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the U.S. False Claims Act and the U.S. Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, under which manufacturers must agree to offer 50 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with

income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- a licensure framework for follow-on biologic products;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program and its implementing regulations;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the Healthcare Reform Law was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in 2013 and will stay in effect through 2024 unless additional congressional action is taken. In 2013, the U.S. American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations.

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

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

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

The research, development and commercialization of new drugs is highly competitive. We will face competition with respect to all drug candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of any approved product will be its indication, label, efficacy, safety profile, drug interactions, method of administration, pricing, coverage, reimbursement and level of promotional activity relative to those of competing drugs.

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

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

Competitive products may render our research and development program obsolete or noncompetitive before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and/or the widespread adoption or increased utilization of any vaccine or development of other products or treatments for the diseases we are targeting could render any of our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for a drug candidate, we will face competition based on the safety and effectiveness of the approved product, the timing of its entry into the market in relation to competitive products in development, the availability and cost of

supply, marketing and sales capabilities, coverage, reimbursement, price, patent position and other factors. Even if we successfully develop drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful.

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

Our drug candidates are regulated by the FDA as biologic products and we intend to seek approval for these products pursuant to the BLA pathway. The U.S. Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biologic products.

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

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

If we obtain FDA approval for any of our drug candidates and begin commercializing those products in the U.S., our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse and other healthcare laws and regulations, including, without limitation, the U.S. Anti-Kickback Statute and the U.S. 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 regulations of U.S. federal, state, local and other countries and 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 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 U.S. Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that impose criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the U.S. Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to "payments or other transfers of value" made to physicians, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members. The period between August 1, 2013 and December 31, 2013 was the first reporting period, and manufacturers were required to report aggregate payment data by March 31, 2014, and were required to report detailed payment data and submit legal attestation to the accuracy of such data during Phase 2 of the program (which began in May 2014). Thereafter, manufacturers must submit reports by the 90th day of each subsequent calendar year;

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

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

If a successful product liability or clinical trial claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, we could incur substantial liability.

The use of our drug candidates in clinical trials and the sale of any products for which we obtain marketing approval will expose us to the risk of product liability and clinical trial liability claims. Product liability claims might be brought against us by consumers, health care providers or others selling or otherwise coming into contact with our products. Clinical trial liability claims may be filed against us for damages suffered by clinical trial subjects or their families. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

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

We currently have clinical trial liability insurance coverage for all of our clinical trials. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient

amounts to protect us against losses due to liability. If and when we obtain marketing approval for any of our drug candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our ordinary share price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of any such clinical trials.

We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties, such as consultants, contract research organizations, medical institutions and clinical investigators, to assist us with these activities. Our reliance on these third parties for clinical development activities results in reduced control over these activities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. Although we have and will enter into agreements with these third parties, we will be responsible for confirming that our clinical trials are conducted in accordance with their general investigational plans and protocols. Moreover, the FDA and other comparable regulatory authorities require us to comply with regulations and standards, commonly referred to as cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If we or any of our third party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with cGCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

To date, we believe our consultants, contract research organizations and other third parties with which we are working have performed well; however, if these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with applicable regulations, we may be required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, we may not be able to enter into arrangements with alternative third-party contractors or to do so on commercially reasonable terms, which may result in a delay of our planned clinical trials. Accordingly, we may be delayed in obtaining regulatory approvals for our drug candidates and may be delayed in our efforts to successfully develop our drug candidates.

In addition, our third-party contractors are not our employees, and except for remedies available to us under our agreements with such third-party contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, 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 third-party manufacturers to supply us with preclinical and clinical trial supplies of all of our drug candidates, and we will depend on third-party manufacturers to supply us with any drug products for commercial sale if we obtain marketing approval from the FDA or any other comparable regulatory authority for any of our drug candidates.

We do not own or operate facilities for the manufacture, packaging, labeling, storage, testing or distribution of preclinical or clinical supplies of any of our drug candidates. We instead contract with and rely on third parties to manufacture, package, label, store, test and distribute pre-clinical and clinical supplies of our drug candidates, and we plan to continue to do so for the foreseeable future. We also rely on third-party consultants to assist us with managing these third-parties and with our manufacturing strategy. If any of these third-parties fail to perform these activities for us, preclinical or clinical development of our drug candidates could be delayed, which could have an adverse effect on our business, financial condition, results of operations and growth prospects.

If the FDA or any other comparable regulatory authority approves any of our drug candidates for commercial sale, we expect to continue to rely, at least initially, on third-parties to manufacture, label, store, test and distribute commercial supplies of such approved drug product. Significant scale-up of manufacturing may require additional comparability validation studies, which the FDA or other comparable regulatory authorities must review and approve. Our third-party manufacturers might not be able to successfully establish such comparability or increase their manufacturing capacity in a timely or economic manner, or at all. If our third-party manufacturers are unable to successfully establish comparability or increase their manufacturing capacity for any drug product, and we are unable to timely establish our own manufacturing capabilities, the commercial launch of that drug product could be delayed or there could be a shortage in supply, which could have an adverse effect on our business, financial condition, results of operations and growth prospects.

Our third-party manufacturers' facilities could be damaged by fire, power interruption, information system failure, natural disaster or other similar event, which could cause a delay or shortage in supplies of our drug candidates, which could have an adverse effect on our business, financial condition, results of operations and growth prospects.

Our drug candidates require, and any future drug product will require, precise, high quality manufacturing, labeling, storage and testing that meet stringent cGMP, other regulatory requirements and other standards. Our third-party manufacturers are subject to ongoing periodic and unannounced inspections by the FDA and other comparable regulatory authorities to ensure compliance with these cGMPs, other regulatory requirements and other standards. We do not have control over, and are dependent upon, our third-party manufacturers' compliance with these cGMPs, regulations and standards. Any failure by a third-party manufacturer to comply with these cGMPs, regulations or standards or that compromises the safety of any of our drug candidates or any drug product could cause a delay or suspension of production of preclinical or clinical supplies of our drug candidates or commercial supplies of drug products, cause a delay or suspension of preclinical or clinical development, product approval and commercialization of our drug candidates or drug products, result in seizure or recall of clinical or commercial supplies, result in fines and civil penalties, result in liability for any patient injury or death or otherwise increase our costs, any of which could have an adverse effect on our business, financial condition, results of operations and growth prospects. If a third-party manufacturer cannot or fails to perform its contractual commitments, does not have sufficient capacity to meet our preclinical, clinical or eventual commercial requirements or fails to meet cGMPs, regulations or other standards, we may be required to replace it or qualify an additional third-party manufacturer. Although we believe there are a number of potential alternative manufacturers, the number of manufacturers with the necessary manufacturing and regulatory expertise and facilities to manufacture biologics like our antibodies is limited. In addition, we could incur significant additional costs and delays in identifying and qualifying any new third-party manufacturer, due to the technology transfer to such new manufacturer and because the FDA and other comparable regulatory authorities must approve any new manufacturer prior to manufacturing our drug candidates. Such approval would require successful technology transfer, comparability and other testing and compliance inspections. Transferring manufacturing to a new manufacturer could therefore interrupt supply, delay our clinical trials and any commercial launch and/or increase our costs for our drug candidates, any of which could have an adverse effect on our business, financial condition, results of operations and growth prospects.

Boehringer Ingelheim Biopharmaceuticals GmbH ("BI") has manufactured and is contracted to continue to manufacture clinical supplies of our drug candidate NEOD001 for its clinical trials. We are dependent on BI to continue to manufacture these clinical supplies. We have contracted with Rentschler Biotechnologie GmbH ("Rentschler") to develop the capability to manufacture and supply drug substance of NEOD001, and to so supply NEOD001 to us for worldwide commercial sale purposes if we apply for and obtain regulatory approval to market NEOD001. In order to be able to use drug substance supplied by Rentschler for commercial purposes, we will need to first establish comparability of drug substance manufactured by Rentschler with clinical supplies manufactured by BI and used by us in clinical development of NEOD001.

BI also manufactured clinical supplies of our drug candidate PRX002/RG7935 for our completed Phase 1a single ascending dose and Phase 1b multiple ascending dose trials. It is intended that Roche, with whom we are collaborating on development of PRX002/RG7935, will manufacture clinical supplies for the contemplated Phase 2 and any subsequent clinical trials.

BI is also our third-party manufacturer of clinical supplies of our drug candidate PRX003. We are dependent on BI to continue to manufacture these clinical supplies.

Rentschler is also our third-party manufacturer of clinical supplies of our drug candidate PRX004. We are dependent on Rentschler to manufacture these clinical supplies in order to initiate clinical trials for PRX004.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on third-party suppliers for the raw materials required for the production of our drug candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our products until a new source of supply, if any, could be identified and qualified. Although we believe there are currently several other suppliers of these raw materials, we may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our drug candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks Related to Our Intellectual Property

If we are unable to adequately protect or enforce the intellectual property relating to our drug candidates our ability to successfully commercialize our drug candidates will be harmed.

Our success depends in part on our ability to obtain patent protection both in the U.S. and in other countries for our drug candidates. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any issued patents may not provide us with sufficient protection for our drug candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes.

In addition, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us or our affiliates. Even if patents have issued or will issue, we cannot guarantee that the claims of these patents are or will be valid or enforceable or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us. Patent applications in the U.S. are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the U.S. Patent and Trademark Office (the "USPTO") for the entire time prior to issuance as a U.S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we or our licensors or co-owners were the first to invent, or the first to file patent applications on, our drug candidates or their use as drugs. In the event that a third party has also filed a U.S. patent application relating to our drug candidates or a similar invention, we may have to participate in interference or derivation proceedings declared by the USPTO to determine priority of invention in the U.S. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a loss of our U.S. patent position. Furthermore, we may not have identified all U.S. and non-U.S. patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our patent applications covering composition-of-matter of our product candidates will be considered patentable by the USPTO and courts in the U.S. or by the patent offices and courts in other countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In 2011, the U.S. Leahy-Smith America Invents Act (the "Leahy-Smith Act") was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, and switch the U.S. patent system from a "first-to-invent" system to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO subsequently developed new regulations and procedures to govern administration of the Leahy-Smith Act, 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 in 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

We may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review, or other patent office proceedings or litigation, in the U.S. or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights.

We may not be able to protect our intellectual property rights throughout the world.

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

We license patent rights from third-party owners. Such licenses may be subject to early termination if we fail to comply with our obligations in our licenses with third parties, which could result in the loss of rights or technology that are material to our business.

We are a party to licenses that give us rights to third-party intellectual property that is necessary or useful for our business, and we may enter into additional licenses in the future. Under these license agreements we are obligated to pay the licensor fees, which may include annual license fees, milestone payments, royalties, a percentage of revenues associated with the licensed technology and a percentage of sublicensing revenue. In addition, under certain of such agreements, we are required to diligently pursue the development of products using the licensed technology. If we fail to comply with these obligations and fail to cure our breach within a specified period of time, the licensor may have the right to terminate the applicable license, in which event we could lose valuable rights and technology that are material to our business.

If the licensor retains control of prosecution of the patents and patent applications licensed to us, we may have limited or no control over the manner in which the licensor chooses to prosecute or maintain its patents and patent applications and have limited or no right to continue to prosecute any patents or patent applications that the licensor elects to abandon.

Litigation regarding patents, patent applications and other proprietary rights may be expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing drug candidates to market and harm our ability to operate.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Although we are not currently aware of any litigation or other proceedings or third-party claims of intellectual property infringement related to our drug candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may hold or obtain patents in the future and allege that the use of our technologies infringes these patent claims or that we are employing their proprietary technology without authorization.

In addition, third parties may challenge or infringe upon our existing or future patents. Proceedings involving our patents or patent applications or those of others could result in adverse decisions regarding:

- the patentability of our inventions relating to our drug candidates; and/or
- the enforceability, validity or scope of protection offered by our patents relating to our drug candidates.

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

If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may:

- incur substantial monetary damages;
- encounter significant delays in bringing our drug candidates to market; and/or
- be precluded from participating in the manufacture, use or sale of our drug candidates or methods of treatment requiring licenses.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

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

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable; however, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

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

Risks Related to Our Ordinary Shares

The market price of our ordinary shares may fluctuate widely.

Our ordinary shares commenced trading on The Nasdaq Global Market on December 21, 2012 and currently trade on The Nasdaq Global Select Market. We cannot predict the prices at which our ordinary shares may trade. The market price of our ordinary shares may fluctuate widely, depending upon many factors, some of which may be beyond our control, including:

- our ability to obtain financing as needed;
- progress in and results from our ongoing or future clinical trials;
- our collaboration with Roche pursuant to the License Agreement to develop and commercialize PRX002/RG7935, as well as any future Licensed Products targeting α -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 U.S. and other countries;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by our competitors;
- changes in estimates or recommendations by securities analysts, if any, who cover our company;
- public concern over our drug candidates;
- litigation;
- future sales of our ordinary shares;
- general market conditions;
- changes in the structure of healthcare payment systems;
- failure of any of our drug candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises;
- period-to-period fluctuations in our financial results;
- overall fluctuations in U.S. equity markets;
- our quarterly or annual results, or those of other companies in our industry;
- announcements by us or our competitors of significant acquisitions or dispositions;
- the operating and ordinary share price performance of other comparable companies;
- investor perception of our company and the drug development industry;
- natural or environmental disasters that investors believe may affect us; or
- fluctuations in the budgets of federal, state and local governmental entities around the world.

These and other external factors may cause the market price and demand for our ordinary shares to fluctuate substantially, which may limit or prevent investors from readily selling their ordinary shares and may otherwise negatively affect the liquidity of our ordinary shares. In particular, stock markets in general have experienced volatility that has often been unrelated to the operating performance of a particular company. These broad market fluctuations may adversely affect the trading price of our ordinary shares. In the past, when the market price of a stock has been volatile, some holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

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

As with any publicly traded company, your percentage ownership in us may be diluted in the future because of equity issuances for acquisitions, capital raising transactions or otherwise. We may need to raise additional capital in the future. If we are able to raise additional capital, we may issue equity or convertible debt instruments, which may severely dilute your ownership interest in us. In addition, we intend to continue to grant option awards to our directors, officers and employees, which would dilute your ownership stake in us. As of March 31, 2017, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plan was 5,843,612.

If we are unable to maintain effective internal controls, our business could be adversely affected.

We are subject to the reporting and other obligations under the U.S. Securities Exchange Act of 1934, as amended, including the requirements of Section 404 of the U.S. Sarbanes-Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. These reporting and

other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with accounting principles generally accepted in the U.S. During the course of our review and testing of our internal controls, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our condensed consolidated financial statements may be materially misstated. We or our independent registered public accounting firm, when required, may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall.

We cannot provide assurance that a material weakness will not occur in the future, or that we will be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 and the related rules and regulations of the SEC when required. A material weakness in internal control over financial reporting is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis by the company's internal controls. If we cannot in the future favorably assess, or our independent registered public accounting firm, when required, is unable to provide an unqualified attestation report on, the effectiveness of our internal controls over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on our share price. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would have an adverse effect on our business, financial position and results of operations.

If we were treated as a passive foreign investment company for U.S. federal income tax purposes, it could result in adverse U.S. federal income tax consequences to United States holders of our ordinary shares .

Significant potential adverse U.S. federal income tax implications generally apply to U.S. investors owning shares of a passive foreign investment company ("PFIC"), directly or indirectly. In general, we would be a PFIC for a taxable year if either (i) 75% or more of its income constitutes passive income (the "income test") or (ii) 50% or more of our assets produce passive income (the "asset test"). Changes in the composition of our active or passive income, passive assets or fair market value may cause us to become a PFIC. A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each taxable year).

We do not believe we were a PFIC for U.S. federal income tax purposes for our taxable years ended December 31, 2016, 2015 or 2014. However, the application of the PFIC rules is subject to uncertainties in a number of respects, and we cannot assure that the U.S. Internal Revenue Service (the "IRS") will not take a contrary position. We also cannot assure that we will not be a PFIC for U.S. federal income tax purposes for any future taxable year.

We may not be able to successfully maintain our tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects.

We are incorporated in Ireland and maintain subsidiaries or offices in Ireland, the U.S. and other jurisdictions. We are able to achieve a low average tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, together with intra-group service agreements. However, changes in tax laws in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the IRS, actively audit and otherwise challenge these types of arrangements, and have done so in our industry. We are subject to reviews and audits by the IRS and other taxing authorities from time to time, and the IRS or other taxing authority may challenge our structure and inter-group arrangements. Responding to or defending against challenges from taxing authorities could be expensive and time consuming, and could divert management's time and focus away from operating our business. We cannot predict whether and when taxing authorities will conduct an audit, challenge our tax structure or the cost involved in responding to any such audit or challenge. If we are unsuccessful, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, all of which could have an adverse effect on our business, financial condition, results of operations or growth prospects.

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

Under current law, we are treated as a foreign corporation for U.S. federal tax purposes. However, changes to the U.S. Internal Revenue Code, U.S. Treasury Regulations or other IRS guidance thereunder could adversely affect our status as a foreign corporation or otherwise affect our effective tax rate. In addition, the U.S. Congress, the IRS, the Organization for Economic Co-operation and Development and other governments and agencies in jurisdictions where we do business have recently focused on issues related to the taxation of multinational corporations, and specifically in the area of "base erosion and profit shifting," where

payments are made between affiliates from a jurisdiction with high tax rates to a jurisdiction with lower tax rates. As a result, the tax laws in the U.S. and other countries in which we do business could change on a prospective or retroactive basis, and any such changes could have an adverse effect on our business, financial condition, results of operations or growth prospects.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our ordinary shares.

It may not be possible to enforce court judgments obtained in the U.S. against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the U.S. currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on federal or state securities laws, would not automatically be enforceable in Ireland.

As an Irish incorporated company, we are governed by the Irish Companies Act 2014 (the "Companies Act"), which differ in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our ordinary shares may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the U.S.

Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our board of directors less ability to control negotiations with hostile offerors.

We are subject to the Irish Takeover Panel Act, 1997, Takeover Rules, 2013. Under those Irish Takeover Rules, our Board is not permitted to take any action that might frustrate an offer for our ordinary shares once our Board has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of ordinary shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our Board has reason to believe an offer is or may be imminent. These provisions may give our Board less ability to control negotiations with hostile offerors and protect the interests of holders of ordinary shares than would be the case for a corporation incorporated in a jurisdiction of the U.S.

Irish law requires that our shareholders renew every five years the authority of our Board of Directors to issue shares and to do so for cash without applying the statutory pre-emption right, and if our shareholders do not renew these authorizations by September 26, 2017 (or any renewal is subject to limitations), our ability to raise additional capital to fund our operations would be limited.

As an Irish incorporated company, we are governed by the Companies Act. The Companies Act requires that every five years our shareholders renew the separate authorities of our Board to (a) allot and issue shares and (b) opt out of the statutory pre-emption right that otherwise applies to share issuances for cash (which pre-emption right would require that shares issued for cash be offered to our existing shareholders on a pro rata basis before the shares may be issued to new shareholders). Our Constitution currently authorizes our Board to issue ordinary shares up to the amount of our authorized share capital, and to opt out of the statutory pre-emption right for such issuances. Under Irish law, these authorizations expire on September 26, 2017, five years after the adoption of our Constitution. Irish law requires that our shareholders renew the authority for our Board to issue ordinary shares by a resolution approved by not less than 50% of the votes cast at a general meeting of our shareholders. Irish law requires that our shareholders renew the authority of our Board to opt out of the statutory pre-emption right in share issuances for cash by a resolution approved by not less than 75% of the votes cast at a general meeting of our shareholders. If these authorizations are not renewed before September 26, 2017, or are renewed with limitations, our Board would be limited in its ability to issue shares, which would limit our ability to raise additional capital to fund our operations, including the research, development and potential commercialization of our product candidates.

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

Transfers of our ordinary shares effected by means of the transfer of book entry interests in DTC should not be subject to Irish stamp duty. However, if a shareholder holds our ordinary shares directly rather than beneficially through DTC any transfer of those ordinary shares could be subject to Irish stamp duty (currently at the rate of 1% of the higher of the price paid or the

market value of the ordinary shares acquired). Payment of Irish stamp duty is generally a legal obligation of the transferee. The potential for stamp duty could adversely affect the price of your ordinary shares.

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

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

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

Although we do not currently anticipate paying cash dividends, if we were to do so in the future, a dividend withholding tax (currently at a rate of 20%) may arise. A number of exemptions from dividend withholding tax exist such that shareholders resident in the U.S. and shareholders resident in other countries that have entered into a double taxation treaty with Ireland may be entitled to exemptions from dividend withholding tax subject to the completion of certain dividend withholding tax declaration forms.

Shareholders entitled to an exemption from Irish dividend withholding tax on any dividends received from us will not be subject to Irish income tax in respect of those dividends, unless they have some connection with Ireland other than their shareholding (for example, they are resident in Ireland). Shareholders who receive dividends subject to Irish dividend withholding tax will generally have no further liability to Irish income tax on those dividends.

Prothena ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax.

Irish capital acquisitions tax ("CAT") could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT. Gifts and inheritances passing between spouses are exempt from CAT. It is recommended that each shareholder consult his or her own tax advisor as to the tax consequences of holding our ordinary shares or receiving dividends from us.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not Applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

See the Exhibit Index following the signature page to this Quarterly Report on Form 10-Q for a list of exhibits filed or furnished with this report, which Exhibit Index is incorporated herein by reference.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Quarterly Report on Form 10-Q to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: May 9, 2017

Prothena Corporation plc
(Registrant)

/s/ Gene G. Kinney

Gene G. Kinney
President and Chief Executive Officer

/s/ Tran B. Nguyen

Tran B. Nguyen
Chief Financial Officer

EXHIBIT INDEX

| Exhibit No. | Description | Previously Filed | | | | Filed Herewith |
|-------------|--|------------------|----------|-------------|---------|----------------|
| | | Form | File No. | Filing Date | Exhibit | |
| 10.1# | Prothena Corporation plc Amended and Restated Incentive Compensation Plan | | | | | X |
| 31.1 | Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 | | | | | X |
| 31.2 | Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 | | | | | X |
| 32.1* | Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 | | | | | X |
| 101.INS+ | XBRL Instance Document | | | | | X |
| 101.SCH+ | XBRL Taxonomy Extension Schema Document | | | | | X |
| 101.CAL+ | XBRL Taxonomy Extension Calculation Linkbase Document | | | | | X |
| 101.DEF+ | XBRL Taxonomy Extension Definition Linkbase Document | | | | | X |
| 101.LAB+ | XBRL Taxonomy Extension Label Linkbase Document | | | | | X |
| 101.PRE+ | XBRL Taxonomy Extension Presentation Linkbase Document | | | | | X |

Indicates management contract or compensatory plan or arrangement.

* Exhibit 32.1 is being furnished and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liability of that section, nor shall such exhibit be deemed to be incorporated by reference in any registration statement or other document filed under the Securities Act of 1933, as amended, or the Exchange Act, except as otherwise specifically stated in such filing.

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

**PROTHENA CORPORATION PLC
AMENDED AND RESTATED INCENTIVE COMPENSATION PLAN**

1. Purpose of the Plan . The purpose of the Plan is to provide a link between compensation and performance, to motivate participants to achieve corporate performance objectives and to enable the Company, its subsidiaries and Affiliated Entities to attract and retain high quality Eligible Employees. This Plan constitutes an amendment and restatement of the Prothena Corporation plc Incentive Compensation Plan.

2. Definitions . As used herein, the following definitions shall apply:

(a) “ Affiliated Entity ” means any entity other than the Company and its subsidiaries that is designated by the Board or the Committee as a participating employer under the Plan; provided, however, that the Company directly or indirectly owns at least 20% of the combined voting power of all classes of stock of such entity or at least 20% of the ownership interests in such entity.

(b) “ Board ” means the Board of Directors of the Company.

(c) “ Bonus ” means a cash payment made pursuant to the Plan.

(d) “ Code ” means the Internal Revenue Code of 1986, as amended.

(e) “ Committee ” means (i) with respect to Bonuses that are not intended to be Performance-Based Compensation, the Compensation Committee of the Board, or such other Board committee (which may include the entire Board) as may be designated by the Board to administer the Plan, and (ii) with respect to Bonuses that are intended to be Performance-Based Compensation, a committee that consists of two or more persons appointed by the Board, all of whom shall be “outside directors” as defined under Section 162(m) of the Code and related Treasury Regulations.

(f) “ Company ” means Prothena Corporation plc.

(g) “ Covered Employee ” means an Employee who is a “covered employee” under Section 162(m) of the Code.

(h) “ Director ” means a non-Employee member of the Board.

(i) “ Effective Date ” means the date that the Plan, as amended and restated herein, is approved by the Board.

(j) “ Eligible Employee ” means any Employee who is selected for participation in the Plan by the Committee.

(k) “ Employee ” means any person who is in the employ of the Company, a subsidiary or an Affiliated Entity, subject to the control and direction of the Company, the subsidiary or the Affiliated Entity as to both the work to be performed and the manner and method of

performance. Neither service as a Director nor fees received from the Company, the subsidiary or the Affiliated Entity for service as a Director shall be sufficient to constitute Employee status.

(l) “Long Term Incentive Plan” means the Prothena Corporation plc 2012 Long Term Incentive Plan, as it may be amended from time to time (or any successor to that plan).

(m) “Performance-Based Compensation” means compensation qualifying as “performance-based compensation” under Section 162(m) of the Code.

(n) “Performance Goal” means any measurable criterion tied to the success of the Company and based on one or more of the business criteria described in Section 6.

(o) “Performance Period” means a fixed period established by the Committee that may range in duration from a minimum period of twelve (12) months to a maximum period of thirty-six (36) months and over which the attainment of the applicable Performance Goals set by the Committee is to be measured.

(p) “Plan” means the Prothena Corporation plc Amended and Restated Incentive Compensation Plan.

3. Administration of the Plan.

(a) The Committee. The Plan shall be administered by the Committee.

(b) Powers of the Committee. Subject the provisions of the Plan (including any other powers given to the Committee hereunder), the Committee shall have the authority, in its discretion, to:

(i) establish the duration of each Performance Period;

(ii) select the Eligible Employees who are to participate in the Plan for such Performance Period;

(iii) determine the specific Performance Goals for each Performance Period and the relative weighting of those goals, establish one or more designated levels of attainment for each such goal and set the Bonus potential for each participant at each corresponding level of attainment;

(iv) certify the level at which the applicable Performance Goals are attained for the Performance Period and determine, on the basis of that certification, the actual Bonus for each participant in an amount not to exceed his or her maximum Bonus potential for the certified level of attainment;

(v) exercise discretionary authority, when appropriate, to reduce the actual Bonus payable to any participant below his or her Bonus potential for the attained level of the Performance Goals for the Performance Period;

(vi) construe and interpret the terms of the Plan and Bonuses awarded under the Plan;

(vii) establish additional terms, conditions, rules or procedures for the administration of the Plan; provided, however, that no Bonus shall be awarded under any such additional terms, conditions, rules or procedures which are inconsistent with the provisions of the Plan; and

(viii) take such other action, not inconsistent with the terms of the Plan, as the Committee deems appropriate.

All decisions and determinations by the Committee shall be final, conclusive and binding on the Company, its subsidiaries, Affiliated Entities, the participants, and any other persons having or claiming an interest hereunder.

(c) Indemnification. In addition to such other rights of indemnification as they may have as members of the Board, members of the Committee who administer the Plan shall be defended and indemnified by the Company, to the extent permitted by law, on an after-tax basis against (i) all reasonable expenses (including attorneys' fees) actually and necessarily incurred in connection with the defense of any claim, investigation, action, suit or proceeding, or in connection with any appeal therein, to which they or any of them may be a party by reason of any action taken or failure to act under or in connection with the Plan or any Bonus awarded hereunder and (ii) all amounts paid by them in settlement thereof (provided such settlement is approved by the Company) or paid by them in satisfaction of a judgment in any such claim, investigation, action, suit or proceeding, except in relation to matters as to which it shall be adjudged in such claim, investigation, action, suit or proceeding that such person is liable for gross negligence, bad faith or intentional misconduct; provided, however, that within 30 days after the institution of such claim, investigation, action, suit or proceeding, such person shall offer to the Company, in writing, the opportunity at the Company's expense to handle and defend the same.

4. Coverage. All Eligible Employees shall be covered by the Plan, except to the extent the Committee may elect to exclude one or more Eligible Employees from participation in a designated Performance Period.

5. Terms and Conditions of Bonus Awards.

(a) Pre-Established Performance Goals for Bonuses Intended to Qualify as Performance-Based Compensation. Payment of Bonuses intended to qualify as Performance-Based Compensation granted to Covered Employees shall be based solely on account of the attainment of one or more pre-established, objective Performance Goals over the designated Performance Period. The Committee shall establish one or more objective Performance Goals with respect to each Covered Employee for a Bonus intended to qualify as Performance-Based Compensation in writing not later than 90 days after the commencement of the Performance Period to which the Performance Goals relate or the date on which twenty-five percent (25%) of such Performance Period has been completed (or such other date as may be required or permitted under Section 162(m) of the Code), provided that the outcome of the Performance Goals must be substantially uncertain

at the time of their establishment. Such Performance Goals shall be based solely on one or more of the business criteria described in the Section 6 and shall be weighted, equally or in such other proportion as the Committee shall determine at the time such Performance Goals are established, for purposes of determining the actual Bonus amounts that may become payable upon the attainment of those goals. For each such Performance Goal, the Committee may establish one or more designated levels of attainment and set the Bonus potential for each Eligible Employee at each designated performance level. Alternatively, the Committee may establish a linear formula for determining the Bonus potential at various points of Performance Goal attainment. Under no circumstance, however, shall the aggregate Bonus potential for any participant for any Performance Period exceed the applicable maximum dollar amount set forth in Section 5(d).

(b) Performance Goals for Bonuses not Intended to Qualify as Performance-Based Compensation . The Performance Goals for Bonuses awarded to Eligible Employees other than Covered Employees or for Bonuses awarded to Covered Employees, in each case, that are not intended to qualify as Performance-Based Compensation, and the determination of final Bonuses pursuant to the achievement of Performance Goals, may conform to the requirements set forth above in Section 5(a) or may be based on such other quantitative or qualitative performance goals, as specified by the Committee. Performance Goals may differ for Bonuses awarded to different Eligible Employees. The Committee may weight the Performance Goals in such manner as the Committee determines at the beginning of the Performance Period.

(c) Committee Certification . As soon as administratively practicable following the completion of the Performance Period, the Committee shall certify the actual levels at which the Performance Goals for that period have been attained and determine, on the basis of such certified levels, the actual Bonus amount to be paid to each Eligible Employee for that Performance Period. Such certification shall be final, conclusive and binding on the participant, and on all other persons, to the maximum extent permitted by law.

(d) Committee Discretion . Except with respect to Bonuses that are not intended to qualify as Performance-Based Compensation, the Committee, in determining the amount of the Bonus actually to be paid to an Eligible Employee, shall in no event award a Bonus in excess of the dollar amount determined on the basis of the Bonus potential established for the particular level at which each of the applicable Performance Goals for the Performance Period is attained. The Committee shall have the discretion to reduce or eliminate the Bonus that would otherwise be payable with respect to one or more Performance Goals on the basis of the certified level of attained performance of those goals. In exercising its discretion to reduce the Bonus payable to any participant, the Committee may utilize such objective or subjective criteria as the Committee deems appropriate in its sole and absolute discretion. With respect to Bonuses that are not intended to qualify as Performance-Based Compensation, the Committee shall have discretion to increase the Bonus that would otherwise be payable with respect to one or more Performance Goals on the basis of the certified level of attained performance of those goals, and in exercising its discretion to increase the Bonus payable to any participant, the Committee may utilize such objective or subjective criteria as the Committee deems appropriate in its sole and absolute discretion. Except with respect to Bonuses that are not intended to qualify as Performance-Based Compensation, the Committee shall not waive any Performance Goal applicable to a participant's Bonus potential for a particular

Performance Period, provided that, the Committee may, in its sole discretion, waive the Performance Goal for a particular Performance Period in the event of the participant's death or disability or under such circumstances as the Committee deems appropriate in the event a Change in Control (as such term is defined in the Long Term Incentive Plan) should occur prior to the completion of that Performance Period.

(e) Individual Limitations on Awards. Notwithstanding any other provision of the Plan, the maximum amount of any Bonus paid to a Covered Employee or other Eligible Employee under the Plan shall be limited to Three Million Dollars (\$3,000,000) per each twelve (12)-month period (or portion thereof) included within the applicable Performance Period.

(f) Payment Date. Payment of such Bonus amounts shall be made as soon as administratively practicable after the Committee certification, but in any event, no later than March 15 of the year following the year in which the Performance Period ends. No participant shall accrue any right to receive a Bonus award under the Plan unless that participant remains in Employee status until the date the Bonus is paid. Accordingly, no Bonus payment shall be made to any participant who ceases Employee status prior to the date a Bonus is paid; provided, however, that the Committee shall have complete discretion to award a full or pro-rated Bonus, based on the level at which the applicable Performance Goals are attained for the Performance Period, to a participant who ceases Employee status prior to the payment by reason of death, disability or a termination of employment by the Company without cause, in each case, as determined by the Committee. Notwithstanding the foregoing, with respect to a Bonus payable for a 12 month Performance Period commencing January 1, an Eligible Employee must have maintained Employee status until at least October 1 of such Performance Period to be eligible to receive a Bonus for such Performance Period.

(g) Withholding Tax. To the extent required by applicable federal, state, local or foreign law, each employer shall withhold all applicable taxes from all Bonus amounts.

6. Business Criteria.

(a) Permitted Criteria. Performance Goals established by the Committee may be based on any one of, or combination of, the following: stock price, earnings per share, price-earnings multiples, net earnings, operating earnings, revenue, number of days sales outstanding in accounts receivable, productivity, margin, EBITDA (earnings before interest, taxes, depreciation and amortization), net capital employed, return on assets, shareholder return, return on equity, return on capital employed, growth in assets, unit volume, sales, cash flow, market share, relative performance to a comparison group designated by the Committee, or strategic business criteria consisting of one or more objectives based on meeting specified revenue goals, market penetration goals, customer growth, geographic business expansion goals, cost targets or goals relating to acquisitions or divestitures. Such Performance Goals may be measured not only in terms of the Company's performance but also in terms of its performance relative to the performance of other entities or may be measured on the basis of the performance of any of the Company's business units or divisions or any parent or subsidiary entity. Performance may also be measured on an absolute basis, relative to internal business plans, or based on growth. As may be applicable, they may also be measured in aggregate or on a per-share basis. Performance Goals need not be uniform as among participants.

(b) Authorized Adjustments. To the extent applicable, subject to the following sentence and unless the Committee determines otherwise, the determination of the achievement of Performance Goals shall be determined based on the relevant financial measure, computed in accordance with U.S. generally accepted accounting principles (“GAAP”), and in a manner consistent with the methods used in the Company’s audited financial statements. To the extent permitted by Section 162(m) of the Code, if applicable, in setting the Performance Goals within the period prescribed in Section 5(a), the Committee may provide for appropriate adjustment as it deems appropriate, including for one or more of the following items: asset write-downs; litigation or claim judgments or settlements; changes in accounting principles; changes in tax law or other laws affecting reported results; changes in commodity prices; severance, contract termination, and other costs related to exiting, modifying or reducing any business activities; costs of, and gains and losses from, the acquisition, disposition, or abandonment of businesses or assets; gains and losses from the early extinguishment of debt; gains and losses in connection with the termination or withdrawal from a pension plan; stock compensation costs and other non-cash expenses; any extraordinary non-recurring items as described in applicable Accounting Principles Board opinions or Financial Accounting Standards Board statements or in management’s discussion and analysis of financial condition and results of operation appearing in the Company’s annual report to stockholders for the applicable year; and any other specified non-operating items as determined by the Committee in setting Performance Goals.

7. Effective Date and Term of Plan. The Plan is effective as of the Effective Date. The Plan shall continue in effect until the Board terminates it.

8. Amendment, Suspension or Termination of the Plan. The Board may at any time amend, suspend or terminate the Plan.

9. General Provisions.

(a) Transferability. No participant in the Plan shall have the right to transfer, alienate, pledge or encumber his or her interest in the Plan, and such interest shall not (to the maximum permitted by law) be subject to the claims of the participant’s creditors or to attachment, execution or other process of law. However, should a participant die before payment is made of the actual Bonus to which he or she has become entitled under the Plan, then that Bonus shall be paid to the executor or other legal representative of his or her estate.

(b) No Rights to Employment. Neither the action of the Company in establishing or maintaining the Plan, nor any action taken under the Plan by the Committee, nor any provision of the Plan itself shall be construed so as to grant any person the right to remain in Employee status for any period of specific duration, and each participant shall at all times remain an Employee at-will and may accordingly be discharged at any time, with or without cause and with or without advance notice of such discharge.

(c) Acknowledgement of Authority. All Bonuses shall be awarded conditional upon the participant’s acknowledgement, by participation in the Plan, that all decisions and determinations of the Committee shall be final and binding on the participant, his or her beneficiaries and any other person having or claiming an interest in such Bonus.

(d) Company Policies. All Bonuses under the Plan shall be subject to any applicable clawback or recoupment policy of the Company adopted from time to time by the Board.

(e) Unfunded Obligation. Eligible Employees eligible to participate in the Plan shall have the status of general unsecured creditors of the Company. Any amounts payable to such Employees pursuant to the Plan shall be unfunded and unsecured obligations for all purposes, including (without limitation) Title I of the Employee Retirement Income Security Act of 1974, as amended. The Company shall not be required to segregate any monies from its general funds, or to create any trusts, or establish any special accounts with respect to such obligations. Employees shall have no claim against the Company for any changes in the value of any assets that may be invested or reinvested by the Company with respect to the Plan.

(f) Reliance on Reports. Each member of the Committee shall be fully justified in relying or acting in good faith upon any report made by the independent public accountants of the Company and its subsidiaries or Affiliated Entities and upon any other information furnished in connection with the Plan by any person or persons other than himself or herself. In no event shall any person who is or shall have been a member of the Committee or of the Board be liable for any determination made or other action taken or any omission to act in reliance upon any such report or information or for any action taken, including the furnishing of information, or failure to act, if in good faith.

(g) Successors. The terms and conditions of the Plan, together with the obligations and liabilities of the Company that accrue hereunder, shall be binding upon any successor to the Company, whether by way of merger, consolidation, reorganization or other change in ownership or control of the Company.

(h) Section 409A. The Plan is intended to comply with the short-term deferral rule set forth in the regulations under Section 409A of the Code in order to avoid application of Section 409A of the Code to the Plan. If and to the extent that any payment under this Plan is deemed to be deferred compensation subject to the requirements of Section 409A of the Code, this Plan shall be administered so that such payments are made in accordance with the requirements of Section 409A of the Code. If an award is subject to Section 409A of the Code, (i) distributions shall only be made in a manner and upon an event permitted under Section 409A of the Code, (ii) payments to be made upon a termination of employment shall only be made upon a “separation from service” under Section 409A of the Code, and (iii) in no event shall a participant, directly or indirectly, designate the calendar year in which a distribution is made except in accordance with Section 409A of the Code. Any award granted under the Plan that is subject to Section 409A of the Code and that is to be distributed to a key employee (as defined below) upon separation from service shall be administered so that any distribution with respect to such award shall be postponed for six months following the date of the participant’s separation from service, if required by Section 409A of the Code. If a distribution is delayed pursuant to Section 409A of the Code, the distribution shall be paid within 30 days after the end of the six-month period. If the participant dies during such six-month period, any postponed amounts shall be paid within 90 days of the participant’s death. The determination of key employees, including the number and identity of persons considered key employees and the identification date, shall be made by the Committee or its delegate each year in

accordance with Section 416(i) of the Code and the “specified employee” requirements of Section 409A of the Code.

(i) Conformity to Section 162(m) of the Code for Bonuses to Covered Employees Intended to Qualify as Performance-Based Compensation. With respect to Bonuses awarded to Covered Employees intended to qualify as Performance-Based Compensation, terms used in the Plan shall be interpreted in a manner consistent with Section 162(m) of the Code and regulations thereunder (including Treasury Regulation Section 1.162-27). If any provision of the Plan with respect such Bonuses or any agreement evidencing such Bonuses hereunder does not comply or is inconsistent with the provisions of Section 162(m)(4)(C) or regulations thereunder (including Treasury Regulation Section 1.162-27(e)) required to be met in order that compensation (other than post-termination compensation) shall constitute Performance-Based Compensation, such provision shall be construed or deemed amended to the extent necessary to conform to such requirements, and no adjustment to a Bonus or its related Performance Goals shall be authorized or made, and no post-termination payment shall be authorized or made under Section 5(f), if and to the extent that such authorization or the making of such adjustment or payment would contravene such requirements.

(j) Governing Law. The validity, construction, interpretation and effect of the Plan shall be governed and construed by and determined in accordance with the laws of the State of Delaware, without giving effect to the conflict of laws provisions thereof.

**CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Gene G. Kinney, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Prothena Corporation plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 9, 2017

/s/ Gene G. Kinney

Gene G. Kinney
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Tran B. Nguyen, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Prothena Corporation plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 9, 2017

/s/ Tran B. Nguyen

Tran B. Nguyen
Chief Financial Officer
(Principal Financial Officer)

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
AND PRINCIPAL FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Gene G. Kinney, President and Chief Executive Officer of Prothena Corporation plc (the "Company") and Tran B. Nguyen, Chief Financial Officer of the Company, each hereby certify that, to the best of his knowledge:

1. The Company's Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2017, to which this Certification is attached as Exhibit 32.1 (the "Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 9, 2017

/s/ Gene G. Kinney

Gene G. Kinney
President and Chief Executive Officer
(Principal Executive Officer)

/s/ Tran B. Nguyen

Tran B. Nguyen
Chief Financial Officer
(Principal Financial Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350 has been provided to the Registrant and will be retained by the Registrant and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933 or the Securities Exchange Act of 1934 (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.