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, 2019

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

77 Sir John Rogerson's Quay, Block C
Grand Canal Docklands
Dublin 2, D02 T804, 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 every Interactive Data File required to be submitted 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 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	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☒
		Emerging growth company	☐

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 ☒

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

Title of Each Class	Trading Symbol	Name of Each Exchange on Which Registered
Ordinary Shares, par value $0.01 per share	**PRTA**	**The Nasdaq Global Select Market**

The number of ordinary shares outstanding as of April 30, 2019 was 39,864,561.

PROTHENA CORPORATION plc
Form 10-Q – QUARTERLY REPORT
For the Quarter Ended March 31, 2019

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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

	March 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 410,106	$ 427,659
Restricted cash, current	1,352	—
Prepaid expenses and other current assets	3,735	3,731
Total current assets	415,193	431,390
Non-current assets:		
Property and equipment, net	4,632	52,835
Operating lease right-of-use assets	27,234	—
Deferred tax assets	8,903	9,702
Restricted cash, non-current	2,704	4,056
Other non-current assets	868	813
Total non-current assets	44,341	67,406
Total assets	$ 459,534	$ 498,796
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 2,103	$ 1,470
Accrued research and development	4,738	5,370
Income taxes payable, current	290	54
Lease liability, current	4,810	—
Build-to-suit lease obligation, current	—	1,645
Restructuring liability	—	461
Other current liabilities	2,965	5,926
Total current liabilities	14,906	14,926
Non-current liabilities:		
Deferred revenue	110,242	110,242
Deferred rent	—	176
Lease liability, non-current	21,703	—
Build-to-suit lease obligation, non-current	—	49,901
Other liabilities	553	553
Total non-current liabilities	132,498	160,872
Total liabilities	147,404	175,798
Commitments and contingencies (Note 6)		
Shareholders' equity:		
Euro deferred shares, €22 nominal value:	—	—
Authorized shares — 10,000 at March 31, 2019 and December 31, 2018		
Issued and outstanding shares — none at at March 31, 2019 and December 31, 2018		
Ordinary shares, $0.01 par value:	399	399
Authorized shares — 100,000,000 at March 31, 2019 and December 31, 2018		
Issued and outstanding shares — 39,864,561 and 39,863,711 at March 31, 2019 and December 31, 2018, respectively		
Additional paid-in capital	926,804	920,594
Accumulated deficit	(615,073)	(597,995)
Total shareholders' equity	312,130	322,998
Total liabilities and shareholders' equity	$ 459,534	$ 498,796

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,	
	2019	2018
Collaboration revenue	$ 186	$ 227
Total revenue	186	227
Operating expenses:		
Research and development	13,296	34,706
General and administrative	9,905	14,229
Restructuring charges (credits)	(61)	—
Total operating expenses	23,140	48,935
Loss from operations	(22,954)	(48,708)
Other income (expense):		
Interest income, net	2,304	200
Other expense, net	(17)	(272)
Total other income (expense), net	2,287	(72)
Loss before income taxes	(20,667)	(48,780)
Provision for (benefit from) income taxes	198	(37)
Net loss	$ (20,865)	$ (48,743)
Basic and diluted net loss per share	$ (0.52)	$ (1.26)
Shares used to compute basic and diluted net loss per share	39,864	38,684

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,	
	2019	**2018**
Operating activities		
Net loss	$ (20,865)	$ (48,743)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	385	797
Share-based compensation	6,205	6,902
Deferred income taxes	(195)	395
Interest expense under build-to-suit lease obligation	—	908
Amortization of right-of-use assets	1,296	—
Changes in operating assets and liabilities:		
Accounts receivable	(5)	(99,772)
Prepaid and other assets	(54)	422
Deferred revenue	—	110,242
Accounts payable, accruals and other liabilities	(2,598)	(2,735)
Restructuring liability	(461)	—
Operating lease liabilities	(1,143)	—
Net cash used in operating activities	(17,435)	(31,584)
Investing activities		
Purchases of property and equipment	(131)	(181)
Proceeds from disposal of fixed assets	8	—
Net cash used in investing activities	(123)	(181)
Financing activities		
Proceeds from subscription of ordinary shares	—	39,758
Proceeds from issuance of ordinary shares upon exercise of stock options	5	4,380
Reduction of build-to-suit lease obligation	—	(954)
Net cash provided by financing activities	5	43,184
Net increase (decrease) in cash, cash equivalents and restricted cash	(17,553)	11,419
Cash, cash equivalents and restricted cash, beginning of the year	431,715	421,676
Cash, cash equivalents and restricted cash, end of the period	$ 414,162	$ 433,095
Supplemental disclosures of cash flow information		
Cash paid (refunds received) for income taxes, net	$ 54	$ —
Supplemental disclosures of non-cash investing and financing activities		
Acquisition of property and equipment included in accounts payable and accrued liabilities	$ 8	$ 79
Right-of-use assets recorded upon adoption of ASC 842	$ 28,530	$ —
Reduction of build-to-suit lease obligation upon adoption of ASC 842	$ (51,546)	$ —
Reduction of amounts capitalized under build-to-suit lease upon adoption of ASC 842	$ (46,760)	$ —
Reduction of capitalized interest under build-to-suit lease upon adoption of ASC 842	$ (1,099)	$ —
Receivable from option exercises	$ —	$ 19

See accompanying Notes to Condensed Consolidated Financial Statements.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the statement of financial position that sum to the total of the same such amounts shown in the Condensed Consolidated Statements of Cash Flows.

	Three Months Ended March 31,	
	2019	2018
Cash and cash equivalents	$ 410,106	$ 429,039
Restricted cash, current	1,352	—
Restricted cash, non-current	2,704	4,056
Total cash, cash equivalents and restricted cash, end of the period	$ 414,162	$ 433,095

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

	Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount			
Balances at December 31, 2018	**39,863,711**	**$ 399**	**$ 920,594**	**$ (597,995)**	**$ 322,998**
Cumulative adjustment to accumulated deficit upon adoption of ASC-842	—	—	—	3,787	3,787
Share-based compensation	—	—	6,205	—	6,205
Issuance of ordinary shares upon exercise of stock options	850	—	5	—	5
Net loss	—	—	—	(20,865)	(20,865)
Balances at March 31, 2019	**39,864,561**	**$ 399**	**$ 926,804**	**$ (615,073)**	**$ 312,130**

	Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount			
Balances at December 31, 2017	**38,482,764**	**$ 385**	**$ 849,154**	**$ (442,350)**	**$ 407,189**
Issuance of ordinary shares under share subscription agreement with Celgene	1,174,536	12	39,746	—	39,758
Share-based compensation	—	—	6,902	—	6,902
Issuance of ordinary shares upon exercise of stock options	164,499	1	4,398	—	4,399
Net loss	—	—	—	(48,743)	(48,743)
Balances at March 31, 2018	**39,821,799**	**$ 398**	**$ 900,200**	**$ (491,093)**	**$ 409,505**

See accompanying Notes to Consolidated Financial Statements.

1. Organization

Description of Business

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

The Company was formed on September 26, 2012 under the laws of Ireland and re-registered as an Irish public limited company on October 25, 2012. The Company's ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012 and currently trade on The Nasdaq Global Select Market.

Liquidity and Business Risks

As of March 31, 2019, the Company had an accumulated deficit of $615.1 million and cash and cash equivalents of $410.1 million.

Based on the Company's business plans, management believes that the Company's cash and cash equivalents at March 31, 2019 are sufficient to meet its obligations for at least the next twelve months. To operate beyond such period, or if the Company elects to increase its spending on research and development programs significantly above current long-term plans or enters into potential licenses and or other acquisitions of complementary technologies, products or companies, the Company may need additional capital. The Company expects to continue to finance future cash needs that exceed its cash from operating activities primarily through its current cash and cash equivalents, its collaborations with Roche and Celgene, and to the extent necessary, through proceeds from public or private equity or debt financings, loans and other collaborative agreements with corporate partners or other arrangements.

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

2. Summary of Significant Accounting Policies

Basis of Preparation and Presentation of Financial Information

These 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 U.S. Securities and Exchange Commission (the "SEC") on March 15, 2019 (the "2018 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.

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, 2019, from the significant accounting policies described in Note 2 of the Notes to Consolidated Financial Statements in the 2018 Form 10-K, with the exception of those noted below.

Recently Adopted Accounting Pronouncement

In August 2018, the SEC issued Final Rule 33-10532, which updates and simplifies certain disclosure requirements. The rule was effective for filings on or after November 5, 2018. However, the SEC released guidance advising it will not object to a registrant adopting the requirement to include changes in stockholders' equity in the Form 10-Q for the first quarter beginning after the effective date of the rule (e.g. for a calendar year-end company, the first quarter of fiscal year 2019). The following amendments from the Final Rule 33-10532 are applicable to the Company: (1) an analysis of changes in stockholders' equity will now be required for the current and comparative year-to-date interim periods; and (2) for market price information, a registrant will disclose the ticker symbol of its common equity instead of disclosure of the high and low trading prices of an entity's common stock for specified quarterly periods. The Company's disclosure reflects the applicable amendments.

In February 2016, the FASB issued Accounting Standards Update 2016-02 Topic 842, Leases ("ASC 842"), which requires lessees to recognize assets and liabilities for leases with lease terms of more than 12 months and disclose key information about leasing arrangements. ASC 842 was subsequently amended by ASU 2018-01, Land Easement Practical Expedient for Transition to Topic 842; ASU 2018-10, Codification Improvements to Topic 842, Leases; ASU 2018-11, Targeted Improvements; ASU 2018-20, Narrow-Scope Improvements for Lessors; and ASU 2019-01, Codification Improvements. Under the new standard, a lessee will recognize liabilities on the balance sheet, initially measured at the present value of the lease payments, and right-of-use (ROU) assets representing its right to use the underlying asset for the lease term. For leases with a term of 12 months or less at the commencement date, a lessee is permitted to make an accounting policy election not to recognize lease assets and lease liabilities. The new standard also eliminates the previous build-to-suit lease accounting guidance, which results in the derecognition of build-to-suit assets and liabilities that remained on the balance sheet after the end of the construction period. 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. The new guidance requires both types of leases to be recognized on the balance sheet. The Company adopted the new standard on January 1, 2019 using the modified retrospective transition method wherein the effective date is its date of initial application. Consequently, prior period amounts are not adjusted and continue to be reported in accordance with the Company’s historical accounting under ASC 840. The new standard provides a number of optional practical expedients in transition. The Company elected the "package of practical expedients", which permitted the Company not to reassess under the new standard its prior conclusions about lease identification, lease classification and initial direct cost. The Company did not elect the use-of-hindsight or the practical expedient pertaining to land easements; the latter not being applicable to the Company. For the Company's build-to-suit lease, Prothena has historically excluded executory costs, when part of the fixed payments in a lease contract, as part of the minimum rental payment disclosed in its financial statements footnote for the Current SSF Facility lease under ASC 840. Executory cost of a lease includes costs of taxes, insurance and maintenance (including common area maintenance). With the selection of practical expedient, the Company believes it is appropriate to continue applying the same accounting policy with its transition to ASC 842 (i.e. exclude the executory cost in determining the minimum rental payment).

As of January 1, 2019, the Company recorded $3.8 million change to the opening balance of the accumulated deficit for the cumulative effect of applying ASC 842, which included a reduction of $1.0 million in deferred tax assets. See Note 6, “Commitments and Contingencies,” which provides additional details on the Company's current lease arrangements. The impact of the adoption of ASC 842 on the accompanying Condensed Consolidated Balance Sheet as of January 1, 2019 was as follows (in thousands):

	December 31, 2018	Adjustments due to the Adoption of Topic 842	January 1, 2019
Property and equipment, net	$ 52,835	$ (47,859)	$ 4,976
Operating lease right-of-use assets	$ —	$ 28,530	$ 28,530
Deferred tax assets	$ 9,702	$ (994)	$ 8,708
Lease liability, current	$ —	$ 4,717	$ 4,717
Other current liabilities[1]	$ 5,926	$ (44)	$ 5,882
Build-to-suit lease obligation, current	$ 1,645	$ (1,645)	$ —
Lease liability, non-current	$ —	$ 22,939	$ 22,939
Build-to-suit lease obligation, non-current	$ 49,901	$ (49,901)	$ —
Deferred rent, non-current	$ 176	$ (176)	$ —
Accumulated deficit	$ (597,995)	$ 3,787	$ (594,208)

[1] Amount as of December 31, 2018 includes Deferred rent, current.

The adjustments due to the adoption of ASC 842 relate to (1) the change in classification of build-to-suit lease under ASC 840 for the Company's current facility in South San Francisco, California to an operating lease under ASC 842 and as a result the Company derecognized its build-to-suit asset of $47.9 million under Property and equipment, net as of December 31, 2018 and related liability of $51.5 million, and (2) recognized an operating lease right-of-use asset of $28.5 million and operating lease liability of $27.7 million on the condensed consolidated balance sheet for the Company's operating lease. The right-of-use asset includes tenant improvements added by the Company wherein the lessor was deemed the accounting owner, net of tenant improvement allowance paid by the lessor. The Company has no debt and has not had an established incremental borrowing rate. For the purpose of estimating the incremental borrowing rate in the adoption of ASC 842, the Company inquired with banks that had business relationship with the Company to determine the Company's collateralized incremental borrowing rate. The discount rate used to determine the lease liability was 4.25%. There is no change in the accounting of the Sub-Sublease of the Current SSF Facility upon adoption of ASC 842. Further, the Company's operating lease at Dublin is not included in the lease liability and right-of-use asset recorded due to its nominal amount.

For the purpose of the adoption of ASC 842, the Company also performed an evaluation of its other contracts with customers and suppliers in accordance with ASC 842 and determined that, except for the office leases described in Note 6, Commitments and Contingencies (a nominal operating lease for medical monitoring equipment and a nominal operating lease for office equipment), none of the Company’s contracts contain a lease.

Leases

At the inception, the Company determines if an arrangement is a lease. If so, the Company evaluates the lease agreement to determine whether the lease is an operating or capital using the criteria in ASC 842. The Company does not recognize right-of-use assets and lease liabilities that arise from short-term leases for any class of underlying assets.

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

Operating Leases

Operating leases are included in the operating lease right-of-use assets, lease liability, current and lease liability, non-current in the Company's Condensed Consolidated Balance Sheets. Operating lease right-of-use assets represent the Company’s right to use an underlying asset for the lease term and lease liabilities represent the Company’s obligation to make lease payments arising from the lease. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of minimum lease payments over the lease term. In determining the present value of lease payments, the Company uses its incremental borrowing rate based on information available at the lease commencement date. The operating lease right-of-use assets also include any lease prepayments made and exclude lease incentives including rent abatements and/or concessions and rent holidays. Tenant improvements made by the Company as a lessee in which they are deemed to be owned by the lessor is viewed as lease prepayments by the Company and included in the operating lease right-of-use assets. Lease expense is recognized on a straight-line basis over the expected lease term. For lease agreements entered after the adoption of ASC 842 that include lease and non-lease components, such components are generally accounted separately.

Segment and Concentration of Risks

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

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

The receivable from Roche recorded in prepaid expenses and other current assets in the Condensed Consolidated Balance Sheet are amounts due from a Roche entity located in Switzerland under the License Agreement that became effective January 22, 2014. Revenue recorded in the Condensed Consolidated Statements of Operations consists of reimbursement from Roche for research and development services. The Company's credit risk exposure is up to the extent recorded on the Company's Condensed Consolidated Balance Sheet.

As of March 31, 2019, $4.6 million of the Company's long-lived assets were held in the U.S. and none were in Ireland. As of December 31, 2018, $52.8 million of the Company's long-lived assets were held in the U.S. and none were in Ireland.

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

Recent Accounting Pronouncements

In November 2018, the FASB issued Accounting Standards Update 2018-18 ("ASU 2018-18"), Collaborative Arrangements: Clarifying the Interaction between Topic 808 and Topic 606, which clarifies when transactions between collaborative arrangement participants are in the scope of ASC 606 and provides some guidance on presentation of transactions not in the scope of ASC 606. This ASU is effective for public business entities for annual and interim periods in fiscal years beginning after December 15, 2019. Early adoption is permitted as long as entities have already adopted the guidance in ASC 606. The Company does not currently expect the adoption of ASU 2018-18 to have an impact on its consolidated financial statements. The Company will continue to evaluate the impact of ASU 2018-18 on its consolidated financial statements in connection with Roche License Agreement and Celgene Collaboration Agreement.

In March 2019, the FASB issued Accounting Standards Update 2019-01 ("ASU 2019-01"), Leases: Codification Improvements. ASU 2019-01 addresses the following three issues: (1) determining the fair value of the underlying assets by lessors that are not manufacturers or dealers; (2) presentation on the statement of cash flows for sales-type and direct financing leases; and (3) clarification of interim disclosure requirements during transition. This update clarifies that entities adopting ASC 842 do not need to provide interim disclosures about the effect on income in the year of adoption. The transition and effective date provision for ASU 2019-01 is only applicable to issue (1) and issue (2), which is for fiscal year beginning after December 15, 2019, and interim periods within those fiscal years. Early application is permitted. Transition and effective date is not applicable for issue (3) because the amendment for that issue is to the original transition requirement in ASC 842. The Company's disclosure related to the adoption of ASC 842 reflects the exemption noted in ASU 2019-01. The remaining two issues are not applicable to the Company.

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 consisted of $385.1 million and $306.2 million in money market funds included in cash and cash equivalents at March 31, 2019 and December 31, 2018, respectively.

4. Composition of Certain Balance Sheet Items

Property and Equipment, net

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

	March 31, 2019	December 31, 2018
Machinery and equipment	$ 9,212	$ 9,693
Leasehold improvements	974	98
Purchased computer software	1,303	1,303
Build-to-suit property[1]	—	52,245
	11,489	63,339
Less: accumulated depreciation and amortization	(6,857)	(10,504)
Property and equipment, net	$ 4,632	$ 52,835

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[1] *The Company derecognized its build-to-suit asset for its current facility in South San Francisco on January 1, 2019 upon adoption of ASC 842 due to a change in classification of its build-to-suit lease under ASC 840 to an operating lease under ASC 842.*

Depreciation expense was $0.4 million and $0.8 million for the three months ended March 31, 2019 and 2018, respectively.

Other Current Liabilities

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

	March 31, 2019	December 31, 2018
Payroll and related expenses	$ 2,182	$ 4,507
Professional services	399	1,097
Deferred rent	—	44
Other	384	278
Other current liabilities	$ 2,965	$ 5,926

5. Net Loss Per Ordinary Share

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

during the three months ended March 31, 2019 and 2018, 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):

	Three Months Ended March 31,	
	2019	2018
Numerator:		
Net loss	$ (20,865)	$ (48,743)
Denominator:		
Weighted-average ordinary shares outstanding	39,864	38,684
Net loss per share:		
Basic and diluted net loss per share	$ (0.52)	$ (1.26)

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

	Three Months Ended March 31,	
	2019	2018
Stock options to purchase ordinary shares	7,253	5,227

6. Commitments and Contingencies

Lease Commitments

The Company adopted ASC 842 effective January 1, 2019. Prior period amounts have not been adjusted and continued to be reported in accordance with the Company's historical accounting under ASC 840. For lease arrangements entered prior to the adoption of ASC 842, right-of-use asset and lease liability are determined based on the present value of minimum lease payments over the remaining lease term and the Company's incremental borrowing rate based on information available as of January 1, 2019. The right-of-use asset also includes any lease prepayments made and excludes unamortized lease incentives including rent abatements and/or concessions and rent holidays. Tenant improvements made by the Company as a lessee in which they are deemed to be owned by the lessor is viewed as lease prepayments by the Company and are included in the right-of-use asset. Lease expense is recognized on a straight-line basis over the expected lease term. For the three months ended March 31, 2019, total operating lease cost was $1.6 million and total cash paid against the operating lease liability was $1.4 million. See Note 2 ,"Summary of Significant Accounting Policies," which provides additional details on the Company's adoption of ASC 842.

Prior to the adoption of ASC 842, the Company recognized rent expense for its operating leases on a straight-line basis over the noncancelable lease term and recorded the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contained escalation clauses, rent abatements and/or concessions, such as rent holidays and landlord or tenant incentives or allowances, the Company applied them in the determination of straight-line rent expense over the lease term. The Company recorded the tenant improvement allowance for operating leases as deferred rent and associated expenditures as leasehold improvements that were being amortized over the shorter of their estimated useful life or the term of the lease. Rent expense was $0.2 million for the three months ended March 31, 2018.

As of March 31, 2019, the Company performed an evaluation of its other contracts with customers and suppliers in accordance with ASC 842 and have determined that, except for the leases described below, a nominal operating lease for medical monitoring equipment and a nominal operating lease for office equipment, none of the Company's contracts contain a lease.

Current SSF Facility

In March 2016, the Company entered into a noncancelable operating sublease (the "Lease") to lease 128,751 square feet of office and laboratory space in South San Francisco, California, U.S. (the "Current SSF Facility"). Subsequently, in April 2016, the Company took possession of the Current SSF Facility. The Lease includes a free rent period and escalating rent payments and has a remaining lease term of 4.8 years 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. Prior to the adoption of ASC 842 on January 1, 2019, this Lease was considered a build-to-suit lease.

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 ASC 840. Accordingly, for accounting purposes, the Company was the deemed owner of the building during the construction period under ASC 840 and the Company capitalized $36.5 million within property and equipment, net, including $1.2 million for capitalized interest and recognized a corresponding build-to-suit obligation in other non-current liabilities in the Consolidated Balance Sheets as of December 31, 2018. The Company has also recognized structural and non-structural tenant improvements totaling $15.8 million as of December 31, 2018 as an addition to the build-to-suit lease property for amounts incurred by the Company during the construction period, of which $14.2 million were reimbursed by the landlord during the year ended December 31, 2016 through the tenant improvement allowance. Under ASC 840, the Company increased its financing obligation for the additional building costs reimbursements received from the landlord during the construction period. For the three months ended March 31, 2018, the Company recorded rent expense associated with the ground lease of $0.1 million and interest expense of $0.9 million in its Condensed Consolidated Statements of Operations. No corresponding amounts were recorded for the three months ended March 31, 2019 due to the adoption of ASC 842.

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 under ASC 840 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 was accounted for under ASC 840 as a financing lease, given the Company's expected continuing involvement after the conclusion of the construction period. Prior to the adoption of the new lease guidance, ASC 842, the build-to-suit lease property was recorded on the Company's Consolidated Balance Sheet as of December 31, 2018 at its historical cost of $52.3 million and the total amount of the build-to-suit lease obligation as of December 31, 2018 was $51.5 million, of which $1.6 million and $49.9 million were classified as current and non-current liability, respectively.

The Lease is considered to be an operating lease under ASC 842 as it does not meet the criteria of a capital lease under ASC 840 and the construction was completed before the adoption of ASC 842. The Company derecognized the build-to-suit property and build-to-suit lease obligations upon adoption of ASC 842 and as of March 31, 2019, the operating lease right-of-use asset and lease liability was $27.2 million and $26.5 million, respectively. The discount rate used to determine the lease liability was 4.25%.

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. The Company is entitled to a $1.4 million reduction in the face amount of the standby letter of credit on the third anniversary of the contractual rent commencement and another $1.4 million on the fifth anniversary of the contractual rent commencement. As a condition to the reduction of the standby letter of credit amount, no uncured default by the Company shall then exist under the Lease. As of March 31, 2019, none of the standby letter of credit amount has been used.

Sub-Sublease of Current SSF Facility

On July 18, 2018, the Company entered into a Sub-Sublease Agreement (the "Sub-Sublease") with Assembly Biosciences, Inc. (the "Sub-Subtenant") for Sub-Subtenant to sub-sublease from the Company approximately 46,641 square feet of office and laboratory space of the Company's Current SSF Facility. Prior to the adoption of ASC 842 on January 1, 2019, this Sub-Sublease was considered an operating lease. There is no change in the accounting of the Sub-Sublease of the Current SSF Facility upon adoption of ASC 842. For the three months ended March 31, 2019, the Company recorded $733,000 sub-lease rental income as an offset to its operating expenses.

The Sub-Sublease provides for initial annual base rent for the complete Sub-Subleased Premises of approximately $2.7 million, with increases of approximately 3.5% in annual base rent on September 1, 2019 and each anniversary thereof. The Sub-Sublease rental income excludes reimbursements for executory costs received from the Sub-Subtenant. The Sub-Sublease became effective on September 24, 2018 and has a term of 5.2 years which terminates on December 15, 2023. The Sub-Sublease will

terminate if the Master Lease or the Sublease terminates. The Company or the Sub-Subtenant may elect, subject to limitations set forth in the Sub-Sublease, to terminate the Sub-Sublease following a material casualty or condemnation affecting the Subleased Premises. The Company may terminate the Sub-Sublease following an event of default, which is defined in the Sub-Sublease to include, among other things, non-payment of amounts owing by the Sub-Subtenant under the Sub-Sublease.

The Company is required under the Lease to pay to the sublandlord 50% of that portion of the cash sums and other economic consideration received from the Sub-Subtenant that exceeds the base rent paid by the Company to the sublandlord after deducting certain of the Company's costs.

Dublin

In September 2018, the Company entered into an agreement to lease 133 square feet of office space in Dublin, Ireland. The lease has a term of one year and expires on November 30, 2019. The Dublin Lease also has an automatic renewal clause, in which the agreement will be extended automatically for successive periods equal to the current term but no less than 3 months, unless the agreement is cancelled by the Company. This operating lease is not included in the lease liability and operating lease right-of-use asset recorded due to its nominal amount.

As of March 31, 2019, the Company is obligated to make lease payments over the remaining term of the lease of approximately €15,000, or $17,000 as converted using an exchange rate as of March 31, 2019.

Future minimum payments under the above-described noncancelable operating leases, including a reconciliation to the lease liabilities recognized in the Condensed Consolidated Balance Sheets, and future minimum rentals to be received under the Sub-Sublease as of March 31, 2019 are as follows (in thousands):

Year Ended December 31,	Operating Leases	Sub-Sublease Rental
2019 (9 months)	4,387	$ 2,067
2020	5,979	2,843
2021	6,165	2,944
2022	6,350	3,047
2023	6,535	3,019
Total	29,416	$ 13,920
Less: Present value adjustment	(2,886)	
Nominal lease payments	(17)	
Lease liability	$ 26,513	

Under ASC 840, future minimum payments under operating lease, build-to-suit lease obligation and future minimum rentals to be received under the Sub-Sublease as of December 31, 2018 was as follows (in thousands):

Year Ended December 31,	Operating Lease	Expected Cash Payments Under Build-To-Suit Lease Obligation	Sub-Sublease Rental
2019	$ 23	$ 5,803	$ 2,746
2020	—	5,979	2,843
2021	—	6,165	2,944
2022	—	6,350	3,047
2023	—	6,535	3,019
Total	$ 23	$ 30,832	$ 14,599

Indemnity Obligations

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

agreements is unlimited; however, the Company has a director and officer liability insurance policy that limits its exposure and enables the Company to recover a portion of any future amounts paid. As a result of its insurance policy coverage, the Company believes the estimated fair value of these indemnification agreements is minimal. Accordingly, the Company had no liabilities recorded for these agreements as of March 31, 2019 and December 31, 2018.

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, 2019, the Company had non-cancelable purchase commitments to suppliers for $1.2 million of which $1.0 million is included in accrued current liabilities, and contractual obligations under license agreements of $1.2 million of which $0.1 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, 2019 (in thousands):

	Total	2019	2020	2021	2022	2023	Thereafter
Purchase Obligations [1]	$ 1,174	$ 1,174	$ —	$ —	$ —	$ —	$ —
Contractual obligations under license agreements [2]	1,160	275	95	95	80	80	535
Total	$ 2,334	$ 1,449	$ 95	$ 95	$ 80	$ 80	$ 535

[1] *Purchase obligations consist of non-cancelable purchase commitments to suppliers.*

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

Legal Proceedings

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

7. Significant Agreements

Roche License Agreement

In December 2013, the Company through its wholly owned subsidiary Prothena Biosciences Limited and Prothena Biosciences Inc entered into a License, Development, and Commercialization Agreement (the "License Agreement") with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") to develop and commercialize certain antibodies that target α-synuclein, including prasinezumab, which are referred to collectively as "Licensed Products." Upon the effectiveness of the License Agreement in January 2014, the Company granted to Roche an exclusive, worldwide license to develop, make, have made, use, sell, offer to sell, import and export the Licensed Products. The Company retained certain rights to conduct development of the Licensed Products and an option to co-promote prasinezumab in the U.S. During the term of the License Agreement, the Company and Roche will work exclusively with each other to research and develop antibody products targeting alpha-synuclein (or α-synuclein) potentially including incorporation of Roche's proprietary Brain Shuttle™ technology to potentially increase delivery of therapeutic antibodies to the brain. The License Agreement provided for Roche making an upfront payment to the Company of $30.0 million, which was received in February 2014; making a clinical milestone payment of $15.0 million upon initiation of the Phase 1 study for prasinezumab, which was received in May 2014; and making a clinical milestone payment of $30.0 million upon dosing of the first patient in the Phase 2 study for prasinezumab, which was achieved in June 2017.

For prasinezumab, Roche is also obligated to pay:

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

- up to an additional $175.0 million upon achievement of ex-U.S. commercial sales milestones; and
- tiered, high single-digit to high double-digit royalties in the teens on ex-U.S. annual net sales, subject to certain adjustments.

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

The Company filed an Investigational New Drug Application ("IND") with the FDA for prasinezumab and subsequently initiated a Phase 1 study in 2014. Following the Phase 1 study, Roche became primarily responsible for developing, obtaining and maintaining regulatory approval for and commercializing Licensed Products. Roche also became responsible for the clinical and commercial manufacture and supply of Licensed Products.

In addition, the Company has an option under the License Agreement to co-promote prasinezumab in the U.S. in the Parkinson's disease indication. If the Company exercises such option, it may also elect to co-promote additional Licensed Products in the U.S. approved for Parkinson's disease. Outside the U.S., Roche will have responsibility for developing and commercializing the Licensed Products. Roche bears all costs that are specifically related to obtaining or maintaining regulatory approval outside the U.S. and will pay the Company a variable royalty based on annual net sales of the Licensed Products outside the U.S.

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

The License Agreement continues on a country-by-country basis until the expiration of all payment obligations under the License Agreement. The License Agreement may also be terminated (i) by Roche at will after the first anniversary of the effective date of the License Agreement, either in its entirety or on a Licensed Product-by-Licensed Product basis, upon 90 days' prior written notice to the Company prior to first commercial sale and 180 days' prior written notice to Prothena after first commercial sale, (ii) by either party, either in its entirety or on a Licensed Product-by-Licensed Product or region-by-region basis, upon written notice in connection with a material breach uncured 90 days after initial written notice, and (iii) by either party, in its entirety, upon insolvency of the other party. The License Agreement may be terminated by either party on a patent-by-patent and country-by-country basis if the other party challenges a given patent in a given country. The Company's rights to co-develop Licensed Products under the License Agreement will terminate if the Company commences certain studies for certain types of competitive products. The Company's rights to co-promote Licensed Products under the License Agreement will terminate if the Company commences a Phase 3 study for such competitive products.

The License Agreement cannot be assigned by either party without the prior written consent of the other party, except to an affiliate of such party or in the event of a merger or acquisition of such party, subject to certain conditions. The License Agreement also includes customary provisions regarding, among other things, confidentiality, intellectual property ownership, patent prosecution, enforcement and defense, representations and warranties, indemnification, insurance, and arbitration and dispute resolution.

Collaboration Accounting

The License Agreement was evaluated under ASC 808, Collaborative Agreements. At the outset of the License Agreement, the Company concluded that it did not qualify as collaboration under ASC 808 because the Company does not share significant risks due to the net profit and loss split (under which Roche incurs substantially more of the costs of the collaboration) and because of the Company's opt-out provision. The Company believes that Roche will be the principal in future sales transactions with third parties as Roche will be the primary obligor bearing inventory and credit risk. The Company will record its share of pre-tax commercial profit generated from the collaboration as collaboration revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods. Prior to commercialization of a Licensed Product, the Company's portion of the expenses related to the License Agreement reflected on its income statement will be limited to R&D expenses. After commercialization, if the Company opts-in to co-detail commercialization, expenses related to commercial capabilities, including expenses related to the establishment of a field sales force and other activities to support the Company's commercialization efforts, will be recorded as sales, general and administrative ("SG&A") expense and will be factored into the computation of the profit

and loss share. The Company will record the receivable related to commercialization activities as collaboration revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Adoption of ASC 606, Revenue from Contracts with Customers

The Company adopted ASC 606, Revenue from Contracts with Customers, as of January 1, 2018 using the modified retrospective transition method. The Company recognized the cumulative effect of applying the new revenue standard as an adjustment to the opening balance of the accumulated deficit as of January 1, 2018.

As of January 1, 2018, the Company did not record any changes to the opening balance of the accumulated deficit since the cumulative effect of applying the new revenue standard was the same as applying ASC 605. The impact of the adoption of ASC 606 to revenues for the three months ended March 31, 2018 was an increase of $0.2 million, which represents the revenue recognized for the development services provided by the Company during the period that is reimbursable by Roche. Historically, the Company recorded such reimbursement as an offset against its R&D expenses under ASC 605. Upon the adoption of ASC 606, the reimbursement for development services is now included as part of the Company's collaboration revenue.

Performance Obligations

The License Agreement was evaluated under ASC 606. The License Agreement includes the following distinct performance obligations: (1) the Company's grant of an exclusive royalty bearing license, with the right to sublicense to develop and commercialize certain antibodies that target α-synuclein, including prasinezumab, and the initial know how transfer which was delivered at the effective date (the "Royalty Bearing License"); (2) the Company's obligation to supply clinical material as requested by Roche for a period up to twelve months (the "Clinical Product Supply Obligation"); (3) the Company's obligation to provide manufacturing related services to Roche for a period up to twelve months (the "Supply Services Obligation"); (4) the Company's obligation to prepare and file the IND (the "IND Obligation"); and (5) the Company's obligation to provide development activities under the development plan during Phase 1 clinical trials (the "Development Services Obligation"). Revenue allocated to the above performance obligations under the License Agreement are recognized when the Company has satisfied its obligations either at a point in time or over a period of time.

The Company concluded that the Royalty Bearing License and the Clinical Product Supply Obligation were satisfied at a point in time. The Royalty Bearing License is considered to be a functional intellectual property, in which the revenue would be recognized at the point in time since (a) the Company concluded that the license to Roche has a significant stand-alone functionality, (b) the Company does not expect the functionality of the intellectual property to be substantially changed during the license period as a result of activities of Prothena, and (c) Prothena's activities transfer a good or service to Roche. The Clinical Product Supply Obligation does not meet criteria for over time recognition; as such, the revenue related to such performance obligation was recognized the point in time at which Roche obtained control of manufactured supplies, which occurred during the first quarter of 2014.

The Company concluded that the Supply Services Obligation, the IND Obligation and the Development Services Obligation were satisfied over time. The Company utilized an input method measure of progress by basing the recognition period on the efforts or inputs towards satisfying the performance obligation (i.e. costs incurred and the time elapsed to complete the related performance obligations). The Company determined that such input method provides an appropriate measure of progress toward complete satisfaction of such performance obligations.

As of March 31, 2019 and December 31, 2018, there were no remaining performance obligations under License Agreement since the obligations related to research and development activities were only for the Phase 1 clinical trial and the remaining obligations were delivered or performed.

Transaction Price

According to ASC 606-10-32-2, the transaction price is the amount of consideration to which an entity expects to be entitled in exchange for transferring promised goods or services to a customer, excluding amounts collected on behalf of third parties (for example, some sales taxes). The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Factors considered in the determination of the transaction price include, among other things, estimated selling price of the license and costs for clinical supply and development costs.

The initial transaction price under the License Agreement, pursuant to ASC 606, was $55.1 million, including $45.0 million for the Royalty Bearing License, $9.1 million for the IND and Development Services Obligations, and $1.1 million for the Supply Services Obligation. The $45.0 million for the Royalty Bearing License included the upfront payment of $30.0 million and the

clinical milestone payment of $15.0 million upon initiation of the Phase 1 clinical trial of prasinezumab, both of which were made in 2014. The remaining transaction price amounts the Company expected to receive as reimbursements were based on costs expected to be paid to third parties and other costs to be incurred by the Company in order to satisfy its performance obligations. They are considered to be variable considerations not subject to constraint. The Company did not incur any incremental costs, such as commissions, to obtain or fulfill the License Agreement.

Under ASC 606, the transaction price was allocated to the performance obligations as follows: $48.9 million to the Royalty Bearing License; $4.6 million to the IND and Development Services Obligations; $1.1 million to the Clinical Product Supply Obligation; and $0.6 million to the Supply Services Obligation. As of March 31, 2019, the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied is $nil. Prior to the adoption of ASC 606, the transaction price was allocated to the deliverables as follows: $35.6 million to the Royalty Bearing License; $3.3 million to the IND and Development Services Obligations; $0.8 million to the Clinical Product Supply Obligation; and $0.4 million to the Supply Services Obligation.

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

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

Significant Payment Terms

Payments for development services are due within 45 days after receiving an invoice from the Company. Variable considerations related to clinical and regulatory milestone payments are constrained due to high likelihood of a revenue reversal. The payment term for all milestone payments are due within 45 days after the achievement of the relevant milestone and receipt by Roche of an invoice for such an amount from the Company.

According to ASC 606-10-32-17, a significant financing component does not exist if a substantial amount of the consideration promised by the customer is variable, and the amount or timing of that consideration varies on the basis of the occurrence or nonoccurrence of a future event that is not substantially within the control of the customer or the entity. Since a "substantial amount of the consideration" promised by Roche to the Company is variable (i.e., is in the form of either milestone payments or sales-based royalties) and the amount of such variable consideration varies based upon the occurrence or nonoccurrence of future events that are not within the control of either Roche or the Company (i.e., are largely subject to regulatory approval), the License Agreement does not have a significant financing component.

Optional Goods and Services

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

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

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

The Company concluded that Roche's option to have the Company perform Research Services did not represent a "material right" to Roche that it would not have received without entering into the License Agreement. As a result, Roche's option to acquire additional Research Services was not considered a performance obligation at the outset of the License Agreement under ASC 606. Accordingly, this deliverable will become new performance obligation for Prothena when Roche asks Prothena to conduct such Research Services. As of March 31, 2019, there were no remaining Research Services performance obligations. Prior to the adoption of ASC 606, the Company recognized Research Services as collaboration revenue as earned.

Post Contract Deliverables

Any development services provided by the Company after performance of the Development Service Obligation are not considered a contractual performance obligation under the License Agreement, since the License Agreement does not require the Company to provide any development services after completion of the Development Service Obligation. However, the collaboration's Joint Steering Committee approved continued funding for additional development services to be provided by the Company (the "Additional Development Services"). Under the License Agreement and upon the adoption of ASC 606, the Company recognizes the reimbursements for Additional Development Services as collaboration revenue as earned.

Revenue and Expense Recognition

The Company recognized $0.2 million and $0.2 million as collaboration revenue for the three months ended March 31, 2019 and 2018, respectively from Roche for Additional Development Services. Cost sharing payments to Roche are recorded as R&D expenses. The Company recognized $2.8 million in R&D expenses for payments made to Roche during the three months ended March 31, 2019, as compared to $2.4 million for the three months ended March 31, 2018. The Company had accounts receivable from Roche of $7,000 and $2,000 recorded in prepaid expenses and other current assets at March 31, 2019 and December 31, 2018, respectively.

Milestone Accounting

Under the License Agreement, only if the U.S. and or global options are exercised, the Company is eligible to receive milestone payments upon the achievement of development, regulatory and various first commercial sales milestones. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods when the milestone is achieved.

The Company excludes the milestone payments and royalties in the initial transaction price calculation because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The clinical and regulatory milestones under the License Agreement after the point at which the Company could opt-out are considered to be variable considerations with constraint due to the fact that active participation in the development activities that generate the milestones is not required under the License Agreement, and the Company can opt-out of these activities. There are no refunds or claw-back provisions and the milestones are uncertain of occurrence even after the Company has opted out. Based on this determination, these milestones will be recognized when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

In June 2017, the Company achieved a $30.0 million clinical milestone under the License Agreement as a result of dosing of first patient in Phase 2 study for prasinezumab. The milestone was accounted for under ASC 605 and was allocated to the units of accounting based on the relative selling price method for income statement classification purposes. As such, the Company recognized $26.6 million of the $30.0 million milestone as collaboration revenue and $3.4 million as an offset to R&D expenses in 2017. The Company did not achieve any clinical and regulatory milestones under the License Agreement during the three months ended March 31, 2019.

Celgene Collaboration Agreement

Overview

On March 20, 2018, the Company, through its wholly owned subsidiary Prothena Biosciences Limited, entered into a Master Collaboration Agreement (the "Collaboration Agreement") with Celgene Switzerland LLC ("Celgene"), a subsidiary of Celgene Corporation, pursuant to which Prothena granted to Celgene a right to elect in its sole discretion to exclusively license rights both in the U.S. (the "US Rights") and on a global basis (the "Global Rights"), with respect to the Company's programs to develop and commercialize antibodies targeting Tau, TDP-43 and an undisclosed target (the "Collaboration Targets"). For each such program, Celgene may exercise its US Rights at the IND filing, and if it so exercises such US Rights would also have a right to expand the license to Global Rights. If Celgene exercises its US Rights for a program, then following the first to occur of (a) completion by the Company, in its discretion and at its cost, of Phase 1 clinical trials for such program or (b) the date on which Celgene elects to assume responsibility for completing such Phase 1 clinical trials (at its cost), Celgene would have decision making authority over development activities and all regulatory, manufacturing and commercialization activities in the U.S.

The Collaboration Agreement provided for Celgene making an upfront payment to the Company of $100.0 million, which was received in April 2018, plus future potential license exercise payments and regulatory and commercial milestones for each program under the Collaboration Agreement, as well as royalties on net sales of any resulting marketed products. In connection with the Collaboration Agreement, the Company and Celgene entered into a Share Subscription Agreement on March 20, 2018, under which Celgene subscribed to 1,174,536 of the Company's ordinary shares for a price of $42.57 per share, for a total of approximately $50.0 million.

Celgene US and Global Rights and Licenses

On a program-by-program basis, following the Company's filing of an IND application for any of the Company's three collaboration programs to Celgene, Celgene may elect in its sole discretion to exercise its US Rights to receive an exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target in the U.S. (the "US License"). If Celgene exercises its US Rights for a collaboration program, it is obligated to pay the Company an exercise fee of approximately $80.0 million per program. Thereafter, following the first to occur of (a) completion by the Company, in its discretion and at its cost, of Phase 1 clinical trials for such program or (b) Celgene's election to assume responsibility to complete such Phase 1 clinical trials (at its cost), Celgene would have the sole right to develop, manufacture and commercialize antibody products targeting the relevant Collaboration Target for such program (the "Collaboration Products") in the U.S.

On a program-by-program basis, following completion of a Phase 1 clinical trial for a collaboration program for which Celgene has previously exercised its US Rights, Celgene may elect in its sole discretion to exercise its Global Rights with respect to such collaboration program to receive a worldwide, exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target (the "Global License"). If Celgene exercises its Global Rights, Celgene would be obligated to pay the Company an additional exercise fee of $55.0 million for such collaboration program. The Global Rights would then replace the US Rights for that collaboration program, and Celgene would have decision making authority over developing, obtaining and maintaining regulatory approval for, manufacturing and commercializing the Collaboration Products worldwide.

After Celgene's exercise of Global Rights for a collaboration program, the Company is eligible to receive up to $562.5 million in regulatory and commercial milestones per program. For obtaining either US Rights or Global Rights for such collaboration program by Celgene, the Company will also be eligible to receive tiered royalties on net sales of Collaboration Products ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds. Such exercise fees, milestones and royalty payments are subject to certain reductions as specified in the Collaboration Agreement, the agreement for US Rights and the agreement for Global Rights.

Celgene will continue to pay royalties on a Collaboration Product-by-Collaboration Product and country-by-country basis, until the latest of (i) expiration of certain patents covering the Collaboration Product, (ii) expiration of all regulatory exclusivity for the Collaboration Product, and (iii) an agreed period of time after the first commercial sale of the Collaboration Product in the applicable country (the "Royalty Term").

Term and Termination

The research term under the Collaboration Agreement continues for a period of six years, which Celgene may extend for up to two additional 12-month periods by paying an extension fee of $10.0 million per extension period. The term of the Collaboration

Agreement continues until the last to occur of the following: (i) expiration of the research term; (ii) expiration of all US Rights terms; and (iii) expiration of all Global Rights terms.

The term of any US License or Global License would continue on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of all Royalty Terms under such agreement.

The Collaboration Agreement may be terminated (i) by either party on a program-by-program basis if the other party remains in material breach of the Collaboration Agreement following a cure period to remedy the material breach, (ii) by Celgene at will on a program-by-program basis or in its entirety, (iii) by either party, in its entirety, upon insolvency of the other party, or (iv) by Prothena, in its entirety, if Celgene challenges a patent licensed by Prothena to Celgene under the Collaboration Agreement.

Share Subscription Agreement

Pursuant to the terms of the Collaboration Agreement, the Company entered into a Share Subscription Agreement (the "SSA") with Celgene, pursuant to which the Company issued, and Celgene subscribed for, 1,174,536 of the Company's ordinary shares (the "Shares") for an aggregate subscription price of approximately $50.0 million, pursuant to the terms and conditions thereof.

Under the SSA, Celgene is subject to certain transfer restrictions. In addition, Celgene will be entitled to request the registration of the Shares with the U.S. Securities and Exchange Commission on Form S-3ASR or Form S-3 following termination of the transfer restrictions if the Shares cannot be resold without restriction pursuant to Rule 144 promulgated under the U.S. Securities Act of 1933, as amended (the "Securities Act").

Collaboration Accounting

The Collaboration Agreement was evaluated under ASC 808, Collaborative Agreements. At the outset of the Collaboration Agreement, the Company concluded that it does not qualify as collaboration under ASC 808 because the Company does not share significant risks due to economics of the collaboration.

Performance Obligations

The Company assessed the Collaboration Agreement and concluded that it represented a contract with a customer within the scope of ASC 606. Per ASC 606, a performance obligation is defined as a promise to transfer a good or service or a series of distinct goods or services. At inception of the Collaboration Agreement, the Company concluded that it does not have material distinct performance obligation as the Company is not obligated to transfer the US License or Global License to Celgene unless Celgene exercises its US Right or Global Right, respectively, and the Company is not obligated to perform development activities under the development plan during preclinical and Phase 1 clinical trials including the regulatory filing of the IND.

The discovery, preclinical and clinical development activities performed by the Company are to be performed at the Company's discretion and therefore are not considered distinct performance obligations under ASC 606. Per the terms of the Collaboration Agreement, the Company may conduct discovery activities to characterize, identify and generate antibodies to become collaboration candidates that target such Collaboration Target, and thereafter may pre-clinically develop collaboration candidates to identify lead candidates that target such Collaboration Target and file an IND with the U.S. Food and Drug Administration (the "FDA") for a Phase 1 clinical trial for such lead candidates.

The Company is not obligated to perform manufacturing activities. Per the terms of the Collaboration Agreement, to the extent that the Company, at its discretion, conducts a program, the Company shall be responsible for the manufacture of collaboration candidates and collaboration products for use in such program, as well as the associated costs. Delivery of manufactured compound (clinical product supply) is not deemed a performance obligation under ASC 606 as the Company is not obligated to transfer supply of collaboration product to Celgene unless Celgene exercises its right to participate in the Phase 1 development.

The options to acquire the US License and Global License for each program will become performance obligations only if and when Celgene chooses to exercise its options for those licenses if those options become available to exercise in the future.

Transaction Price

According to ASC 606-10-32-2, the transaction price is the amount of consideration to which an entity expects to be entitled in exchange for transferring promised goods or services to a customer, excluding amounts collected on behalf of third parties (for example, some sales taxes). The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Factors considered in the determination of the transaction price included, among other things, estimated selling price of the license and costs for clinical supply and development costs.

The initial transaction price under the Collaboration Agreement, pursuant to ASC 606, was $110.2 million, including the $100.0 million upfront payment and $10.2 million premium on the ordinary shares purchased under the SSA.

The Company evaluated the potential obligations to transfer the US Licenses and Global Licenses to Celgene under ASC 606-10-55-42 and 55-43 to determine whether it gave Celgene a "material right" and concluded that Celgene's options to exercise its US Rights or Global Rights represented a "material right" to Celgene that it would not have received without entering into the Collaboration Agreement. However, the obligations to transfer the US Licenses and Global Licenses to Celgene were not considered performance obligations at the outset of the Collaboration Agreement under ASC 606, and will become performance obligations only if and when Celgene chooses to exercise its options.

In addition, the Company did not include the option fees in the initial transaction price because such fees are variable consideration that are contingent on the options to the US Rights and the Global Rights being exercised. Upon the exercise of the US Rights and the Global Rights for a program, the Company will have the obligation to deliver the US License and Global License, respectively, for such program. The Company will include the option fees in the transaction price at a point in time when the Company can conclude that it is probable that a significant revenue reversal will not occur. In addition, the Company did not include in the initial transaction price certain clinical and regulatory milestone payments since these variable considerations are constrained due to the likelihood of a significant revenue reversal.

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

The relative selling price method is based on the Company's best estimate of the selling price of the respective US License or Global License for that program. The best estimate of selling price for the US License and Global License by program was based on a discounted cash flow model. The key assumptions used in the discounted cash flow model used to determine the best estimate of selling price for the US License and Global License included the market opportunity for commercialization of each program in the U.S. or globally depending on the license, the probability of successfully developing and commercializing a given program target, the estimated remaining development costs for the respective program, and the estimated time to commercialization of the drug for that program.

Significant Payment Terms

The upfront payment of $100.0 million was due within ten business days after the effective date of the Collaboration Agreement and was received in April 2018, while all option fees and milestone payments are due within 30 days after the achievement of the relevant milestone by Celgene or receipt by Celgene of an invoice for such an amount from the Company.

The Collaboration Agreement does not have a significant financing component since a substantial amount of consideration promised by Celgene to the Company is variable and the amount of such variable consideration varies based upon the occurrence or nonoccurrence of future events that are not within the control of either Celgene or the Company. Variable considerations related to clinical and regulatory milestone payments and option fees are constrained due to the likelihood of a significant revenue reversal.

Milestone and Royalties Accounting

The Company is eligible to receive milestone payments of up to $90.0 million per program upon the achievement of certain specified regulatory milestones and milestone payments of up to $375.0 million per program upon the achievement of certain specified commercial sales milestones under the US License for such program. The Company is also eligible to receive milestone payments of up to $187.5 million per program upon the achievement of certain specified regulatory milestones and milestone payments of up $375.0 million per program upon the achievement of certain specified commercial sale milestones under the Global License for such program. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible

amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company excluded the milestone payments and royalties in the initial transaction price because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue at a point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company did not achieve any clinical and regulatory milestones under the Collaboration Agreement during the three months ended March 31, 2019.

8. Shareholders' Equity

Ordinary Shares

As of March 31, 2019, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of $0.01 per ordinary share and 39,864,561 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, 2019, 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, 2019. 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.

Celgene Share Subscription Agreement

In connection with the Celgene Collaboration Agreement, the Company entered into a Share Subscription Agreement (the "SSA") with Celgene, pursuant to which the Company issued, and Celgene subscribed for, 1,174,536 of the Company's ordinary shares (the "Shares") for an aggregate subscription price of approximately $50.0 million, of which the fair value of $39.8 million was recorded in shareholders' equity and the premium of $10.2 million was recorded as deferred revenue from Celgene.

Under the SSA, Celgene is subject to certain transfer restrictions. In addition, Celgene will be entitled to request the registration of the Shares with the SEC on Form S-3ASR or Form S-3 following termination of the transfer restrictions if the Shares cannot be resold without restriction pursuant to Rule 144 promulgated under the Securities Act.

9. Share-Based Compensation

2018 Long Term Incentive Plan

In May 2018, the Company's shareholders approved the 2018 Long Term Incentive Plan (the "2018 LTIP"), which provides for the grant of ISOs, NQSOs, SARs, restricted shares, RSUs, performance bonus awards, performance share units awards, dividend equivalents and other share or cash-based awards to eligible individuals. Options under the 2018 LTIP may be granted for periods up to ten years. All options issued to date have had a ten year life. Under the 2018 LTIP, the number of ordinary shares authorized for issuance under the 2018 LTIP is equal to the sum of (a) 1,800,000 shares, (b) 1,177,933 shares that were available for issuance under the 2012 LTIP as of the May 15, 2018 effective date of the 2018 LTIP, and (c) any shares subject to issued and outstanding awards under the 2012 Long Term Incentive Plan (the "2012 LTIP") that expire, are cancelled or otherwise terminate following the effective date of the 2018 LTIP; provided, that no more than 2,500,000 shares may be issued pursuant to the exercise of ISOs.

Amended and Restated 2012 Long Term Incentive Plan

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

Shares Available for Grant

The Company granted 852,975 and 1,093,100 options during the three months ended March 31, 2019 and 2018, respectively, in aggregate under the 2012 LTIP and the 2018 LTIP. The Company's option awards generally vest over four years. As of March 31, 2019, 1,008,188 ordinary shares remained available for grant under the 2018 LTIP, and options to purchase 7,253,048 ordinary shares in aggregate under the 2012 LTIP and the 2018 LTIP were outstanding with a weighted-average exercise price of approximately $24.69 per share.

Share-based Compensation Expense

The Company estimates the fair value of share-based compensation on the date of grant using an option-pricing model. The Company uses the Black-Scholes model to value share-based compensation, excluding RSUs, which the Company values using the fair market value of its ordinary shares on the date of grant. The Black-Scholes option-pricing model determines the fair value of share-based payment awards based on the share price on the date of grant and is affected by assumptions regarding a number of complex and subjective variables. These variables include, but are not limited to, the Company's share price, volatility over the expected life of the awards and actual and projected employee stock option exercise behaviors. Since the Company does not have sufficient historical employee share option exercise data, the simplified method has been used to estimate the expected life of all options. The Company uses its historical volatility for the Company's stock to estimate expected volatility starting January 1, 2018. 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 2023 related to unvested share-based payment awards at March 31, 2019 is $58.2 million. The weighted-average period over which the unearned share-based compensation is expected to be recognized is 3.10 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, 2019 and 2018 was based on awards granted under the 2012 LTIP and the 2018 LTIP. The following table summarizes share-based compensation expense for the periods presented (in thousands):

	Three Months Ended March 31,	
	2019	**2018**
Research and development	$ 2,099	$ 2,258
General and administrative	4,106	4,644
Total share-based compensation expense	$ 6,205	$ 6,902

For the three months ended March 31, 2019, and 2018, the Company recognized tax benefits from share-based awards of $1.2 million and $1.1 million, respectively.

The fair value of the options granted to employees and non-employee directors during the three months ended March 31, 2019 and 2018 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,	
	2019	**2018**
Expected volatility	81.5%	67.2%
Risk-free interest rate	2.5%	2.8%
Expected dividend yield	—%	—%
Expected life (in years)	6.0	6.0
Weighted average grant date fair value	$9.48	$20.67

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, 2019:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2018	6,726,715	$ 26.82	7.39	$ 2,169
Granted	852,975	13.44		
Exercised	(850)	6.41		
Canceled	(325,792)	39.28		
Outstanding at March 31, 2019	7,253,048	$ 24.69	7.86	$ 3,270
Vested and expected to vest at March 31, 2019	6,743,549	$ 25.10	7.75	$ 3,262
Vested at March 31, 2019	2,635,745	$ 31.53	5.62	$ 3,211

The total intrinsic value of options exercised was approximately $6,100 and $2.1 million during the three months ended March 31, 2019 and 2018, respectively, determined as of the date of exercise.

10. Restructuring

In May 2018, the Company commenced a reorganization plan to reduce its operating costs and better align its workforce with the needs of its business following the Company's April 23, 2018 announcement of its decision to discontinue further development of NEOD001. Restructuring charges incurred under this plan primarily consisted of employee termination benefits and contract termination costs primarily associated with exit fees relating to third-party manufacturers that we contracted with for NEOD001 clinical and commercial supplies.

Restructuring charges incurred under this plan primarily consisted of employee termination benefits and contract termination costs primarily associated with exit fees relating to third-party manufacturers that we contracted with for NEOD001 clinical and commercial supplies. Employee termination benefits included severance costs, employee-related benefits, supplemental one-time termination payments and non-cash share-based compensation expense related to the acceleration of stock options. Charges and other costs related to the workforce reduction and structure realignment were presented as restructuring costs in the Condensed Consolidated Statements of Operations. The Company recorded a restructuring credit of approximately $61,000 for the three months ended March 31, 2019. The Company has completed all of its restructuring activities as of March 31, 2019 and does not expect to incur additional costs associated with the restructuring. The cumulative amount incurred to date is $16.1 million as of March 31, 2019.

The following table summarizes the restructuring liability and utilization by cost type associated with the restructuring activities during the three months ended March 31, 2019 (in thousands):

	Restructuring Liability				
	Termination Benefits	Contract Termination Costs	Assets Impairment	Other	Total
Balance at December 31, 2018	$ 461	$ —	$ —	$ —	$ 461
Restructuring charges (credit)	(61)	—	—	—	(61)
Reductions for cash payments	(400)	—	—	—	(400)
Balance at March 31, 2019	$ —	$ —	$ —	$ —	$ —

11. Income Taxes

The major taxing jurisdictions for the Company are Ireland and the U.S. The Company recorded an income tax provision of $198,000 for the three months ended March 31, 2019 as compared to an income tax benefit of $37,000 for three months ended March 31, 2018. 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 net tax shortfall from cancellations 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 ASU 2016-09 on January 1, 2017. Pursuant to the adoption of ASU 2016-09, tax attributes previously tracked off balance sheet have been recorded as deferred tax assets, offset by a valuation allowance. Further, excess benefits of stock compensation have been recorded as a benefit to the tax provision for all periods presented. For the three months ended March 31, 2019 and 2018, the Company recorded a net tax shortfall of $0.7 million and $0.3 million, respectively, all of which were recorded 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.

On January 1, 2019, the Company adopted ASC 842, Leases and it recorded a reduction in deferred tax assets of $1.0 million as part of the $3.8 million change in the opening balance of the accumulated deficit for the cumulative effect of applying ASC 842 (See Note 2, "Summary of Significant Accounting Policies").

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 tax credit carryforwards, share-based compensation and other temporary differences. The Company maintains a valuation allowance against certain U.S. federal and state and Irish deferred tax assets. Each reporting period, the Company evaluates the need for a valuation allowance on its deferred tax assets by jurisdiction.

No provision for income tax in Ireland has been recognized on undistributed earnings of the Company's U.S. and Swiss subsidiaries. The Company considers the U.S. earnings to be indefinitely reinvested. The Company expects to distribute the remaining cash from its Swiss subsidiary to its Irish parent in 2019 however, the Company considers any potential tax associated with the distribution of Swiss earnings to be insignificant. Unremitted earnings may be subject to withholding taxes (potentially at 5% in the U.S. and 5% in Switzerland) and Irish taxes (potentially at a rate of 12.5%) if they were to be distributed as dividends. However, Ireland allows a credit against Irish taxes for U.S. and Swiss taxes withheld, and the Company's current year net operating losses in Ireland are sufficient to offset any potential dividend income received from its overseas subsidiaries.

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 objective to fundamentally change the course of progressive, life-threatening diseases; our goal of advancing a pipeline of therapeutic candidates for a number of potential indications and novel targets; our expected research and development ("R&D") and general and administrative ("G&A") expenses in 2019; our expectation that we have made substantially all cash payments under our restructuring plan; our expectation of continued impacts on our income tax expense from fluctuations in our stock price; the sufficiency of our cash and cash equivalents to meet our obligations; our anticipated need for additional capital; and our estimates of certain future contractual obligations. Forward-looking statements may include words such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective" "plan," "predict," "potential," "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 Part II Item 1A - Risk Factors of this Form 10-Q:

- our ability to obtain additional financing in future offerings and/or obtain funding from future collaborations;
- our operating losses;
- our ability to successfully complete research and development of our drug candidates;
- our ability to develop, manufacture and commercialize products;
- our collaborations with third parties, including Roche and Celgene;
- our ability to protect our patents and other intellectual property;
- our ability to hire and retain key employees;
- tax treatment of our separation from Elan and subsequent distribution of our ordinary shares;
- our ability to maintain financial flexibility and sufficient cash, cash equivalents and investments and other assets capable of being monetized to meet our liquidity requirements;
- potential disruptions in the U.S. and global capital and credit markets;

- government regulation of our industry;
- the volatility of our ordinary share price;
- business disruptions; and
- the other risks and uncertainties described in Part II Item 1A - Risk Factors 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 Consolidated Financial Statements and Notes contained in our Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (the "SEC") on March 15, 2019 (the "2018 Form 10-K").

Overview

Prothena Corporation plc is a clinical-stage neuroscience company focused on the discovery and development of novel therapies with the potential to fundamentally change the course of progressive, life-threatening diseases. Fueled by a deep scientific understanding built over decades of neuroscience research, we are advancing a pipeline of therapeutic candidates for a number of indications and novel targets including Parkinson's disease and other related synucleinopathies (prasinezumab, or PRX002/RG7935) and ATTR amyloidosis (PRX004), as well as tau for the potential treatment of Alzheimer's disease and other neurodegenerative disorders, and TDP-43 for the potential treatment of ALS (amyotrophic lateral sclerosis) and FTD (frontotemporal dementia).

We were formed on September 26, 2012 under the laws of Ireland and re-registered as an Irish public limited company on October 25, 2012. Our ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012 and currently trade on The Nasdaq Global Select Market.

Recent Developments

In April, we reported final results from the Phase 3 VITAL Amyloidosis study of NEOD001 (birtamimab) in newly diagnosed, treatment naïve patients with AL Amyloidosis and cardiac dysfunction (N=260), which was discontinued in 2018, and that we are exploring potential business development opportunities to advance NEOD001. The final hazard ratio (HR) for the composite primary endpoint (time to all-cause mortality or time to cardiac hospitalization more than 90 days after first infusion of study drug) of 0.835 (95% CI: 0.5799, 1.2011; p=0.3300) was consistent with the futility analysis reported in April 2018. Post hoc analyses of all-cause mortality revealed a potential survival benefit favoring NEOD001 in the category of patients at highest risk for early mortality (Mayo Stage IV, n=77) with a HR of 0.544 (95% CI: 0.2738, 1.0826; p=0.0787). This potential survival benefit was more pronounced in Mayo Stage IV patients during the initial 12 months of treatment, with a HR of 0.498 (95% CI: 0.2404, 1.0304; p=0.0556).

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.

Except for the accounting policies for leases that was updated as a result of adopting ASC 842, there were no significant changes to our critical accounting policies and estimates during the three months ended March 31, 2019 from the critical accounting policies and estimates disclosed in Management's Discussion and Analysis of Financial Condition and Results of Operations in our 2018 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, 2019 , as compared to the recent accounting pronouncements described in our 2018 Form 10-K, that are of significance or potential significance to us.

Results of Operations

Comparison of Three Months Ended March 31, 2019 and 2018

Revenue

	Three Months Ended March 31,		Percentage Change
	2019	2018	
	(Dollars in thousands)		
Collaboration revenue	$ 186	$ 227	(18)%
Total revenue	$ 186	$ 227	(18)%

Total revenue was $0.2 million and $0.2 million for the three months ended March 31, 2019 and 2018, respectively.

Collaboration revenue includes reimbursements for development services under our License Agreement with Roche. See Note 7, "Significant Agreements" to the Condensed Consolidated Financial Statements regarding the Roche License Agreement for more information.

Operating Expenses

	Three Months Ended March 31,		Percentage Change
	2019	2018	
	(Dollars in thousands)		
Research and development	$ 13,296	$ 34,706	(62)%
General and administrative	9,905	14,229	(30)%
Restructuring charges (credits)	(61)	—	nm
Total operating expenses	$ 23,140	$ 48,935	(53)%

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nm = not meaningful

Total operating expenses consist of R&D expenses, general and administrative ("G&A") expenses and restructuring charges (credits). Our operating expenses were $23.1 million and $48.9 million for the three months ended March 31, 2019 and 2018, respectively.

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

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

Research and Development Expenses

Our R&D expense decreased by $21.4 million, or 62%, for the three months ended March 31, 2019, compared to the same period in the prior year. The decrease for the three months ended March 31, 2019 was primarily due to lower clinical costs associated primarily with the discontinuation of the NEOD001 program, lower consulting expense, lower personnel costs (including share-based compensation expense) and lower manufacturing cost associated with the discontinuation of 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 nonclinical and drug development and materials, equipment and facilities costs that are allocated to clearly related R&D activities.

The following table sets forth the R&D expenses for our major programs (specifically, any program with successful first dosing in a Phase 1 clinical trial, which were NEOD001, prasinezumab, PRX003 and PRX004) and other R&D expenses for the three months ended March 31, 2019 and 2018 and the cumulative amounts to date (in thousands):

	Three Months Ended March 31,		Cumulative to Date
	2019	2018	
NEOD001[1]	$ 619	$ 25,596	$ 309,263
Prasinezumab (PRX002/RG7935)[2]	3,415	2,607	68,945
PRX003[3]	64	194	59,074
PRX004[4]	4,345	4,072	51,025
Other R&D[5]	4,853	2,237	
	$ 13,296	$ 34,706	

(1) *Cumulative R&D costs to date for NEOD001 include the costs incurred from the date when the program has been separately tracked in preclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount. In April 2018, we announced that we were discontinuing development of NEOD001. Since that date we have incurred costs associated with the close out of our Phase 2b PRONTO, Phase 3 VITAL as well as the open label extension studies of NEOD001.*

(2) *Cumulative R&D costs to date for prasinezumab and related antibodies include the costs incurred from the date when the program was separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount. Prasinezumab costs include payments to Roche for our share of the development expenses incurred by Roche related to prasinezumab programs and, through December 31, 2017, is net of reimbursements from Roche for development and supply services recorded as an offset to R&D expense. For the three months ended March 31, 2019 and 2018, $0.2 million and $0.2 million, respectively, of reimbursements from Roche for development services were recorded as part of collaboration revenue.*

(3) *Cumulative R&D costs to date for PRX003 include the costs incurred from the date when the program has been separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount. Based on the Phase 1b multiple ascending dose study results announced in September 2017, we announced that we will not advance PRX003 into mid-stage clinical development for psoriasis or psoriatic arthritis as previously planned.*

(4) *Cumulative R&D costs to date for PRX004 include the costs incurred from the date when the program was separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount.*

(5) *Other R&D is comprised of preclinical development and discovery programs that have not progressed to first patient dosing in a Phase 1 clinical trial.*

As a result of the restructuring and the discontinuation of NEOD001 program in 2018, we expect our R&D expenses to decrease in 2019 compared to the prior year.

General and Administrative Expenses

Our G&A expenses decreased by $4.3 million, or 30%, for the three months ended March 31, 2019 compared to the same period in the prior year. The decrease for the three months ended March 31, 2019 was primarily due to lower personnel costs (including share based compensation expense) and lower consulting expenses as a result of the discontinuation of the NEOD001 program.

As a result of the restructuring in 2018, we expect our G&A expenses to decrease in 2019 compared to the prior year.

Restructuring and Impairment Related Charges

In May 2018, we commenced a reorganization plan to reduce our operating costs and better align our workforce with the needs of our business following our decision in April 2018 to discontinue further development of NEOD001. For the three months ended March 31, 2019, we recorded a restructuring credit of approximately $61,000 primarily due to an adjustment in previously recorded employee termination benefits. See Note 10, “Restructuring” to the Condensed Consolidated Financial Statements for more information.

Other Income (Expense)

	Three Months Ended March 31,		Percentage Change
	2019	2018	
	(Dollars in thousands)		
Interest income	$ 2,304	$ 1,108	108 %
Interest expense	—	(908)	(100)%
Interest income, net	2,304	200	1,052 %
Other income (expense)	(17)	(272)	(94)%
Total other income (expense), net	$ 2,287	$ (72)	(3,276)%

Interest income, net increased by $2.1 million, or 1,052%, for the three months ended March 31, 2019, compared to the same periods in the prior year. The increase for the three months ended March 31, 2019 was primarily due to higher interest income in our cash and money market accounts and no recorded interest expense associated with the build-to-suit accounting upon the adoption of ASC 842 in 2019.

Other income (expense), net for the three months ended March 31, 2019 and 2018 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
	2019	2018	
	(Dollars in thousands)		
Provision for (benefit from) income taxes	$ 198	$ (37)	(635)%

The provision for income taxes for the three months ended March 31, 2019 was $0.2 million and the benefit from income taxes for three months ended March 31, 2018 was $37,000. The change in provision for (benefit from) income taxes was primarily due to an increase in tax shortfall related to options cancellation in the three months ended March 31, 2019. Our income tax expense will continue to be impacted by fluctuations in stock price between the grant dates and the exercise or cancellation dates of stock options.

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.

Liquidity and Capital Resources

Overview

	March 31, 2019	December 31, 2018
Working capital	$ 400,287	$ 416,464
Cash and cash equivalents	410,106	427,659
Total assets	459,534	498,796
Total liabilities	147,404	175,798
Total shareholders' equity	312,130	322,998

Working capital was $400.3 million as of March 31, 2019, a decrease of $16.2 million from working capital of $416.5 million as of December 31, 2018. This decrease in working capital during the three months ended March 31, 2019 was primarily due to cash use of $23.1 million for operating expenses (adjusted to exclude non-cash charges).

As of March 31, 2019, we had $410.1 million in cash and cash equivalents. Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in the future in order to continue the research and development of our drug candidates. As of March 31, 2019, $108.3 million of our outstanding cash and cash equivalents related to U.S. operations are considered permanently reinvested. We do not intend to repatriate these funds. However, if these funds were repatriated back to Ireland we would incur a withholding tax from the dividend distribution.

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

Cash Flows for the three months ended March 31, 2019 and 2018

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,	
	2019	2018
Net cash used in operating activities	$ (17,435)	$ (31,584)
Net cash used in investing activities	(123)	(181)
Net cash provided by financing activities	5	43,184
Net increase in cash and cash equivalents and restricted cash	$ (17,553)	$ 11,419

Cash Used in Operating Activities

Net cash used in operating activities was $17.4 million for the three months ended March 31, 2019, was primarily due to $23.1 million for operating expenses (adjusted to exclude non-cash charges) and a decrease in accounts payable, accruals and other liabilities and restructuring liabilities.

Net cash used in operating activities was $31.6 million for the three months ended March 31, 2018, primarily due to use of $48.9 million for operating expenses (adjusted to exclude non-cash charges), an increase in receivable from Celgene and a decrease in accounts payable and accrued liabilities, which were partially offset by an increase in deferred revenue.

Cash Used in Investing Activities

Net cash used in investing activities was $0.1 million and $0.2 million for the three months ended March 31, 2019 and 2018, respectively. Net cash used in investing activities for the three months ended March 31, 2019 and 2018 were primarily related to purchases of property and equipment.

Cash Provided by Financing Activities

Net cash provided by financing activities was $5,000 for the three months ended March 31, 2019, primarily from proceeds from issuances of ordinary shares upon exercise of stock options.

Net cash provided by financing activities was $43.2 million for the three months ended March 31, 2018, primarily from the $39.8 million proceeds from Celgene's subscription of ordinary shares at market value, and to a lesser extent, from $4.4 million proceeds from issuances of ordinary shares upon exercises of stock options.

Off-Balance Sheet Arrangements

At March 31, 2019, we were not a party to any off-balance sheet arrangements that have, or are reasonably likely to have, a current or future effect on our financial condition, changes in financial condition, revenue or expenses, results of operations, liquidity, capital expenditures or capital resources.

Contractual Obligations

Our contractual obligations as of March 31, 2019 consisted of minimum cash payments under operating leases of $29.4 million, purchase obligations of $1.2 million (of which $1.0 million is included in accrued current liabilities), and contractual obligations under license agreements of $1.2 million (of which $0.1 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 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 $29.4 million remains outstanding as of March 31, 2019.

In September 2018, we entered into an agreement to lease an office space in Dublin, Ireland. The lease term expires on November 2019. As of March 31, 2019, we are obligated to make lease payments over the remaining term of the lease of approximately €15,000, or $17,000 as converted using an exchange rate as of March 31, 2019.

The following is a summary of our contractual obligations as of March 31, 2019 (in thousands):

	Total	2019	2020	2021	2022	2023	Thereafter
Operating leases [1]	$ 29,416	$ 4,387	$ 5,979	$ 6,165	$ 6,350	$ 6,535	$ —
Purchase obligations	1,174	1,174	—	—	—	—	—
Contractual obligations under license agreements [2]	1,160	275	95	95	80	80	535
Total	$ 31,750	$ 5,836	$ 6,074	$ 6,260	$ 6,430	$ 6,615	$ 535

[1] *See Note 6,* "*Commitments and Contingencies*" *to our Condensed Consolidated Financial Statements.*

[2] *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 drug supplies which are denominated in Euros. We recorded a loss on foreign currency exchange rate differences of approximately $16,000 and $272,000 during the three months ended March 31, 2019 and 2018, respectively. If we continue or increase our business activities that require the use of foreign currencies, we may incur further losses if the Euro and other such currencies continue to strengthen against the U.S. dollar.

Interest Rate Risk

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

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

Credit Risk

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

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

ITEM 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 U.S. 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, 2019, 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

During the quarter ended March 31, 2019, we implemented certain internal controls in connection with our adoption of ASC 842. There were no other changes in our internal control over financial reporting that occurred during our most recent fiscal quarter that have 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

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

We may at times be party to ordinary routine litigation incidental to our business. When appropriate in management's estimation, we may record reserves in our financial statements for pending legal proceedings.

ITEM 1A. RISK FACTORS

Investing in our ordinary shares involves a high degree of risk. Our Annual Report on Form 10-K for 2018 (filed with the SEC on March 15, 2019) 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 $155.6 million, $153.2 million and $160.1 million for the years ended December 31, 2018, 2017 and 2016, respectively. We expect to continue to incur substantial losses for the foreseeable future as we:

- support the Phase 2 PASADENA clinical trial for prasinezumab (PRX002/RG7935) being conducted by Roche, conduct our Phase 1 clinical trial for PRX004 and possibly initiate additional clinical trials for these and other programs;
- develop and possibly commercialize our product candidates, including prasinezumab and PRX004;
- undertake nonclinical development of other product candidates and initiate clinical trials, if supported by nonclinical data; and
- pursue our early stage research and seek to identify additional drug candidates; and
- potentially acquire rights from third parties to drug candidates or technologies 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, 2019, we had cash and cash equivalents of $410.1 million. Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in the future in order to continue the research and development, and eventual commercialization, of our drug candidates. Our future capital requirements will depend on many factors that are currently unknown to us, including, without limitation:

- the timing of initiation, progress, results and costs of our clinical trials, including the Phase 2 clinical trial for prasinezumab and our Phase 1 clinical trial for PRX004;
- the timing, initiation, progress, results and costs of these and our other research, development and possible commercialization activities;
- the results of our research, nonclinical and clinical studies;
- the costs of manufacturing our drug candidates for clinical development as well as for future commercialization needs;
- if and when appropriate, the costs of preparing for commercialization of our drug candidates;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- our ability to establish research collaborations, strategic collaborations, licensing or other arrangements;
- the timing, receipt and amount of any payments or royalties that we might receive under current or potential future collaborations;
- the costs to satisfy our obligations under current and potential future collaborations; and
- the timing, receipt and amount of revenues or royalties, if any, from any approved drug candidates.

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

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

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

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

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

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

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

In June 2016, a majority of voters in the United Kingdom (the "UK") elected in a national referendum to withdraw from the European Union (the "EU"). In March 2017, the UK government formally initiated the withdrawal process, which is still underway. That withdrawal has created significant uncertainty about the future relationship between the UK and the EU, including with respect to the laws and regulations that will apply as the UK determines which EU laws to replace or replicate upon withdrawal. The pending withdrawal has also given rise to calls for the governments of other EU member states to consider withdrawal. These developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict access to capital, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

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

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

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

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

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

We may be adversely affected by earthquakes or other natural disasters.

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

disasters or similar events. Accordingly, such a natural disaster or similar event could have an adverse effect on our business, financial condition or results of operations.

We may experience breaches or similar disruptions of our information technology systems or data.

Our business is increasingly dependent on critical, complex and interdependent information technology systems to support business processes as well as internal and external communications. The size and complexity of those systems make them vulnerable to breakdown, malicious intrusion and computer viruses. We have developed systems and processes that are designed to protect our information technology systems and prevent data loss and other security breaches, including systems and processes designed to reduce the impact of a security breach. However, such measures cannot provide absolute security. Any breakdown, malicious intrusion or computer virus could result in the impairment of key business processes or breach of data security, which could cause us to lose trade secrets or other intellectual property or lead to unauthorized disclosure of personal data of our employees, third parties with which we do business, clinical trial participants or others. Such an event could have an adverse effect on our business, financial condition or results of operations.

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

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

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

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

The success of our business depends substantially upon our ability to discover, develop, obtain regulatory approval for and commercialize our drug candidates successfully. Our research and development programs are prone to the significant and likely risks of failure inherent in drug development, which can result from the failure of the drug candidate to be sufficiently effective, the safety profile of the drug candidate, a clinical trial that is not sufficiently enrolled or powered or adequately designed to detect a drug effect, or other reasons. We intend to continue to invest most of our time and financial resources in our research and development programs.

Although we have an ongoing Phase 2 clinical trial for prasinezumab and an ongoing Phase 1 clinical trial for PRX004, there is no assurance that the results of these trials will support further development of these drug candidates. In addition, we currently do not, and may never, have any other drug candidates in clinical trials and we have not identified drug candidates for many of our research programs.

Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate with substantial evidence gathered in adequate and well-controlled clinical trials that the drug candidate is safe and effective for use for that target indication. In the U.S., this must be done to the satisfaction of the U.S. Food and Drug Administration (the "FDA"); in the EU this must be done to the satisfaction of the EMA; and in other countries this must be done to the satisfaction of comparable regulatory authorities.

Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. Despite our efforts, our drug candidates may not:

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

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

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

- obtaining and maintaining commercial manufacturing arrangements with third-party manufacturers;
- developing the marketing and sales capabilities, internal and/or in collaboration with pharmaceutical companies or contract sales organizations, to market and sell any approved drug; and
- acceptance of any approved drug in the medical community and by patients and third-party payers.

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

We have entered into collaborations and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration, and might not commit sufficient efforts and resources or might misapply those efforts and resources;
- we may have limited influence or control over the approaches to development and commercialization of products candidates in the territories in which our collaboration partners lead development and commercialization;
- collaborators might not pursue research, development and commercialization of collaboration product candidates or might elect not to continue or renew research, development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competing products, availability of funding or other factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators might delay, provide insufficient resources to, or modify or stop clinical trials for collaboration product candidates or require a new formulation of a product candidate for clinical testing;
- collaborators could develop or acquire products outside of the collaboration that compete directly or indirectly with our product candidates or require a new formulation of a product candidate for clinical testing;
- collaborators with sales, marketing and distribution rights to one or more product candidates might not commit sufficient resources to sales, marketing and distribution or might otherwise fail to successfully commercialize those product candidates;
- collaborators might not properly maintain or defend our intellectual property rights or might use our intellectual property improperly or in a way that jeopardizes our intellectual property or exposes us to potential liability;
- collaboration activities might result in the collaborator having intellectual property covering our activities or product candidates, which could limit our rights or ability to research, develop or commercialize our product candidates;
- disputes might arise between us and a collaborator that could cause a delay or termination of the collaboration or result in costly litigation that diverts management attention and resources; and
- collaborations might be terminated, which could result in a need for additional capital to pursue further development or commercialization of our product candidates.

In addition, funding provided by a collaborator might not be sufficient to advance product candidates under the collaboration. For example, although Celgene made a $100 million upfront payment to us and made a $50 million equity investment in us upon entering into the Collaboration Agreement, we might need additional funding to advance product candidates prior to when Celgene decides whether to exercise its license rights to those product candidates. We also note that, on January 3, 2019, Bristol-Myers Squibb (BMS) and Celgene announced that they had entered into an agreement for BMS to acquire Celgene. If and when that acquisition is completed, BMS might take a different approach to our collaboration with Celgene or determine not to continue that collaboration.

If a collaborator terminates a collaboration or a development program under a collaboration, including by failing to exercise a license or other option under the collaboration, whether because we fail to meet a milestone or otherwise, any potential revenue from the collaboration would be significantly reduced or eliminated. In addition, we will likely need to either secure other funding to advance research, development and/or commercialization of the relevant product candidate or abandon that program, the development of the relevant product candidate could be significantly delayed, and our cash expenditures could increase significantly if we are to continue research, development and commercialization of the relevant product candidates.

Any one or more of these risks, if realized, could reduce or eliminate future revenue from product candidates under our collaborations, and could have a material adverse effect on our business, financial condition, results of operations and/or growth prospects.

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

We cannot predict whether we will encounter problems with the Phase 2 clinical trial for prasinezumab, our Phase 1 clinical trial for PRX004 or any other future clinical trials that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing or planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular drug candidate:

- conditions imposed on us by the FDA, the EMA or other comparable regulatory authorities regarding the scope or design of our clinical trials;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards ("IRBs") or other reviewing entities at clinical sites selected for participation in our clinical trials;
- insufficient supply or deficient quality of our drug candidates or other materials necessary to conduct our clinical trials;
- delays in obtaining regulatory authority agreement for the conduct of our clinical trials;
- lower than anticipated enrollment and/or retention rate of subjects in our clinical trials, which can be impacted by a number of factors, including size of patient population, design of trial protocol, trial length, eligibility criteria, perceived risks and benefits of the study drug, patient proximity to trial sites, patient referral practices of physicians, availability of other treatments for the relevant disease and competition from other clinical trials;
- slower than expected rates of events in trials with a composite primary endpoint that is event-based;
- serious and unexpected drug-related side effects experienced by subjects in clinical trials; or
- failure of our third-party contractors and collaborators to meet their contractual obligations to us or otherwise meet their development or other objectives in a timely manner.

We are dependent upon Roche with respect to further development of prasinezumab. Under the terms of our collaboration with Roche, Roche is responsible for that further development, including the conduct of the ongoing Phase 2 clinical trial and any future clinical trial of that drug candidate.

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

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;

- inspection of the clinical trial operations or trial sites by the FDA, the EMA or other regulatory authorities resulting in the imposition of a clinical hold on or imposition of additional conditions for the conduct of the trial;
- interpretation of data by the FDA, the EMA or other regulatory authorities;
- requirement by the FDA, the EMA or other regulatory authorities to perform additional studies;
- failure to achieve primary or secondary endpoints or other failure to demonstrate efficacy or adequate safety;
- unforeseen safety issues; or
- lack of adequate funding to continue the clinical trial.

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

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

The regulatory approval processes of the FDA, the EMA and other comparable regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.

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

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

- the FDA, the EMA or comparable regulatory authorities may disagree with the design, implementation or conduct of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, the EMA or comparable regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, the EMA or comparable regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA, the EMA or comparable regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of a Biologic License Application ("BLA") to the FDA, a Marketing Authorization Application ("MAA") to the EMA or similar applications to comparable regulatory authorities;
- the FDA, the EMA or comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; or
- the approval policies or regulations of the FDA, the EMA or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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

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

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

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

Both before and after regulatory approval to market a particular drug candidate, adverse event reporting, manufacturing, labeling, packaging, storage, distribution, advertising, promotion, record keeping and reporting related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as continued compliance with current good manufacturing practice ("cGMP") requirements and current good clinical practice ("cGCP") requirements for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or not previously observed in clinical trials, or with our third-party manufacturers or manufacturing processes, or failure to comply with the regulatory requirements of the FDA, the EMA and other comparable regulatory authorities could subject us to administrative or judicially imposed sanctions, including:

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

The FDA's, the EMA's or other comparable regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If side effects are identified during the time our drug candidates are in development or after they are approved and on the market, we may choose to or be required to perform lengthy additional clinical trials, discontinue development of the affected drug candidate, change the labeling of any such products, or withdraw any such products from the market, any of which would hinder or preclude our ability to generate revenues.

Undesirable side effects caused by our drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA or other comparable regulatory authorities. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. Even if any of our drug candidates receives marketing approval, as greater numbers of patients use a drug following its approval, an increase in the incidence or severity of side effects or the incidence of other post-approval problems that were not seen or anticipated during pre-approval clinical trials could result in a number of potentially significant negative consequences, including:

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

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

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

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

Risks Related to the Commercialization of Our Drug Candidates

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

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

- the indication and label for the product and the timing of introduction of competitive products;
- demonstration of clinical safety and efficacy compared to other products;
- prevalence, frequency and severity of adverse side effects;

- availability of coverage and adequate reimbursement from managed care plans and other third-party payers;
- convenience and ease of administration;
- cost-effectiveness;
- other potential advantages of alternative treatment methods; and
- the effectiveness of marketing and distribution support of the product.

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

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

The success of sales of prasinezumab in the U.S. will be dependent on the ability of Roche to successfully develop in collaboration with us, and launch and commercialize prasinezumab, if approved by the FDA, pursuant to the License Agreement we entered into in December 2013. Our collaboration with Roche is complex, particularly with respect to future U.S. commercialization of prasinezumab, with respect to financial provisions, allocations of responsibilities, cost estimates and the respective rights of the parties in decision making. Accordingly, significant aspects of the development and commercialization of prasinezumab require Roche to execute its responsibilities under the arrangement, or require Roche's agreement or approval, prior to implementation, which could cause significant delays that may materially impact the potential success of prasinezumab in the U.S. In addition, Roche may under some circumstances independently develop products that compete with prasinezumab, or Roche may decide to not commit sufficient resources to the development, commercialization, marketing and distribution of prasinezumab. If we are not able to collaborate effectively with Roche on plans and efforts to develop and commercialize prasinezumab, our business could be materially adversely affected.

Furthermore, the terms of the License Agreement provide that Roche has the ability to terminate such arrangement for any reason after the first anniversary of the License Agreement at any time upon 90 days' notice (if prior to first commercial sale) or 180 days' notice (if after first commercial sale). For example, Roche may determine that the outcomes of clinical trials have made prasinezumab a less attractive commercial product and terminate our collaboration. If the License Agreement is terminated, our business and our ability to generate revenue from sales of prasinezumab could be substantially harmed as we will be required to develop, commercialize and build our own sales and marketing organization or enter into another strategic collaboration in order to develop and commercialize prasinezumab in the U.S. Such efforts may not be successful and, even if successful, would require substantial time and resources to carry out.

The manner in which Roche launches prasinezumab, including the timing of launch and potential pricing, will have a significant impact on the ultimate success of prasinezumab in the U.S, and the success of the overall commercial arrangement with Roche. If launch of commercial sales of prasinezumab in the U.S. by Roche is delayed or prevented, our revenue will suffer and our stock price may decline. Further, if launch and resulting sales by Roche are not deemed successful, our business would be harmed and our stock price may decline. Any lesser effort by Roche in its prasinezumab sales and marketing efforts may result in lower revenue and thus lower profits with respect to the U.S. The outcome of Roche's commercialization efforts in the U.S. could also have a negative effect on investors' perception of potential sales of prasinezumab outside of the U.S., which could also cause a decline in our stock price.

Furthermore, pursuant to the License Agreement, we are responsible for 30% of all development and commercialization costs for prasinezumab for the treatment of Parkinson's disease in the U.S., and for any future Licensed Products and/or indications that we opt to co-develop, in each case unless we elect to opt out of profit and loss sharing. If we elect to opt out of profit and loss sharing, we will instead receive sales milestones and royalties, and our revenue, if any, from prasinezumab will be reduced.

Our right to co-develop prasinezumab and other Licensed Products under the License Agreement will terminate if we commence certain studies for a competitive product that treats Parkinson's disease or other indications that we opted to co-develop. In addition, our right to co-promote prasinezumab and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease.

Moreover, under the terms of the License Agreement, we rely on Roche to provide us estimates of their costs, revenue and revenue adjustments and royalties, which estimates we use in preparing our quarterly and annual financial reports. If the underlying assumptions on which Roche's estimates were based prove to be incorrect, actual results or revised estimates supplied by Roche

that are materially different from the original estimates could require us to adjust the estimates included in our reported financial results. If material, these adjustments could require us to restate previously reported financial results, which could have a negative effect on our stock price.

Our ability to receive any significant revenue from prasinezumab will be dependent on Roche's efforts and our participation in profit and loss sharing, and may result in lower levels of income than if we marketed or developed our product candidates entirely on our own. Roche may not fulfill its obligations or carry out marketing activities for prasinezumab as diligently as we would like. We could also become involved in disputes with Roche, which could lead to delays in or termination of development or commercialization activities and time-consuming and expensive litigation or arbitration. If Roche terminates or breaches the License Agreement, or otherwise decides not to complete its obligations in a timely manner, the chances of successfully developing, commercializing or marketing prasinezumab would be materially and adversely affected.

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

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

In the event that Roche does not diligently develop and commercialize prasinezumab, the License Agreement provides us the right to terminate the License Agreement in connection with a material breach uncured for 90 days after notice thereof. However, our ability to enforce the provisions of the License Agreement so as to obtain meaningful recourse within a reasonable timeframe is uncertain. Further, any decision to pursue available remedies including termination would impact the potential success of prasinezumab, including inside the U.S., and we may choose not to terminate as we may not be able to find another partner and any new collaboration likely will not provide comparable financial terms to those in our arrangement with Roche. In the event of our termination, this may require us to develop and commercialize prasinezumab on our own, which is likely to result in significant additional expense and delay. Significant changes in Roche's business strategy, resource commitment and the willingness or ability of Roche to complete its obligations under our arrangement could materially affect the potential success of the product. Furthermore, if Roche does not successfully develop and commercialize prasinezumab outside of the U.S., our potential to generate future revenue outside of the U.S. would be significantly reduced.

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

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

We have entered into the License Agreement with Roche for the development of prasinezumab and may develop our own sales force and marketing infrastructure to co-promote prasinezumab in the U.S. for the treatment of Parkinson's disease and any future Licensed Products approved for Parkinson's disease in the U.S. If we exercise our co-promotion option and are unable to develop our own sales force and marketing infrastructure to effectively commercialize prasinezumab or other Licensed Products, our ability to generate additional revenue from potential sales of prasinezumab or such products in the U.S. may be harmed. In addition, our right to co-promote prasinezumab and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease.

For any other products that may be approved, if we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable.

If government and third-party payers fail to provide coverage and adequate reimbursement rates for any of our drug candidates that receive regulatory approval, our revenue and prospects for profitability will be harmed.

In both U.S. and non-U.S. markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payers. Such third-party payers include government health programs such as Medicare, managed care providers,

private health insurers, and other organizations. There is significant uncertainty related to the third-party coverage and reimbursement of newly approved drugs. Coverage and reimbursement may not be available for any drug that we or our collaborators commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Third-party payers often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Third-party payers are also increasingly attempting to contain healthcare costs by demanding price discounts or rebates limiting both coverage and the amounts that they will pay for new drugs, and, as a result, they may not cover or provide adequate payment for our drug candidates. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize any product candidates for which marketing approval is obtained.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or licensing approval is granted. In some countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, and negatively impact our ability to generate revenue from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

U.S. and other governments continue to propose and pass legislation designed to reduce the cost of healthcare. In the U.S., we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the U.S. will continue to put pressure on pharmaceutical product pricing. For example, in 2010, the U.S. Patient Protection and Affordable Care Act, as amended by the U.S. Health Care and Education Reconciliation Act (collectively, the "Healthcare Reform Law"), was enacted. The Healthcare Reform Law substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the Healthcare Reform Law of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the minimum rebates a manufacturer must pay under the U.S. Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the U.S. False Claims Act and the U.S. Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, under which manufacturers must agree to offer 50 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a licensure framework for follow-on biologic products;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program and its implementing regulations;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

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

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

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

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

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

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

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

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

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

Our drug candidates are regulated by the FDA as biologic products and we intend to seek approval for these products pursuant to the BLA pathway. The U.S. Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes

legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biologic products.

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

We are subject to healthcare and other laws and regulations, including anti-bribery, anti-kickback, fraud and abuse, false claims, physician payment transparency and health information privacy and security laws and regulations, which could expose us to criminal, civil and/or administrative sanctions and penalties, exclusion from governmental healthcare programs or reimbursements, contractual damages and reputational harm.

Our operations and activities are directly, or indirectly through our service providers and collaborators, subject to numerous healthcare and other laws and regulations, including, without limitation, those relating to anti-bribery, anti-kickback, fraud and abuse, false claims, physician payment transparency and health information privacy and security, in the U.S., the EU and other countries and jurisdictions in which we conduct our business. These laws include:

- the U.S. Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- U.S. federal and state false claims laws, including the False Claims Act, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the U.S. Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements in connection with the delivery of or payment for healthcare benefits, items or services, and under the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH") imposes obligations, including mandatory contractual terms, on certain types of individuals and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information and places restrictions on the use of such information for marketing communications;

- the U.S. Physician Payment Sunshine Act, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to "payments or other transfers of value" made to physicians and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members;

- laws and regulations that apply to sales or marketing arrangements; apply to healthcare items or services reimbursed by non-governmental third-party payers, including private insurers; require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines; that restrict payments that may be made to healthcare providers; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and

- similar and other laws and regulations in the U.S. (federal, state and local), in the EU (including member countries) and other countries and jurisdictions.

Further, the Healthcare Reform Law, among other things, amended the intent requirements of the U.S. Anti-Kickback Statute and the criminal statutes governing healthcare fraud. A person or entity can now be found guilty of violating the statute without

actual knowledge of the statute or specific intent to violate it. In addition, the Healthcare Reform Law provided that the government may assert that a claim including items or services resulting from a violation of the U.S. Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the U.S. False Claims Act.

Ensuring our compliance with applicable healthcare and other laws and regulations involves substantial costs, and it is possible that governmental authorities or third parties will assert that our business practices fail to comply with these laws and regulations. If our operations are found to be in violation of any of such laws and regulations, we may be subject to significant civil, criminal and administrative damages, penalties and fines, as well exclusion from participation in government healthcare programs, curtailment or restructuring of our operations and reputational harm, any of which could have a material adverse effect on our business, financial condition or results of operations.

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

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

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

We currently have clinical trial liability insurance coverage for all of our clinical trials. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for any of our drug candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our ordinary share price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Related to Our Dependence on Third Parties

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

We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties, such as consultants, contract research organizations, medical institutions and clinical investigators, to assist us with these activities. Our reliance on these third parties for clinical development activities results in reduced control over these activities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. Although we have and will enter into agreements with these third parties, we will be responsible for confirming that our clinical trials are conducted in accordance with their general investigational plans and protocols. Moreover, the FDA, the EMA and other comparable regulatory authorities require us to comply with regulations and standards, commonly referred to as cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If we or any of our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or other comparable regulatory authorities may require us to perform additional clinical trials

before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with cGCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

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

In addition, our third-party contractors are not our employees, and except for remedies available to us under our agreements with such third-party contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. If third-party contractors do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

If we do not establish additional strategic collaborations, we may have to alter our research and development plans.

Our drug research and development programs and potential commercialization of our drug candidates will require substantial additional cash to fund expenses. Our strategy includes potentially collaborating with additional leading pharmaceutical and biotechnology companies to assist us in furthering development and potential commercialization of some of our drug candidates, in some or all geographies. It may be difficult to enter into one or more of such collaborations in the future. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all, in which case we may have to curtail the development of a particular drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our drug candidates to market and generate product revenue.

We have no manufacturing capacity and depend on third-party manufacturers to supply us with nonclinical and clinical trial supplies of all of our drug candidates, and we will depend on third-party manufacturers to supply us with any drug products for commercial sale if we obtain marketing approval from the FDA, the EMA or any other comparable regulatory authority for any of our drug candidates.

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

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

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

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

Roche, with whom we are collaborating on development of prasinezumab, is manufacturing clinical supplies for the Phase 2 clinical trial for prasinezumab and is expected to do so for any subsequent clinical trials of prasinezumab. We are dependent on Roche to continue to manufacture these clinical supplies.

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

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

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

Risks Related to Our Intellectual Property

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

Our success depends in part on our ability to obtain patent protection both in the U.S. and in other countries for our drug candidates. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights

under any issued patents may not provide us with sufficient protection for our drug candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- incur substantial monetary damages;
- 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 nonclinical research and clinical trials;
- our collaborations with third parties, including with Roche and Celgene;
- failure or delays in advancing our nonclinical drug candidates or other drug candidates we may develop in the future into clinical trials;
- results of clinical trials conducted by others, including on drugs that would compete with our drug candidates;
- issues in manufacturing our drug candidates;
- regulatory developments or enforcement in the U.S. and other countries;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by our competitors;
- changes in estimates or recommendations by securities analysts, if any, who cover our company;
- public concern over our drug candidates;
- litigation;
- future sales of our ordinary shares;
- general market conditions;
- changes in the structure of healthcare payment systems;
- failure of any of our drug candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises;
- period-to-period fluctuations in our financial results;
- overall fluctuations in U.S. equity markets;

- our quarterly or annual results, or those of other companies in our industry;
- announcements by us or our competitors of significant acquisitions or dispositions;
- the operating and ordinary share price performance of other comparable companies;
- investor perception of our company and the drug development industry;
- natural or environmental disasters that investors believe may affect us;
- changes in tax laws or regulations applicable to our business or the interpretations of those tax laws and regulations by taxing authorities; or
- fluctuations in the budgets of federal, state and local governmental entities around the world.

These and other external factors may cause the market price and demand for our ordinary shares to fluctuate substantially, which may limit or prevent investors from readily selling their ordinary shares and may otherwise negatively affect the liquidity of our ordinary shares. In particular, stock markets in general have experienced volatility that has often been unrelated to the operating performance of a particular company. These broad market fluctuations may adversely affect the trading price of our ordinary shares. Some companies that experienced volatility in the trading price of their stock have been the subject of securities class action litigation.

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

As described in Note 6, "Commitments and Contingencies - Legal Proceedings" of the Notes to Consolidated Financial Statements and Item 1 - Legal Proceedings of this Form 10-Q, a purported class action lawsuit has been filed against us and certain of our current and former officers. This lawsuit seeks, among other things, compensatory damages and attorneys' fees and costs. We believe that the lawsuit lacks merit and we intend to vigorously defend against it. However, this lawsuit, like any litigation, is subject to inherent uncertainties, the outcome is necessarily uncertain and we might not prevail. Moreover, defending against the lawsuit could result in substantial costs and be time-consuming and distracting to our management and internal resources, which could have an adverse effect on our business, results of operations or financial condition.

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

As with any publicly traded company, your percentage ownership in us may be diluted in the future because of equity issuances for acquisitions, capital raising transactions or otherwise. We may need to raise additional capital in the future. If we are able to raise additional capital, we may issue equity or convertible debt instruments, which may severely dilute your ownership interest in us. In addition, we intend to continue to grant option awards to our directors, officers and employees, which would dilute your ownership stake in us. As of March 31, 2019, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plan was 8,261,236.

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

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

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

on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall.

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

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

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

We do not believe we were a PFIC for U.S. federal income tax purposes for our taxable years ended December 31, 2018, or any prior year. However, the application of the PFIC rules is subject to uncertainties in a number of respects, and we cannot assure that the U.S. Internal Revenue Service (the "IRS") will not take a contrary position. We also cannot assure that we will not be a PFIC for U.S. federal income tax purposes for any future taxable year.

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

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

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

Under current law, we are treated as a foreign corporation for U.S. federal tax purposes. However, changes to the U.S. Internal Revenue Code, U.S. Treasury Regulations or other IRS guidance thereunder could adversely affect our status as a foreign corporation or otherwise affect our effective tax rate. In addition, the U.S. Congress, the IRS, the Organization for Economic Co-operation and Development and other governments and agencies in jurisdictions where we do business have recently focused on issues related to the taxation of multinational corporations, and specifically in the area of "base erosion and profit shifting," where payments are made between affiliates from a jurisdiction with high tax rates to a jurisdiction with lower tax rates. As a result, the tax laws in the U.S. and other countries in which we do business could change on a prospective or retroactive basis, and any such changes could have an adverse effect on our business, financial condition, results of operations or growth prospects.

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

It may not be possible to enforce court judgments obtained in the U.S. against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is uncertainty as to whether the courts of Ireland would

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

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

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

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

Irish law requires that our shareholders renew every five years the authority of our Board of Directors to issue shares and to do so for cash without applying the statutory pre-emption right, and if our shareholders do not renew these authorizations by May 17, 2022 (or any renewal is subject to limitations), our ability to raise additional capital to fund our operations would be limited.

As an Irish incorporated company, we are governed by the Companies Act. The Companies Act requires that every five years our shareholders renew the separate authorities of our Board to (a) allot and issue shares, and (b) opt out of the statutory pre-emption right that otherwise applies to share issuances for cash (which pre-emption right would require that shares issued for cash be offered to our existing shareholders on a pro rata basis before the shares may be issued to new shareholders). At our shareholders' annual general meeting held on May 17, 2017, our shareholders authorized our Board to issue ordinary shares up to the amount of our authorized share capital, and to opt out of the statutory pre-emption right for such issuances. Under Irish law, these authorizations will expire on May 17, 2022, five years after our shareholders last renewed these authorizations. Irish law requires that our shareholders renew the authority for our Board to issue ordinary shares by a resolution approved by not less than 50% of the votes cast at a general meeting of our shareholders. Irish law requires that our shareholders renew the authority of our Board to opt out of the statutory pre-emption right in share issuances for cash by a resolution approved by not less than 75% of the votes cast at a general meeting of our shareholders. If these authorizations are not renewed before May 17, 2022, or are renewed with limitations, our Board would be limited in its ability to issue shares, which would limit our ability to raise additional capital to fund our operations, including the research, development and potential commercialization of our product candidates.

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

Irish stamp duty may be payable in respect of transfers of our ordinary shares (currently at the rate of 1% of the price paid or the market value of the shares acquired, if greater).

Under the Irish Stamp Duties Consolidation Act, 1999 (the "Stamp Duties Act"), a transfer of our ordinary shares from a seller who holds shares through DTC to a buyer who holds the acquired shares through DTC should not be subject to Irish stamp duty. Shareholders may also transfer their shares into or out of DTC without giving rise to Irish stamp duty provided that there is no change in the beneficial ownership of such shares and the transfer into or out of DTC is not effected in contemplation of a subsequent sale of such shares to a third party; in order to benefit from this exemption from Irish stamp duty, the seller must confirm to us that there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and there is no agreement for the sale of the shares by the beneficial owner to a third party being contemplated.

A transfer of our ordinary shares (i) by a seller who holds shares outside of DTC to any buyer, or (ii) by a seller who holds the shares through DTC to a buyer who holds the acquired shares outside of DTC, may be subject to Irish stamp duty. Payment of any Irish stamp duty is generally a legal obligation of the transferee.

Any Irish stamp duty payable on transfers of our ordinary shares could adversely affect the price of those shares.

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

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

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

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

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

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

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

ITEM 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

EXHIBIT INDEX

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
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

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\# *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.*

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 7, 2019

Prothena Corporation plc
(Registrant)

/s/ Gene G. Kinney

Gene G. Kinney
President and Chief Executive Officer

/s/ Tran B. Nguyen

Tran B. Nguyen
Chief Operating Officer and Chief Financial Officer

Exhibit 31.1

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 7, 2019

/s/ Gene G. Kinney

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

Exhibit 31.2

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 7, 2019

/s/ Tran B. Nguyen

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

Exhibit 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

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, 2019, 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 7, 2019

/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.