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, 2021

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 VK60, Ireland
(Address of principal executive offices including Zip Code)

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

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**

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, a smaller reporting company, or an emerging growth 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, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

The number of ordinary shares outstanding was 44,175,792 as of May 4, 2021.

PROTHENA CORPORATION PLC
Form 10-Q – QUARTERLY REPORT
For the Quarter Ended March 31, 2021

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Note Regarding Forward-Looking Statements

In addition to historical information, this Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. 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. In addition, any statements that refer to expectations, projections, or other characterizations of future events or circumstances are forward-looking statements.

These forward-looking statements, which reflect our beliefs, objectives, and expectations as of the date hereof, are estimates based on our best judgment. These statements relate to, among other things, our goal of building a protein dysregulation platform; the treatment potential and proposed mechanisms of action of drug candidates; plans for future clinical studies of our drug candidates; our collaborations with Roche and Bristol Myers Squibb and amounts we may receive under such collaborations; the sufficiency of our cash position to fund advancement of a broad pipeline; and our anticipated need for additional capital.

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 set forth below, those discussed under Part II Item 1A “Risk Factors” of this Quarterly Report on Form 10-Q, and in our other filings with the U.S. Securities and Exchange Commission:

- 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 Bristol Myers Squibb;
- 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 the market price of our ordinary shares;
- the outbreak of the novel strain of coronavirus SARS-CoV-2; and
- business disruptions.

Except as required by law or by the rules and regulations of the U.S. Securities and Exchange Commission, 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 Quarterly Report on Form 10-Q.

Summary of Risks Affecting Our Business

Our business is subject to numerous risks and uncertainties. The following summary highlights some of the risks you should consider with respect to our business and prospects. These risks are described more fully in Part II Item 1A “Risk Factors” of this Quarterly Report on Form 10-Q which includes a more complete discussion of the risks summarized below as well as a discussion of other risks related to our business, our prospects, and your investment in our ordinary shares.

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

- The COVID-19 pandemic has adversely affected our business and could have a material adverse effect on our liquidity, results of operations, financial condition, or business, including our nonclinical and clinical development programs.
- 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.
- We have entered into collaborations with Roche and Bristol-Myers Squibb and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.
- 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.
- 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.
- 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 future success depends on our ability to retain key personnel and to attract, retain, and motivate qualified personnel.

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, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 342,993	$ 295,380
Accounts receivable	1	15
Prepaid expenses and other current assets	7,955	2,537
Restricted cash, current	1,352	1,352
Total current assets	352,301	299,284
Non-current assets:		
Property and equipment, net	2,295	2,551
Operating lease right-of-use assets	16,411	17,811
Deferred tax assets	7,022	11,644
Restricted cash, non-current	1,352	1,352
Other non-current assets	338	333
Total non-current assets	27,418	33,691
Total assets	$ 379,719	$ 332,975
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 4,212	$ 4,117
Accrued research and development	9,355	9,044
Income taxes payable, current	—	36
Lease liability, current	5,617	5,512
Other current liabilities	4,272	7,139
Total current liabilities	23,456	25,848
Non-current liabilities:		
Deferred revenue, non-current	110,242	110,242
Lease liability, non-current	10,884	12,326
Other liabilities	553	553
Total non-current liabilities	121,679	123,121
Total liabilities	145,135	148,969
Commitments and contingencies (Note 6)		
Shareholders' equity:		
Euro deferred shares, €22 nominal value:	—	—
Authorized shares — 10,000 at March 31, 2021 and December 31, 2020		
Issued and outstanding shares — none at March 31, 2021 and December 31, 2020		
Ordinary shares, $0.01 par value:	442	399
Authorized shares — 100,000,000 at March 31, 2021 and December 31, 2020		
Issued and outstanding shares — 44,175,792 and 39,921,413 at March 31, 2021 and December 31, 2020, respectively		
Additional paid-in capital	1,053,906	966,636
Accumulated deficit	(819,764)	(783,029)
Total shareholders' equity	234,584	184,006
Total liabilities and shareholders' equity	$ 379,719	$ 332,975

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,	
	2021	**2020**
Collaboration revenue	$ 110	$ 141
License revenue	50	—
Total revenue	160	141
Operating expenses:		
Research and development	21,144	15,248
General and administrative	11,125	9,741
Total operating expenses	32,269	24,989
Loss from operations	(32,109)	(24,848)
Other income (expense):		
Interest income, net	11	1,137
Other income (expense), net	23	(24)
Other income, net	34	1,113
Loss before income taxes	(32,075)	(23,735)
Provision for (benefit from) income taxes	4,660	(166)
Net loss	$ (36,735)	$ (23,569)
Basic and diluted net loss per share	$ (0.91)	$ (0.59)
Shares used to compute basic and diluted net loss per share	40,250	39,909

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,	
	2021	**2020**
Operating activities		
Net loss	$ (36,735)	$ (23,569)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	304	384
Share-based compensation	6,176	5,536
Deferred income taxes	4,622	(495)
Amortization of right-of-use assets	1,400	1,345
Changes in operating assets and liabilities:		
Accounts receivable	14	(106)
Prepaid and other assets	(5,259)	(4,278)
Accounts payable, accruals and other liabilities	(2,851)	(748)
Operating lease liabilities	(1,337)	(1,236)
Net cash used in operating activities	(33,666)	(23,167)
Investing activities		
Purchases of property and equipment	(48)	(22)
Net cash used in investing activities	(48)	(22)
Financing activities		
Proceeds from issuance of ordinary shares in public offering, net	78,367	—
Proceeds from issuance of ordinary shares upon exercise of stock options	2,960	151
Net cash provided by financing activities	81,327	151
Net increase (decrease) in cash, cash equivalents and restricted cash	47,613	(23,038)
Cash, cash equivalents and restricted cash, beginning of the year	298,084	378,427
Cash, cash equivalents and restricted cash, end of the period	$ 345,697	$ 355,389
Supplemental disclosures of cash flow information		
Cash paid for income taxes, net	$ 402	$ 417
Supplemental disclosures of non-cash investing and financing activities		
Acquisition of property and equipment included in accounts payable and accrued liabilities	$ —	$ 24
Receivable from option exercises	$ 123	$ —
Offering costs included in accounts payable and accrued liabilities	$ 313	$ —

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,	
	2021	2020
Cash and cash equivalents	$ 342,993	$ 352,685
Restricted cash, current	1,352	—
Restricted cash, non-current	1,352	2,704
Total cash, cash equivalents and restricted cash, end of the period	$ 345,697	$ 355,389

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

	Three Months Ended March 31, 2021				
	Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount			
Balances at December 31, 2020	**39,921,413**	**$ 399**	**$ 966,636**	**$ (783,029)**	**$ 184,006**
Share-based compensation	—	—	6,176	—	6,176
Issuance of ordinary shares upon exercise of stock options	229,379	3	3,080	—	3,083
Issuance of ordinary shares in public offering, net of issuance costs of $5.5 million	4,025,000	40	78,014	—	78,054
Net loss	—	—	—	(36,735)	(36,735)
Balances at March 31, 2021	**44,175,792**	**$ 442**	**$ 1,053,906**	**$ (819,764)**	**$ 234,584**

	Three Months Ended March 31, 2020				
	Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount			
Balances at December 31, 2019	**39,898,561**	**399**	**944,407**	**(671,885)**	**272,921**
Share-based compensation	—	—	5,536	—	5,536
Issuance of ordinary shares upon exercise of stock options	12,852	—	151	—	151
Net loss	—	—	—	(23,569)	(23,569)
Balances at March 31, 2020	**39,911,413**	**$ 399**	**$ 950,094**	**$ (695,454)**	**$ 255,039**

See accompanying Notes to Consolidated Financial Statements.

Notes to the Condensed Consolidated Financial Statements
(unaudited)

1. Organization

Description of Business

Prothena Corporation plc ("Prothena" or the "Company") is a late-stage clinical company with a robust pipeline of novel investigational therapeutics built on protein dysregulation expertise with the potential to change the course of devastating rare peripheral amyloid and neurodegenerative diseases.

Fueled by its deep scientific expertise built over decades of research, the Company is advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which its ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. The Company's wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, PRX004 for the potential treatment of ATTR amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012 that targets Aβ (Amyloid beta). The Company's partnered programs include prasinezumab, in collaboration with Roche for the potential treatment of Parkinson's disease and other related synucleinopathies, and programs that target tau (PRX005), TDP-43 and an undisclosed target in collaboration with Bristol Myers Squibb for the potential treatment of Alzheimer's disease, amyotrophic lateral sclerosis (ALS).

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, 2021, the Company had an accumulated deficit of $819.8 million and cash and cash equivalents of $343.0 million.

In March 2021, the Company sold an aggregate of 4,025,000 ordinary shares for net proceeds of approximately $78.1 million, after deducting the underwriting discount and estimated offering expenses, in an underwritten public offering.

Based on the Company's business plans, management believes that the Company's cash and cash equivalents at March 31, 2021, 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 Bristol Myers Squibb, 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; the outbreak of the novel strain of coronavirus SARS-CoV-2; 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 February 26, 2021 (the "2020 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, research and development expenses and leases. 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, 2021, from the significant accounting policies described in Note 2 of the Notes to Consolidated Financial Statements in the 2020 Form 10-K.

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 receivables recorded in the Condensed Consolidated Balance Sheet include amounts due from a Roche entity located in Switzerland. Collaboration 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, 2021, $2.3 million of the Company’s property and equipment, net were held in the U.S. and none were in Ireland. As of December 31, 2020, $2.6 million of the Company's property and equipment, net 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

There were no new accounting pronouncements or changes to accounting pronouncements during the three months ended March 31, 2021 that are of significance or potential significance 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 $273.1 million and $226.1 million in money market funds included in cash and cash equivalents at March 31, 2021, and December 31, 2020, respectively.

4. Composition of Certain Balance Sheet Items

Property and Equipment, net

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

	March 31, 2021	December 31, 2020
Machinery and equipment	$ 9,350	$ 9,343
Leasehold improvements	1,318	1,278
Purchased computer software	1,424	1,423
	12,092	12,044
Less: accumulated depreciation and amortization	(9,797)	(9,493)
Property and equipment, net	$ 2,295	$ 2,551

Depreciation expense was $0.3 million and $0.4 million for the three months ended March 31, 2021 and 2020, respectively.

Other Current Liabilities

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

	March 31, 2021	2020
Payroll and related expenses	$ 3,516	$ 5,927
Professional services	510	696
Other	246	516
Other current liabilities	$ 4,272	$ 7,139

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, 2021, and 2020, 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,	
	2021	2020
Numerator:		
Net loss	$ (36,735)	$ (23,569)
Denominator:		
Weighted-average ordinary shares outstanding	40,250	39,909
Net loss per share:		
Basic and diluted net loss per share	$ (0.91)	$ (0.59)

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,	
	2021	2020
Stock options to purchase ordinary shares	8,825	8,412

6. Commitments and Contingencies

Lease Commitments

The Company currently has two leases relating to its facilities in South San Francisco and Dublin, Ireland.

Current SSF Facility

The Company has a noncancelable operating sublease (the “Lease”) covering 128,751 square feet of office and laboratory space in South San Francisco, California, U.S. (the “Current SSF Facility”). The Lease includes a free rent period and escalating rent payments and has a remaining lease term of 2.75 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. The Lease is considered an operating lease under ASC 842. Prior to the Company's adoption of ASC 842, this Lease was considered a build-to-suit lease.

The Company’s 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 such improvements are deemed to be owned by the lessor, are 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. Total operating lease cost was $1.6 million and $1.6 million for the three months ended March 31, 2021 and 2020, respectively. Total cash paid against the operating lease liability was $1.5 million and $1.5 million for the three months ended March 31, 2021 and 2020, respectively.

The discount rate used to determine the lease liability was 4.25%. To estimate the Company's collateralized incremental borrowing rate, the Company inquired with banks that had a business relationship with the Company. Furthermore, the Company's operating lease in Dublin is not included in the lease liability and right-of-use asset recorded due to its nominal amount. As of March 31, 2021, 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 and a nominal operating lease for office equipment, none of the Company's contracts contain a 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 initial measurement of right-of-use asset for the Lease includes the tenant improvement added by the Company wherein the lessor was deemed the accounting owner, net of the tenant improvement allowance received from the sublandlord and the master landlord.

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 was 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, which was received in 2019, 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, 2021, none of the remaining standby letter of credit amount of $2.7 million 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") to sub-sublease approximately 46,641 square feet of office and laboratory space of the Current SSF Facility to the Sub-Subtenant. The Sub-Sublease is considered an operating lease under ASC 842. For the three months ended March 31, 2021 and 2020, the Company recorded $0.7 million and $0.7 million, respectively, of 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 Lease or the corresponding master lease 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

The Company entered into an agreement to lease 133 square feet of office space in Dublin, Ireland (the "Dublin Lease"). The current lease term expires on November 30, 2021. The Dublin Lease also has an automatic renewal clause, pursuant to which the agreement will be extended automatically for successive periods equal to the current term but no less than three 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, 2021, the Company is obligated to make lease payments over the remaining term of the Dublin Lease of approximately €16,000, or $19,000 as converted using an exchange rate as of March 31, 2021.

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, 2021, are as follows (in thousands):

Year Ended December 31,	Operating Leases	Sub-Sublease Rental
2021 (9 months)	4,662	2,216
2022	6,350	3,047
2023	6,535	3,019
2024	—	—
Total	17,547	$ 8,282
Less: Present value adjustment	(1,027)	
Nominal lease payments	(19)	
Lease liability	$ 16,501	

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, 2021 and 2020.

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, 2021, the Company had non-cancelable purchase commitments to suppliers for $11.9 million of which $3.6 million is included in accrued current liabilities, and contractual obligations under license agreements of $0.7 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, 2021 (in thousands):

	Total	2021	2022	2023	2024	2025	Thereafter
Purchase Obligations [1]	$ 11,921	$ 11,921	$ —	$ —	$ —	$ —	$ —
Contractual obligations under license agreements [2]	740	135	70	70	60	60	345
Total	$ 12,661	$ 12,056	$ 70	$ 70	$ 60	$ 60	$ 345

[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.*

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 bore 100% of the cost of conducting the research collaboration under the License Agreement during the research term, which expired December 31, 2017. 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 studies, 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 prasinezumab for the Parkinson's disease indication in the U.S. on a 70%/30% basis with the Company receiving 30% of the profit and losses provided that the Company has not exercised its opt-out right.

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

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

Collaboration Accounting

The License Agreement was evaluated under ASC 808, Collaborative Agreements. At the outset of the 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.

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, 2021, and December 31, 2020, 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, 2021, 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, 2021 and December 31, 2020, there were no remaining Research Services performance obligations.

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 the Company recognizes the reimbursements for Additional Development Services as collaboration revenue as earned.

Revenue and Expense Recognition

The Company recognized $0.1 million and $0.1 million as collaboration revenue from Roche for the three months ended March 31, 2021 and 2020, respectively. Cost sharing payments to Roche are recorded as R&D expenses. The Company recognized $4.4 million and $3.9 million in R&D expenses for payments made to Roche during the three months ended March 31, 2021 and 2020, respectively. The Company had accounts receivable from Roche of $1,000 and $3,000 at March 31, 2021 and December 31, 2020, 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.

Collaboration Agreement with Bristol Myers Squibb

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 (which was acquired by Bristol Myers Squibb ("BMS") in November 2019), 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, BMS 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 BMS 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 BMS elects to assume responsibility for completing such Phase 1 clinical trials (at its cost), BMS 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.

BMS US and Global Rights and Licenses

On a program-by-program basis, beginning on the effective date of the Collaboration Agreement and ending on the date that the IND Option term expires for such program (which generally occurs sixty days after the date on which Prothena delivers to BMS the first complete data package for an IND that was filed for a lead candidate from the relevant program), BMS 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 BMS 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) BMS's election to assume responsibility to complete such Phase 1 clinical trials (at its cost), BMS 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 BMS has previously exercised its US Rights, BMS 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 BMS exercises its Global Rights, BMS 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 BMS would have decision making authority over developing, obtaining and maintaining regulatory approval for, manufacturing and commercializing the Collaboration Products worldwide.

After BMS'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. Following an exercise by BMS of either US Rights or Global Rights for such collaboration program, 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.

BMS 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 BMS 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 BMS 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 BMS challenges a patent licensed by Prothena to BMS 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, BMS (formerly Celgene) is subject to certain transfer restrictions. In addition, BMS 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.

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 is not obligated to transfer the US License or Global License to BMS unless BMS exercises its US Rights or Global Rights, 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 are not promised goods or services and therefore are not considered performance obligations under ASC 606, unless and until the Company agrees to perform the Phase 1 clinical studies (after the IND option exercise) that are determined to be performance obligations at the time the option is exercised. 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. In the event the Company agrees to be involved in a Phase 1 clinical study, the Company will further evaluate whether any such promise represents a performance obligation at the time the option is exercised. If it is concluded that the Company has obligated itself to an additional performance obligation besides the license granted at IND option exercise, then the effects of the changes in the arrangement will be evaluated under the modification guidance of ASC 606.

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 BMS unless BMS exercises its right to participate in the Phase 1 development.

Compensation for the Company's provision of inventory supply, to the extent requested by BMS would be paid to Prothena by BMS at a reasonable stand-alone selling price for such supply. Given that (i) there is substantial uncertainty about the development of the programs, (ii) the pricing for the inventory is at its standalone selling price and (iii) the manufacturing services require the entity to transfer additional goods or services that are incremental to the goods and services provided prior to the resolution of the contingency, the Company's supply of product is not a material right. Therefore, the inventory supply is not considered a performance obligation unless and until, requested by BMS.

In addition to the grant of the US License after BMS exercises its US Rights for a program, BMS is entitled to receive certain ancillary development services from the Company, such as technology transfer assistance, regulatory support, safety data reporting activities and transition supply, if requested by BMS.

In addition to the grant of the Global License after BMS exercises the Global Rights for a program, BMS is entitled to receive certain ancillary development services from Prothena, such as ongoing clinical trial support upon request by BMS, transition supply, if requested by BMS, and regulatory support for coordination of pharmacovigilance matters.

The Company evaluated the potential obligations to transfer the US Licenses and Global Licenses and performance of the ancillary development services subsequent to exercise of the US Rights and Global Rights, if the options are exercised by BMS, under ASC 606-10-55-42 and 55-43 to determine whether the US Rights or the Global Rights provided BMS a “material right” and concluded that BMS’s options to exercise its US Rights and Global Rights represented “material rights” to BMS that it would not have received without entering into the Agreement.

There are a total of six options including US Rights and Global Rights to acquire a US License and a Global License, respectively, and rights to request certain development services (following exercise of the US Rights and Global Rights, respectively) for each of the three programs. Per ASC 606, the US Rights and Global Rights are material rights and therefore are performance obligations. The goods and services underlying the options are not accounted for as separate performance obligations, but rather become performance obligations, if and when, an option is exercised.

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 expects that the initial transaction price will be allocated across the US Rights and Global Rights for each program in a range of approximately $15-$25 million and $10-$18 million, respectively.

The Company did not include the option fees in the initial transaction price because such fees 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 and provide certain ancillary development services if requested by BMS, subsequent to its exercise of the US Rights and Global Rights, respectively, for such program. The Company will include the option fees in the transaction price at the point in time a material right is exercised. In addition, the Company did not include in the initial transaction price certain clinical and regulatory milestone payments since they relate to licenses for which BMS has not yet exercised its option to obtain and 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 BMS (formerly 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 BMS (which would be when BMS exercises the US Right or Global Right and receives control of the US License or Global License for at least one of the programs), or when the IND Option term expires if BMS does not exercise the US Right (which is generally sixty days after the date on which Prothena delivers to BMS the first complete data package for an IND that was filed for a lead candidate from the relevant program), or when the Phase 1 Option term expires if BMS does not exercise the Global Right (which is generally ninety days after the date on which Prothena delivers to BMS the first complete data package for a Phase 1 clinical trial for a lead candidate from the relevant program) or at the termination of the Collaboration Agreement, whichever occurs first. At such point that the Company transfers control of goods or services to BMS, or when the option expires, the Company will recognize revenue as a continuation of the original contract. Under this approach, the Company will treat the consideration allocated to the material right as an addition to the consideration for the goods or services underlying the contract option.

At inception of the Collaboration Agreement, the Company estimated the standalone selling price for each performance obligation (i.e., the US Rights and Global Rights by program). The estimate of standalone selling price for the US Rights and Global Rights by program was based on the adjusted market assessment approach using a discounted cash flow model. The key assumptions used in the discounted cash flow model 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, the estimated time to commercialization of the drug for that program and a discount rate.

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 BMS or receipt by BMS 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 BMS to the Company is variable and the amount of such variable consideration varies based upon the occurrence or non-occurrence of future events that are not within the control of either BMS 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, 2021, and 2020.

8. Shareholders' Equity

Ordinary Shares

As of March 31, 2021, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of $0.01 per ordinary share and 44,175,792 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, 2021, 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, 2021. 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.

March 2021 Offering

In March 2021, the Company completed an underwritten public offering of an aggregate of 4,025,000 of its ordinary shares at a public offering price of $20.75 per ordinary share. The Company received aggregate net proceeds of approximately $78.1 million, after deducting the underwriting discount and offering costs.

9. Share-Based Compensation

2018 Long Term Incentive Plan

In May 2018, the Company's shareholders approved the 2018 Long Term Incentive Plan. In May 2020, the Company's shareholders approved an amendment to the 2018 Long Term Incentive Plan (as amended, the "2018 LTIP") to increase the number of ordinary shares available for issuance under that Plan by 1,500,000 ordinary shares. Under the 2018 LTIP, the number of ordinary shares authorized for issuance under the 2018 LTIP is equal to the sum of (a) 3,300,000 ordinary shares, (b) 1,177,933 ordinary 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 ordinary 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 ordinary shares may be issued pursuant to the exercise of ISOs. The 2018 LTIP 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 granted to date, with the exception of options granted pursuant to the Option Exchange (as discussed below), have had a ten year life.

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. All options under the 2012 LTIP were granted for periods of ten years.

2020 Employment Inducement Incentive Plan

On February 25, 2020, the Company's Board of Directors approved the 2020 Employment Inducement Incentive Plan. The 2020 EIIP provides for the grant of NQSOs, SARs, restricted shares, RSUs, performance bonus awards, performance share units awards, or other share or cash-based awards to eligible individuals. Options under the 2020 EIIP may be granted for periods up to ten years. All options issued to date have had a ten year life. As of December 31, 2020, the number of ordinary shares authorized for issuance under the 2020 EIIP was 710,000. During the three months ended March 31, 2021, the 2020 EIIP was further amended to increase the ordinary shares available for issuance under that Plan by 75,000 ordinary shares. As of March 31, 2021, the number of ordinary shares authorized for issuance under the 2020 EIIP was 785,000 and no ordinary shares remained available for future awards under the 2020 EIIP, although the Company's Board of Directors reserves the right to amend the 2020 EIIP to increase the number of ordinary shares available and to make additional awards to key new hires.

Shares Available for Grant

The Company granted 2,550,977 (1,372,587 of which were replacement options granted pursuant to the Option Exchange (as discussed below) and 1,455,450 options during the three months ended March 31, 2021, and 2020, respectively, in aggregate under its equity plans. The Company's option awards generally vest over four years. As of March 31, 2021, 1,434,506 ordinary shares remained available for grant under the 2018 LTIP and options to purchase 8,825,499 ordinary shares in aggregate under the Company's equity plans were outstanding with a weighted-average exercise price of approximately $16.23 per share.

2020 Option Exchange Program

On May 19, 2020, the Company's shareholders approved a proposal to allow for a one-time option exchange program (the "Option Exchange") designed to give its employees, including our named executive officers, and non-employee directors of the Company, who are employed by or providing services to the Company through the completion of the Option Exchange, the opportunity to exchange eligible options for new replacement options with an exercise price equal to the fair market value of the Company's ordinary shares on the date the replacement options are granted. Any new replacement options would be subject to a new initial one-year vesting period from the replacement option grant date and after such initial one-year vesting period would vest in substantially equal installments on the remaining original vesting dates of each exchanged option. Additionally, any new replacement options would have a term equal to the remaining term of the applicable exchanged option.

On November 9, 2020, the Company commenced the Option Exchange which closed on February 12, 2021. Options to purchase approximately 2.1 million ordinary shares were exchanged for options to purchase approximately 1.4 million ordinary shares with an exercise price of $22.85 per share. Options were eligible to exchange if they had an exercise price equal to or greater than $17.63 per share, were granted prior to April 23, 2018, under the 2012 LTIP, and were held by an eligible participant. No incremental share-based compensation expense was recognized for the Option Exchange.

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 2025 related to unvested share-based payment awards at March 31, 2021, is $44.8 million. The weighted-average period over which the unearned share-based compensation is expected to be recognized is 2.27 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, 2021, and 2020 was based on awards granted under the 2012 LTIP, the 2018 LTIP, and the 2020 EIIP. The following table summarizes share-based compensation expense for the periods presented (in thousands):

	Three Months Ended March 31,	
	2021	**2020**
Research and development	$ 1,954	$ 2,017
General and administrative	4,222	3,519
Total share-based compensation expense	$ 6,176	$ 5,536

The Company recognized tax benefits from share-based awards of $1.2 million and $1.1 million for the three months ended March 31, 2021 and 2020, respectively.

With the exception of options granted pursuant to the Option Exchange, the fair value of the options granted to employees and non-employee directors during the three months ended March 31, 2021, and 2020 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,	
	2021	**2020**
Expected volatility	81.3 %	81.5 %
Risk-free interest rate	1.0 %	1.2 %
Expected dividend yield	—	— %
Expected life (in years)	6.0	6.0
Weighted average grant date fair value	$ 15.09	$ 8.32

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, 2021:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	8,744,765	$ 20.42	7.19	$ 4,656
Granted [1]	2,550,977	22.39		
Exercised	(229,379)	13.43		
Forfeited[2]	(236,876)	30.60		
Expired[3]	(2,003,988)	40.98		
Outstanding at March 31, 2021	8,825,499	$ 16.23	7.44	$ 81,230
Vested and expected to vest at March 31, 2021	8,290,411	$ 16.15	7.37	$ 77,128
Vested at March 31, 2021	3,356,692	$ 14.60	6.48	$ 37,958

[1] *Includes replacement options to purchase 1,372,587 ordinary shares granted pursuant to the Option Exchange.*

[2] *Includes unvested options to purchase 179,959 ordinary shares that were exchanged pursuant to the Option Exchange.*

[3] *Includes vested options to purchase 1,934,446 ordinary shares that were exchanged pursuant to the Option Exchange.*

The total intrinsic value of options exercised was approximately $2.5 million and $35,000 during the three months ended March 31, 2021, and 2020, respectively, determined as of the date of exercise.

10. Income Taxes

The major taxing jurisdictions for the Company are Ireland and the U.S. The Company recorded an income tax provision of $4.7 million and an income tax benefit of $0.2 million for the three months ended March 31, 2021 and 2020, respectively. The provision for income taxes differs from the statutory tax rate of 12.5% applicable to Ireland primarily due to Irish net operating losses for which a tax provision benefit is not recognized, 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.

On January 1, 2021, the Company adopted the Accounting Standards Update 2019-12 ("ASU 2019-12"), Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. There were no impacts from the provisions of ASU 2019-12 on the Company's tax provision for the three months ended March 31, 2021.

Pursuant to ASU 2016-09, the Company recorded a net tax shortfall of a $0.1 million for the three months ended March 31, 2021, and a net tax shortfall of $0.1 million for the three months ended March 31, 2020, all of which were recorded as part of its income tax provision in the Condensed Consolidated Statements of Operations.

On January 1, 2019, the Company adopted ASC 842, 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.

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's deferred tax assets ("DTA") are composed primarily of its Irish subsidiaries' net operating loss carryforwards, state net operating loss carryforwards available to reduce future taxable income of the Company's U.S. subsidiaries, 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.

For the three months ended March 31, 2021, the Company recorded a reduction in DTA of $4.6 million, primarily due to changes in the Company's 162(m) limitations of $3.5 million as a result of the Company's option exchange program that closed on February 12, 2021, which was considered a material modification from a tax perspective and a $0.9 million DTA reduction related to the newly issued American Rescue Plan Act, which expanded the list of covered employees.

No provision for income tax in Ireland has been recognized on undistributed earnings of the Company's U.S. subsidiaries. The Company considers the U.S. earnings to be indefinitely reinvested. Unremitted earnings may be subject to withholding taxes (potentially at 5% in the U.S.) 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. taxes withheld, and as of March 31, 2021, the Company's current year net operating losses in Ireland are sufficient to offset any potential dividend income received from its overseas subsidiaries.

11. Subsequent Event

On May 10, 2021, the Company announced that the first patient was dosed in the global Phase 2b PADOVA study of prasinezumab in early Parkinson's disease, which is being conducted by Roche. Prasinezumab is the focus of a worldwide collaboration between the Company and Roche. In connection with the dosing of the first patient in the PADOVA study, the Company will receive a $60.0 million milestone payment.

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

In addition to historical information, this Quarterly Report on Form 10-Q contains forward-looking statements which may cause our actual results to differ materially from expectations, plans and anticipated results discussed in forward-looking statements. Factors that could cause our actual results to differ materially include, but are not limited to, the risks and uncertainties set forth in the "Summary of Risks Affecting Our Business" at the beginning of this Quarterly Report on Form 10-Q, Part II Item 1A "Risk Factors" of this Quarterly Report on Form 10-Q, and in our other filings with the U.S. Securities and Exchange Commission.

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 SEC on February 26, 2021 (the "2020 Form 10-K").

Overview

Prothena is a late-stage clinical company with a robust pipeline of novel investigational therapeutics built on protein dysregulation expertise with the potential to change the course of devastating rare peripheral amyloid and neurodegenerative diseases. Fueled by our deep scientific expertise built over decades of research, we are advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which our ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged.

Our wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, PRX004 for the potential treatment of ATTR amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012 that targets Aβ (Amyloid beta). Our partnered programs include prasinezumab, in collaboration with Roche for the potential treatment of Parkinson's disease and other related synucleinopathies, and programs that target tau (PRX005), TDP-43, and an undisclosed target in collaboration with Bristol Myers Squibb for the potential treatment of Alzheimer's disease, amyotrophic lateral sclerosis (ALS), or other neurodegenerative diseases.

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

Birtamimab for the Potential Treatment of AL Amyloidosis

Birtamimab is an investigational humanized antibody that targets toxic misfolded light chain that causes organ dysfunction and failure in patients with AL amyloidosis. AL amyloidosis is a rare, progressive, and fatal disease where immunoglobulin light chain proteins produced by clonal plasma cells misfold, aggregate, and deposit as amyloid in vital organs. These toxic aggregates and amyloid deposits cause progressive damage and failure of vital organs, including the heart.

Birtamimab binds to both soluble and insoluble amyloid aggregates in multiple organs and promotes the clearance of amyloid deposits via phagocytosis. This depleter mechanism of action broadly targets misfolded kappa and lambda light chain to clear deposited amyloid that causes organ dysfunction and failure in patients with AL amyloidosis. Birtamimab has been granted Fast Track Designation by the U.S. Food and Drug Administration (FDA) for the treatment of Mayo Stage IV patients

with AL amyloidosis to reduce the risk of mortality and has been granted Orphan Drug Designation by both the FDA and European Medicines Agency (EMA).

It is estimated that 200,000 to 400,000 patients globally suffer from this rare disease, with approximately 60,000 to 120,000 (or 30%) of those patients being categorized as Mayo Stage IV. Patients categorized at diagnosis as Mayo Stage IV have poor outcomes with current standard-of-care that aims to reduce the production of new protein but does not directly target and clear the toxic amyloid that deposits in organs. There are currently no approved treatments for AL amyloidosis and there is an urgent unmet medical need for therapies that improve survival in patients at risk for early mortality due to amyloid deposition.

Confirmatory Phase 3 AFFIRM-AL Study Design under SPA Agreement with FDA

Based on further analyses regarding data from the VITAL study and multiple in-depth discussions with the FDA, we announced plans on February 1, 2021 to advance birtamimab into the confirmatory Phase 3 AFFIRM-AL study in Mayo Stage IV patients with AL amyloidosis. AFFIRM-AL is a registration-enabling Phase 3 study that will be conducted with a primary endpoint of all-cause mortality at $p \leq 0.10$ under a Special Protocol Assessment (SPA) agreement with the FDA.

AFFIRM-AL will be a global, multi-center, double-blind, placebo-controlled, 2:1 randomized, time-to-event study expected to enroll approximately 150 newly diagnosed, treatment naïve patients with AL amyloidosis categorized as Mayo Stage IV. It has been designed to evaluate the primary endpoint of all-cause mortality with a significance level of $p \leq 0.10$. Secondary endpoints will assess change from baseline to month 9 in quality of life as measured by SF-36v2 PCS and functional capacity as measured by 6MWT distance.

An interim analysis will be conducted when approximately 50% of the events have occurred, allowing the independent data monitoring committee to recommend either continuing the study or stopping early for overwhelming efficacy. Patients will receive 24 mg/kg of birtamimab or placebo by intravenous infusion every 28 days, with all patients receiving concurrent standard of care therapy consisting of a first line bortezomib-containing regimen.

More information on the Phase 3 VITAL study can be found in the Investors section of www.prothena.com or by searching NCT#02312206 on clinicaltrials.gov.

Prasinezumab for the Potential Treatment of Parkinson's Disease and Other Synucleinopathies

Prasinezumab is an investigational monoclonal antibody targeting alpha-synuclein designed to slow the progressive neurodegeneration associated with synuclein misfolding and/or the cell-to-cell transmission of the pathogenic, aggregated forms of synuclein in Parkinson's disease and other synucleinopathies. Prasinezumab is the focus of a worldwide collaboration between Prothena and Roche. Parkinson's disease is a progressive degenerative disorder of the central nervous system (CNS) that affects approximately one in 100 people over the age of 60, with incidence increasing based on an aging population. With an estimated seven to 10 million people living with Parkinson's disease worldwide today, it is the most common neurodegenerative movement disorder and fastest growing neurological disorder. There are currently no disease-modifying treatments available that target the underlying cause of Parkinson's disease and can slow its progression.

Phase 2b PADOVA Study

On October 20, 2020, we announced that based on positive signals of efficacy consistent with disease modification in the PASADENA study, Roche and Prothena plan to advance prasinezumab into a Phase 2b study (PADVOA) to further assess the efficacy of prasinezumab in an expanded patient population. PADOVA will be conducted by Roche and is a Phase 2b, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of prasinezumab in patients with early Parkinson's disease who are on stable symptomatic (levodopa) medication. The study will enroll 575 patients randomized to receive either prasinezumab or placebo via intravenous infusion every 4 weeks. The primary endpoint is time to meaningful progression on motor signs of the disease, as assessed by ≥5 point increase in Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III score from baseline. Additional information can be found on clinicaltrials.gov by searching NCT#04777331.

Prasinezumab is the first anti-alpha synuclein antibody to advance into late-stage development. On May 10, 2021, we announced that the first patient was dosed in the PADOVA study. In connection with the dosing of the first patient, we will receive a $60.0 million milestone payment.

On March 11, 2021, Roche gave two oral presentations at the 15th International Conference on Alzheimer's and Parkinson's Diseases (AD/PD 2021) highlighting data from a new pre-specified exploratory subgroup analyses from Part 1 of

the Phase 2 PASADENA study showing slowing of clinical decline with prasinezumab was even more evident in subgroups with faster disease progression. Separately, Roche presented new digital biomarker data from its remote monitoring technology used in the study that was consistent with a potential disease modifying effect of prasinezumab in slowing Parkinson's disease progression and in line with the Phase 2 PASADENA study results.

PRX004 for the Potential Treatment of ATTR Amyloidosis

PRX004 is an investigational antibody designed to deplete amyloid associated with disease pathology in hereditary and wild type ATTR amyloidosis without affecting the native tetrameric form of the protein. PRX004's proposed mechanism of action is to deplete both circulating non-native TTR to prevent further deposition and deposited amyloid to improve organ function. PRX004 has been shown in preclinical studies to inhibit amyloid fibril formation, neutralize soluble aggregate forms of non-native TTR, and promote clearance of insoluble amyloid fibrils through antibody-mediated phagocytosis. This differentiated depleter mechanism of action could be developed as a monotherapy approach to ATTR amyloidosis and might also complement existing therapeutic approaches which either stabilize or reduce production of the native TTR tetramer. It is estimated that between 400,000 to 1.4 million patients suffer from ATTR-cardiomyopathy (ATTR-CM). Within this population, between 130,000 to 490,000 patients are estimated to be moderate-to-advanced and categorized as New York Heart Association Class III and IV.

On April 18, 2021, we gave an oral presentation featuring results from the Phase 1 study of PRX004 in ATTR amyloidosis at the American Association of Neurology (AAN) 2021 Virtual Annual Meeting. PRX004 showed favorable results as demonstrated by slowing of neuropathy progression for all 7 evaluable patients at 9 months, including improvement in neuropathy in 3 of the 7 patients, and improved cardiac systolic function for all 7 patients. In this Phase 1 study, PRX004 was found to be generally safe and well tolerated across all dose levels.

The long-term extension portion of the Phase 1 study was disrupted by the COVID-19 pandemic. As a result, 7 patients received all infusions through 9 months and were considered evaluable for efficacy. For all of the evaluable patients, slowing of neuropathy progression was evidenced by a +1.29 point mean change in Neuropathy Impairment Score (NIS), which was more favorable than expected progression of +9.2 points in untreated and placebo-treated patients with hereditary ATTR peripheral neuropathy based on analysis of published historical data. Improvement in neuropathy for 3 of these 7 evaluable patients demonstrated by a mean change in NIS of -3.33 points at 9 months and improvement in cardiac function for all 7 evaluable patients demonstrated by a decrease in global longitudinal strain (GLS) of –1.21% at 9 months (centrally read). These results were previously highlighted by the Company on December 9, 2020.

Based on the results of the Phase 1 study, we are planning to advance PRX004 into a late-stage study in moderate-to-advanced ATTR-cardiomyopathy patients. This is an area of urgent need which directly aligns with PRX004's differentiated depleter mechanism that targets the amyloid that puts patients at risk of early mortality due to organ dysfunction and failure.

PRX005 for the Potential Treatment of Alzheimer's Disease

PRX005 is an investigational antibody that targets tau, a protein implicated in diseases including AD, FTD, progressive supranuclear palsy (PSP), chronic traumatic encephalopathy (CTE) and other tauopathies. Cell-to-cell transmission of pathogenic tau in the extracellular space is thought to be the primary mechanism for the spread of tau pathology in Alzheimer's disease and has been well established in vitro and in vivo. The cell-to-cell transmission and accumulation of pathogenic tau correlates with progression of symptomatology and clinical decline in Alzheimer's disease. Several antibodies targeting various tau epitopes are currently being investigated for their ability to intervene in this pathogenic pathway and treat Alzheimer's disease, but antibodies that target mid-domain regions of tau may demonstrate superior attributes.

On March 11, 2021, we gave an oral presentation at AD/PD 2021 highlighting new preclinical data demonstrating that targeting the microtubule binding region (MTBR) of tau with PRX005 resulted in superior attributes for the potential treatment of Alzheimer's disease. PRX005 demonstrated superior attributes in multiple in vitro assays, displaying superior activity against tau uptake and neurotoxicity. In vivo treatment with PRX005 in transgenic tau mice and a seeding model reduced intraneuronal tau pathology and downstream behavioral deficits. PRX005 is being developed as part of the Company's global neuroscience collaboration with Bristol Myers Squibb.

March 2021 Offering

In March 2021, we completed an underwritten public offering of an aggregate of 4,025,000 of our ordinary shares at a public offering price of $20.75 per ordinary share. The Company received aggregate net proceeds of approximately $78.1 million after deducting the underwriting discount and estimated offering costs.

Critical Accounting Policies and Estimates

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

There were no significant changes to our critical accounting policies and estimates during the three months ended March 31, 2021, from the critical accounting policies and estimates disclosed in Management's Discussion and Analysis of Financial Condition and Results of Operations in our 2020 Form 10-K.

Recent Accounting Pronouncements

There have been no new accounting pronouncements or changes to accounting pronouncements during the three months ended March 31, 2021, as compared to the recent accounting pronouncements described in our 2020 Form 10-K, that are of significance or potential significance to us.

Results of Operations

Comparison of Three Months Ended March 31, 2021 and 2020

Revenue

	Three Months Ended March 31,		
	2021	2020	Percentage Change
	(Dollars in thousands)		
Collaboration revenue	110	141	(22)%
License revenue	50	—	nm
Total revenue	160	141	13 %

n/m = not meaningful

Total revenue was $0.2 million and $0.1 million for the three months ended March 31, 2021 and 2020, respectively.

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

License revenue includes fees paid under the License Agreement entered into on March 1, 2020, between the Company's wholly owned subsidiary, Prothena Biosciences Limited, and F. Hoffmann-La Roche Ltd.

Operating Expenses

	Three Months Ended March 31,		
	2021	2020	Percentage Change
	(Dollars in thousands)		
Research and development	21,144	15,248	39 %
General and administrative	11,125	9,741	14 %
Total operating expenses	32,269	24,989	29 %

Total operating expenses consist of R&D expenses and general and administrative ("G&A") expenses. Our operating expenses were $32.3 million and $25.0 million for the three months ended March 31, 2021 and 2020, 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 birtamimab (formerly 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 the 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 increased by $5.9 million or 39%, for the three months ended March 31, 2021, compared to the same period in the prior year. The increase for the three months ended March 31, 2021 was primarily due to higher R&D consulting expense, higher personnel expenses, higher manufacturing costs primarily related to our PRX012 and birtamimab programs and to a lesser extent PRX004 as well as a credit for insurance claim related to the PRX003 program recorded in the first quarter of 2020 with no corresponding amount this year, higher clinical trial expense primarily related to birtamimab partially offset by lower PRX004 clinical trial expenses, and higher collaboration expense related to the prasinezumab program with Roche.

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 birtamimab, prasinezumab, PRX003, PRX004 and other R&D expenses for the three months ended March 31, 2021 and 2020 and the cumulative amounts to date (in thousands):

	Three Months Ended March 31,		Cumulative to Date
	2021	2020	
Birtamimab (NEOD001) [1]	$ 6,510	$ 1,060	$ 329,899
Prasinezumab (PRX002/RG7935)[2]	$ 4,876	$ 4,344	$ 103,215
PRX003 [3]	$ 28	$ (288)	$ 58,986
PRX004 [4]	$ 1,441	$ 3,828	76,403
Other R&D [5]	$ 8,289	$ 6,304	
	$ 21,144	$ 15,248	

[1] *Cumulative R&D costs to date for birtamimab (NEOD001) include the costs incurred from the date when the program was separately tracked in preclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount.*

[2] *Cumulative R&D costs to date for 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. For the three months ended March 31, 2021 and 2020, $0.1 million and $0.1 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 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. 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.*

We expect our R&D expenses to increase in 2021 over the prior year, primarily due to increased spending for our late stage programs, birtamimab and PRX004.

General and Administrative Expenses

Our G&A expenses increased by $1.4 million, or 14%, for the three months ended March 31, 2021, compared to the same period in the prior year. The increase for the three months ended March 31, 2021, compared to the prior year, was primarily due to higher personnel costs including share based compensation and costs for our director and officer insurance premiums.

We expect our G&A expenses to increase in 2021 compared to the prior year, primarily related to higher personnel costs including share based compensation and increases in our director and officer insurance premiums.

Other Income (Expense)

	Three Months Ended March 31,		
	2021	2020	Percentage Change
	(Dollars in thousands)		
Interest income	$ 11	$ 1,137	(99)%
Other income (expense), net	23	(24)	(196)%
Total other income, net	$ 34	$ 1,113	(97)%

Interest income decreased by $1.1 million, or 99%, for the three months ended March 31, 2021, compared to the same periods in the prior year, primarily due to lower interest income from our cash and money market accounts resulting from lower interest rates. Other income (expense), net for the three months ended March 31, 2021 and 2020, was primarily foreign exchange gains (losses) from transactions with vendors denominated in Euros.

Provision for (benefit from) Income Taxes

	Three Months Ended March 31,		
	2021	2020	Percentage Change
	(Dollars in thousands)		
Provision for (benefit from) income taxes	$ 4,660	$ (166)	(2,907)%

The provision for income taxes for the three months ended March 31, 2021 was $4.7 million and the benefit from income taxes for the three months ended March 31, 2020 was $0.2 million. The provision for income taxes increased by $4.8 million for the three months ended March 31, 2021, compared to the same periods in the prior year. The change in provision for (benefit from) income taxes for the three months ended March 31, 2021, was primarily due to a decrease in deferred tax asset related to the Company's February 12, 2021 option exchange program and a change in our share-based compensation 162(m) limitations associated with the increase in the number of covered employees under the American Rescue Plan Act.

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, 2021	December 31, 2020
Working capital	$ 328,845	$ 273,436
Cash and cash equivalents	342,993	295,380
Total assets	379,719	332,975
Total liabilities	145,135	148,969
Total shareholders' equity	234,584	184,006

Working capital was $328.8 million as of March 31, 2021, an increase of $55.4 million from working capital of $273.4 million as of December 31, 2020. This increase in working capital during the three months ended March 31, 2021, was primarily attributable to a higher cash and cash equivalents balance resulting from the net proceeds of approximately $78.1

million from our public offering in March 2021, and to a lesser extent, proceeds from stock option exercises of approximately $3.1 million, partially offset by cash use of $32.3 million for operating expenses (adjusted to exclude non-cash charges).

As of March 31, 2021, we had $343.0 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, 2021, $155.9 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 BMS (formerly 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, 2021 and 2020

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,	
	2021	2020
Net cash used in operating activities	(33,666)	(23,167)
Net cash used in investing activities	(48)	(22)
Net cash provided by financing activities	81,327	151
Net increase (decrease) in cash, cash equivalents and restricted cash	47,613	(23,038)

Cash Used in Operating Activities

Net cash used in operating activities was $33.7 million for the three months ended March 31, 2021, primarily due to use of $32.3 million for operating expense (adjusted to exclude non-cash charges of approximately $12.5 million) and cash paid for prepaid expenses, other current liabilities, and operating lease payments.

Net cash used in operating activities was $23.2 million for the three months ended March 31, 2020, primarily due to use of $25.0 million for operating expenses (adjusted to exclude non-cash charges), cash paid for prepaid expenses and other current assets and operating lease payments.

Cash Used in Investing Activities

Net cash used in investing activities was $48,000 and $22,000 for the three months ended March 31, 2021 and 2020, respectively. Net cash used in investing activities for the three months ended March 31, 2021 and 2020 was primarily related to purchases of property and equipment.

Cash Provided by Financing Activities

Net cash provided by financing activities was $81.3 million and $0.2 million for the three months ended March 31, 2021 and 2020, respectively, which were primarily from net proceeds from issuance of ordinary shares in public offering of $78.4 million and to a lesser extent, proceeds from issuances of ordinary shares upon exercises of stock options of $3.0 million.

Off-Balance Sheet Arrangements

At March 31, 2021, 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, 2021, consisted of minimum cash payments under operating leases of $17.5 million, purchase obligations of $11.9 million (of which $3.6 million is included in accrued current liabilities), and contractual obligations under license agreements of $0.7 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 $17.5 million remains outstanding as of March 31, 2021.

In September 2018, we entered into an agreement to lease an office space in Dublin, Ireland. The current lease term expires on November 30, 2021. The Dublin Lease also has an automatic renewal clause, pursuant to 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 us. As of March 31, 2021, we are obligated to make lease payments over the remaining term of the lease of approximately €16,000, or $19,000 as converted using an exchange rate as of March 31, 2021.

The following is a summary of our contractual obligations as of the filing date (in thousands):

	Total	2021	2022	2023	2024	2025	Thereafter
Operating leases [1]	$ 17,547	$ 4,662	$ 6,350	$ 6,535	$ —	$ —	$ —
Purchase obligations[2]	14,913	14,913	—	—	—	—	—
Contractual obligations under license agreements [3]	740	135	70	70	60	60	345
Total	$ 33,200	$ 19,710	$ 6,420	$ 6,605	$ 60	$ 60	$ 345

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

[2] *Purchase obligations as of the filing date includes additional $3.0 million purchase commitments to our contract manufacturers.*

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

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Foreign Currency Risk

Our business is primarily conducted in U.S. dollars except for our agreements with contract manufacturers for drug supplies which are denominated in Euros. For the three months ended March 31, 2021 we recorded a gain on foreign currency exchange rate differences of approximately $24,000 and a loss of $23,000 during the three months ended March 31, 2020. If we increase our business activities that require the use of foreign currencies, we may be exposed to 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

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. The Company's credit risk exposure is up to the extent recorded on the Company's Condensed Consolidated Balance Sheets.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer (“CEO”) and chief financial officer (“CFO”) evaluated the effectiveness of our disclosure controls and procedures pursuant to Rule 13a-15 under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), as of the end of the period covered by this Form 10-Q. Based on this evaluation, our CEO and CFO concluded that, as of March 31, 2021, our disclosure controls and procedures are designed and are effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC’s rules and forms, and that such information is accumulated and communicated to our management, including our CEO and CFO, as appropriate, to allow timely decisions regarding required disclosure.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in management’s evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during our first fiscal quarter ended March 31, 2021, that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

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

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

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings. We may at times be 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 2020 (filed with the SEC on February 26, 2021) 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 materially and adversely affect 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 in our ordinary shares. 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 $111.1 million, $77.7 million and $155.6 million for the years ended December 31, 2020, 2019, and 2018, respectively. We expect to continue to incur substantial losses for the foreseeable future as we:

- support the Phase 3 AFFIRM-AL clinical trial for birtamimab expected to initiate in mid-2021, the Phase 2 PASADENA clinical trial for prasinezumab (PRX002/RG7935) being conducted by Roche, the Phase 2b PADOVA clinical trial for prasinezumab, the Phase 2/3 clinical trial for PRX004 expected to initiate in the fourth quarter of 2021, the Phase 1 clinical trial for PRX005 expected to initiate in the third quarter of 2021, the Phase 1 clinical trial for PRX012 expected to initiate in the first quarter of 2022, and possibly initiate additional clinical trials for these and other programs;
- develop and possibly commercialize our drug candidates, including birtamimab, prasinezumab, PRX004, PRX005, and PRX012;
- undertake nonclinical development of other drug candidates and initiate clinical trials, if supported by nonclinical data;
- 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, 2021, we had cash and cash equivalents of $343.0 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 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 progress, results, and costs of our clinical trials, including the Phase 3 clinical trial for birtamimab expected to initiate in mid-2021, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2/3 clinical trial for PRX004 expected to initiate in the fourth quarter of 2021, the Phase 1 clinical trial for PRX005 expected to initiate in the third quarter of 2021, and the Phase 1 clinical trial for PRX012 expected to initiate in the first quarter of 2022;

- the timing, initiation, progress, results, and costs of these and our other research, development, and possible commercialization activities;
- the results of our research and 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 strategic collaborations, licensing, or other arrangements;
- the timing, receipt, and amount of any capital investments, cost-sharing contributions or reimbursements, milestone 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 drug 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 drug 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 drug 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 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 drug 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 COVID-19 pandemic has adversely affected our business and could have a material adverse effect on our liquidity, results of operations, financial condition or business, including our nonclinical and clinical development programs.

The outbreak of the novel strain of coronavirus SARS-CoV-2, which causes coronavirus disease (“COVID-19”), has evolved into a global pandemic. While it is not possible at this time to estimate the overall impact that COVID-19 could have on our business, the continued rapid spread of COVID-19, and the measures taken by the governments and local authorities of

affected countries and local jurisdictions, has disrupted our Phase 2 clinical trial for prasinezumab and could disrupt and delay our planned clinical trials, our research and nonclinical studies, the manufacture or shipment of both drug substance and finished drug product for our drug candidates for preclinical testing and clinical trials and materially adversely impact our liquidity, results of operations, financial condition, or business, including the following:

- our Phase 2 clinical trial for prasinezumab has been disrupted and this and other clinical trials pursued by us and our collaboration partners may be further delayed or interrupted, including as a result of (i) interruptions of supply to clinical trial sites of drug candidate or other equipment or materials, (ii) inability or unwillingness of site investigators or other study personnel to travel to study sites, dispense drug product, or otherwise treat or monitor study participants or follow study protocols, or conduct necessary data collection or verification, (iii) inability or unwillingness of study participants to travel to clinical trial sites, receive infusions, or otherwise continue to participate in the study, (iv) diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, or (v) interruptions in contracting with essential third-party vendors;
- we, or our collaboration partners, may be delayed in or prevented from initiating new clinical trials of current or prospective drug candidates because of (i) delays or difficulties in manufacturing drug product, (ii) delays or difficulties preparing regulatory submissions, (iii) delays or difficulties contracting with essential third-party vendors (such as contract research organizations), (iv) delays or difficulties enlisting site investigators or initiating clinical trial sites, (v) delays or difficulties recruiting or enrolling study participants, or (vi) delays or difficulties supplying drug product or other equipment or materials to clinical trial sites or other locations;
- we may experience delays or interruptions in our business operations due to our key personnel, or a significant number of our personnel, becoming infected with COVID-19 and therefore being unable to work, even remotely, for an extended period of time;
- interruption or delays in the operations of the U.S. Food and Drug Administration (the “FDA”) and comparable foreign regulatory agencies may impact review, inspection, and approval timelines for any of our development programs;
- the pandemic may adversely affect our collaboration partners, Roche and/or Bristol Myers Squibb (“BMS”), in ways that adversely impacts our collaborations with them;
- business development opportunities may become more limited or difficult to undertake;
- our costs may significantly increase to manage impacts to our business to complete our planned operations within our projected timelines;
- changes in local regulations as part of a response to COVID-19 may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or discontinuation of the clinical trials altogether;
- we may experience delays in necessary interactions with local regulators, ethics committees, and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; or
- our liquidity needs may be adversely impacted by the economic effects of the pandemic on financial markets.

Any one or more of these risks could have a material adverse effect on our liquidity, results of operations, financial condition or business, including the progress of, and timelines for, our nonclinical and clinical development programs.

In addition, the spread of COVID-19 has caused a broad impact globally, and may materially affect us economically. For example, if the subtenant to the office space that we subleased in South San Francisco, California defaults on its payment obligations, we will not receive sublease income to offset our lease payments to the landlord of the South San Francisco office space until such time as we are able to secure a new subtenant and enter into a new sublease agreement. The spread of COVID-19 has had a negative impact on the commercial real estate market and there can be no assurance that we would be able to re-sublet the space for the same rent that the current subtenant is obligated to pay us or at all.

While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the market price of our ordinary shares.

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

Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the European Union ("EU") on January 31, 2020, commonly referred to as Brexit. The United Kingdom remained in the EU customs union and the single market for a transition period which expired on December 31, 2020. On December 24, 2020, the United Kingdom and the EU reached agreement in principle on their future trading relationship and entered into the EU-UK Trade and Cooperation Agreement which was formally ratified by the parties and as of May 1, 2021, is fully in force. However, because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the United Kingdom and the EU as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains as to aspects of the future relationship between the United Kingdom and the EU. The uncertainty surrounding Brexit has 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/or 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/or 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 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. Despite the implementation of security measures, our internal computer systems, and those of our current and any future CROs and other contractors, consultants, and collaborators, are vulnerable to damage from cyberattacks, "phishing" attacks, computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication or electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication, and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to or to sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Any breakdown, malicious intrusion, or computer virus could result in the impairment of key business processes or breach of data security, which could result in a material disruption of our development programs and cause interruptions in our business operations, whether due to a loss of our 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. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, such a breach may require notification to governmental agencies, the media, or individuals pursuant to applicable data privacy and security law and regulations. Such an event could have an adverse effect on our business, financial condition, or results of operations.

Changes in and failures to comply with U.S. and foreign privacy and data protection laws, regulations, and standards may adversely affect our business, operations, and financial performance.

We and our partners may be subject to federal, state, and foreign data privacy and security laws and regulations. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect our business and may increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations, including state security breach notification laws, federal and state health information privacy laws (including HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and regulations promulgated thereunder), and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues. For example, the California Consumer Privacy Act (the "CCPA") went into effect January 1, 2020. The CCPA, among other things, imposes new data privacy obligations on covered companies and provides expanded privacy rights to California residents, including the right to access, delete, and opt out of certain disclosures of their information. The CCPA provides for civil penalties for violations, as well as a private right of action with statutory damages for certain data breaches, which may increase the frequency and likelihood of data breach litigation. Although the law includes limited exceptions for health-related information, including clinical trial data, such exceptions may not apply to all of our operations and processing activities. Further, the California Privacy Rights Act (the "CPRA") recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In addition, the CCPA has prompted a number of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business. If we fail to comply with applicable laws and regulations we could be subject to penalties or sanctions, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or applicable state laws.

We are also or may become subject to rapidly evolving data protection laws, rules, and regulations in foreign jurisdictions. For example, the European Union General Data Protection Regulation (the "GDPR") governs certain collection and other processing activities involving personal data about individuals in the European Economic Area. Among other things, the GDPR imposes requirements regarding the security of personal data, the rights of data subjects to access and delete personal data, requires having lawful bases on which personal data can be processed and transferred outside of the European Economic Area, requires changes to informed consent practices, and requires more detailed notices for clinical trial participants and investigators. In addition, the GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of our annual global revenue). The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from

violations of the GDPR. Relatedly, from January 1, 2021, companies have to comply with the GDPR and the United Kingdom GDPR ("UK GDPR"), which together with the amended UK Data Protection Act 2018, retains the GDPR in United Kingdom national law. The UK GDPR mirrors the fines under the GDPR, i.e. fines up to the greater of £17.5 million or 4% of global turnover. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. These changes will lead to additional costs and increase our overall risk exposure. Currently there is a four to six-month grace period agreed in the EU and United Kingdom Trade and Cooperation Agreement, ending June 30, 2021 at the latest, whilst the parties discuss an adequacy decision. The European Commission published a draft adequacy decision on February 19, 2021. If adopted, the decision will enable data transfers from EU member states to the United Kingdom for a four-year period, subject to subsequent extensions.

Compliance with U.S. and foreign data privacy and security laws, rules, and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. If we fail to comply with any such laws, rules, or regulations, we may face government investigations and/or enforcement actions, fines, civil or criminal penalties, private litigation, or adverse publicity that could adversely affect our business, financial condition, and 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.

There is no assurance that the results of the Phase 3 clinical trial for birtamimab expected to initiate in mid-2021, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2/3 clinical trial for PRX004 expected to initiate in the fourth quarter of 2021, the Phase 1 clinical trial for PRX005 expected to initiate in the third quarter of 2021, and the Phase 1 clinical trial for PRX012 expected to initiate in the first quarter of 2022 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 FDA; in the EU, this must be done to the satisfaction of the European Medicines Agency (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 any drug candidates that obtain regulatory approval. Successful commercialization 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 with Roche and BMS and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.

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

- collaborators may have significant control or 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 research, development, and/or commercialization of products candidates in the territories in which our collaboration partners lead research, development, and/or commercialization;
- collaborators might not pursue research, development, and/or commercialization of collaboration drug candidates or might elect not to continue or renew research, development, and/or commercialization programs based on nonclinical and/or 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 research or clinical development for collaboration drug candidates or require a new formulation of a drug candidate for clinical testing;
- collaborators could develop or acquire products outside of the collaboration that compete directly or indirectly with our drug candidates or require a new formulation of a drug candidate for nonclinical and/or clinical testing;
- collaborators with sales, marketing, and distribution rights to one or more drug candidates might not commit sufficient resources to sales, marketing, and distribution or might otherwise fail to successfully commercialize those drug 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 drug candidates, which could limit our rights or ability to research, develop, and/or commercialize our drug candidates;
- collaborators might not be in compliance with laws applicable to their activities under the collaboration, which could impact the collaboration or us;
- 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 research, development, and/or commercialization of our drug candidates.

In addition, funding provided by a collaborator might not be sufficient to advance drug candidates under the collaboration. For example, although BMS (formerly 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 drug candidates prior to when BMS decides whether to exercise its license rights to those drug candidates. We also note that, on

November 20, 2019, BMS acquired Celgene. BMS might take a different approach to our collaboration or determine not to continue that collaboration whether for reasons related to that collaboration or otherwise.

If a collaborator terminates a collaboration or a 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. For example, under our Collaboration Agreement with BMS, an $80 million option payment would be payable upon BMS's exercise of U.S. rights for PRX005. However, BMS may, at its sole discretion, choose not to exercise its option to such U.S. rights for PRX005 and thus would not owe to us the applicable option payment. In addition, we will likely need to either secure other funding to advance research, development, and/or commercialization of the relevant drug candidate or abandon that program, the development of the relevant drug candidate could be significantly delayed, and our cash expenditures could increase significantly if we are to continue research, development, and/or commercialization of the relevant drug candidates.

Any one or more of these risks, if realized, could reduce or eliminate future revenue from drug 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, if at all, which would require us to incur additional costs and delay or prevent our receipt of any revenue from potential product sales.

We cannot predict whether we will encounter problems with the Phase 3 clinical trial for birtamimab expected to initiate in mid-2021, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2/3 clinical trial for PRX004 expected to initiate in the fourth quarter of 2021, the Phase 1 clinical trial for PRX005 expected to initiate in the third quarter of 2021, the Phase 1 clinical trial for PRX012 expected to initiate in the first quarter of 2022, or any other future clinical trials that will cause us or any regulatory authority to delay, suspend or terminate 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 authorization 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 drug candidate, 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/or growth prospects.

Separately, in response to the COVID-19 global pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a

risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic, including providing guidance regarding the conduct of clinical trials. If global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, or impact reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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.

Although we have obtained agreement with the FDA on a special protocol assessment ("SPA"), for our Phase 3 AFFIRM-AL trial of birtamimab, a SPA does not guarantee approval of birtamimab or any other particular outcome from regulatory review.

On January 27, 2021, the FDA agreed to an SPA for our Phase 3 AFFIRM-AL clinical trial of birtamimab. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate proposed critical design features of certain clinical trials that are intended to form the primary basis for determining a drug candidate's efficacy and safety. Upon specific request by a clinical trial sponsor, the FDA will evaluate the study protocol and statistical analysis plan and respond to a sponsor's questions regarding protocol design and scientific and regulatory requirements. FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether specific elements of the protocol design for the trial, such as entry criteria, endpoints, size, duration, and planned analyses, are acceptable to support an application for regulatory approval of the drug candidate with respect to the effectiveness of and safety for the indication studied. All agreements and disagreements between the FDA and the sponsor regarding a SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Although the FDA has agreed to the SPA for our Phase 3 AFFIRM-AL clinical trial, a SPA agreement does not guarantee approval of a drug candidate. Even if the FDA agrees to the design, execution, and analysis proposed in a protocol reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, a SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor fails to comply with the agreed upon study protocol, or the relevant data, assumptions, or information provided by the sponsor in a request for the SPA change or are found to be false or to omit relevant facts. In addition, even after a SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to the modification of the study protocol and/or statistical analysis plan. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than the sponsor, the FDA may not deem the data sufficient to support an application for regulatory approval.

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. 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 problems with our third-party manufacturers or manufacturing processes, or failure to comply with the regulatory requirements of the FDA, the EMA, or 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 policies of the FDA, the EMA, or other comparable regulatory authority 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, if they are approved by applicable regulatory authorities, after they are 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, or to 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, if approved, will be 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, even if prasinezumab was approved by the FDA, Roche may determine that the outcomes of clinical trials 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, if approved by the FDA, 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 drug 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, if prasinezumab is approved by applicable regulatory authorities, 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 drug candidate. 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 drug 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 "ACA"), was enacted. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the ACA 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 now agree to offer 70 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 ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in 2013 and will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020, through March 31, 2021, 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.

Since its enactment, there have been judicial, executive, and Congressional challenges to certain aspects of the ACA. The U.S. Supreme Court is currently reviewing the constitutionality of the ACA in its entirety, although it is unclear how the Supreme Court will rule. It is also unclear how other efforts, if any, to challenge, repeal, or replace the ACA will impact the law. The ultimate content, timing, or effect of any healthcare reform legislation on the U.S. healthcare industry is unclear.

We expect that 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 current 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. Any processes adopted by the FDA to implement the BPCIA 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, and physician payment transparency 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. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- U.S. federal 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. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- 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. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians (as defined by statute) and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse midwives;
- state 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.

On September 4, 2018, we received a subpoena from the U.S. Department of Justice requesting the production of documents relating to our NEOD001 development program. We completed the production of documents in July 2019. Since that time, the Department of Justice has not requested that we provide any additional information.

We cannot predict the outcome of this matter or whether any government agency will take further action. If further action is taken, it could divert the attention of management and require the devotion of a substantial amount of time and resources.

Ensuring our compliance with applicable 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 actions are found to be in violation of any laws and regulations, we may be subject to significant civil, criminal, and administrative damages, penalties, and fines, as well as 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;
- 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 cGMPs. 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, development, and/or commercialization plans.

Research, development, 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 research, development, and/or 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 product 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/or 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 candidate 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/or 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/or 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 product, cause a delay or suspension of nonclinical or clinical development, product approval and/or commercialization of our drug candidates or drug product, 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/or 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/or growth prospects.

Rentschler Biopharma SE (“Rentschler”) and Catalent Pharma Solutions, LLC (“Catalent”) are our third-party manufacturers of clinical supplies of our drug candidate birtamimab. We are dependent on Rentschler and Catalent to manufacture these clinical supplies.

Roche, with whom we are collaborating on development of prasinezumab, manufactured 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 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 initiate any subsequent clinical trials for PRX004.

Catalent and Berkshire Sterile Manufacturing, LLC (“Berkshire”) are our third-party manufacturers of clinical supplies of our drug candidate PRX005. We are dependent on Catalent and Berkshire to manufacture these clinical supplies in order to initiate any clinical trial for PRX005.

Catalent is our third-party manufacturer of clinical supplies of our drug candidate PRX012. We are dependent on Catalent to manufacture these clinical supplies in order to initiate any clinical trial for PRX012.

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, factual and scientific

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. Additionally, our ability to obtain patent protection for our drug candidates also depends on our collaborators, partners, contractors, and employees involved in the generation of intellectual property to carry out their contractual duties, including those to assign or license relevant intellectual property rights developed on our behalf to us.

In addition, the strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal, factual, and scientific analyses and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. 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 drug 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.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our drug candidates in any jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our drug candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

We may be subject to a third-party preissuance submission of prior art to the USPTO and foreign patent agencies, 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 result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Any failure to obtain or maintain patent protection with respect to our drug candidates could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is costly, time-consuming, and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs, and may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or the Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. 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 and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third-party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our drug candidates and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. 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, financial condition, results of operations, and/or growth prospects.

Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by Congress, the federal courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We cannot predict how future decisions by Congress, the federal courts or the USPTO may impact the value of our patents.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Although an inadvertent lapse, including due to the effect of the COVID-19 pandemic on us or our patent maintenance vendors, can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application or invalidity of an issued patent include failure to respond to official actions within prescribed time limits, non-payment of fees, failure to properly legalize and submit formal documents, and failure to submit certain prior art. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing, and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such drug candidates are

commercialized. Even if patents covering our drug candidates are obtained, once a patent covering a drug candidate has expired, we may be open to competition, including biosimilar or generic medications. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drug candidates similar or identical to ours. Our patents issued as of December 31, 2020, are anticipated to expire on dates ranging from 2023 to 2040, subject to any patent extensions that may be available for such patents. If patents are issued on our patent applications pending as of December 31, 2020, the resulting patents are projected to expire on dates ranging from 2025 to 2041. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. A patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each first regulatory review period for a product, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators, or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our drug candidates or as a result of questions regarding co-ownership of potential joint inventions. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our drug candidates. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We or our licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that we or our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our patents, including in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

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

Patents are of national or regional effect, and filing, prosecuting, maintaining, and defending patents on drug candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can have a different scope and strength than do those in the United States. In addition, the laws of some foreign countries, particularly certain developing countries, do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained

patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing.

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 or technology 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, including due to the impact of the COVID-19 pandemic on our business operations or our use of the intellectual property licensed to us in an unauthorized manner, 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, harming our ability to develop, manufacture, and/or commercialize our platform or drug candidates.

In addition, the agreements under which we license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. Our business also would suffer if any current or future licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights.

In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant research programs or drug candidates and our business, financial condition, results of operations, and/or growth prospects could suffer.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- whether we are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our drug candidates, and what activities satisfy those diligence obligations;
- the priority of invention of patented technology;
- the amount and timing of payments owed under license agreements; and
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

We depend, in part, on our licensors to file, prosecute, maintain, defend, and enforce patents and patent applications 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. If our licensors or any future licensees having rights to file, prosecute, maintain, and defend our patent rights fail to conduct these activities for patents or patent applications covering any of our drug candidates, including due to the impact of the COVID-19 pandemic on our licensors' business operations, our ability to develop and commercialize those drug candidates may be adversely affected and we may not be able to prevent competitors from making, using, or selling competing products. We cannot be certain that such activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with some of our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners.

We may wish to form collaborations in the future with respect to our drug candidates, but may not be able to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans.

Our drug candidates may also require specific components to work effectively and efficiently, and rights to those components may be held by others. We may be unable to in-license any compositions, methods of use, processes or other third party intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, which would harm our business. If we fail to obtain licenses to necessary third-party intellectual property rights, we may need to cease use of the compositions or methods covered by such third-party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Any delays in entering into new collaborations or strategic partnership agreements related to our drug candidates could delay the development and commercialization of our drug candidates in certain geographies, which could harm our business prospects, financial condition, and results of operations.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our drug candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional drug candidates that we may seek to acquire.

Moreover, some of our owned and in-licensed patents or patent applications or future patents are or may be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. Any of

the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

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, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post-grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post-grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. 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. Furthermore, patent reform and changes to patent laws add uncertainty to the possibility of challenge to our patents in the future. We cannot assure you that our drug candidates and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties.

In addition, third parties may challenge our existing or future patents. Competitors may also infringe our patents or other intellectual property or the intellectual property of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. 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; and/or
- findings that our drug candidates, products, or activities infringe third party patents or other intellectual property rights.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business including distracting our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Third parties asserting their patent or other intellectual property rights against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our drug candidates or force us to cease some of our business operations. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, cause development delays, and may impact our reputation. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

In the event we are able to establish third-party infringement of our patents, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

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, including treble damages and attorneys' fees for willful infringement;
- obtain one or more licenses from third parties and potentially pay royalties;
- redesign our infringing products, which may be impossible on a cost-effective basis or require substantial time and monetary expenditure;
- 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.

In that event, we would be unable to further develop and commercialize our drug candidates, which could harm our business significantly.

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 current or future trademarks or trade names may be challenged, infringed, circumvented, declared generic or descriptive, or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

Moreover, any name we have proposed to use with our drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

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. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. In addition, others may independently discover our trade secrets and proprietary information, and we would have no right to prevent them from using that technology or information to compete with us. 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. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition.

We may be subject to claims that our employees, collaborators, partners, contractors, or advisors have wrongfully used or disclosed alleged trade secrets of third parties.

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. Likewise, our collaborators, partners, contractors, and advisors may have in the past, or may currently, work with or for universities, 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 third parties is not disclosed to us or used in their work for us, we may be subject to claims that we or our employees, collaborators, partners, contractors, or advisors have used or disclosed intellectual property, including trade secrets or other proprietary information, of third parties. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates, if such technologies or features are found to incorporate, be derived from, or benefited from the knowledge of the trade secrets or other proprietary information of third parties. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make drug candidates that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in-license will result in issued patents with claims that cover our drug candidates or uses thereof in the United States or in other foreign countries;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents are valid, enforceable and infringed;

- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications.

Should any of these events occur, they could significantly harm our business, results of operations, and prospects.

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 BMS;
- 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 by us or by existing shareholders;
- 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. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

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

As with any publicly traded company, your percentage ownership in us may be diluted in the future because of equity issuances for acquisitions, capital raising transactions or otherwise. We may need to raise additional capital in the future. If we are able to raise additional capital, we may issue equity or convertible debt instruments, which may severely dilute your ownership interest in us. In addition, we intend to continue to grant option awards to our directors, officers and employees, which would dilute your ownership stake in us. As of March 31, 2021, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plan was 10,260,005.

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. In addition, under Section 404(b) of the U.S. Sarbanes-Oxley Act, if we are either an “accelerated filer” or “large accelerated filer,” our independent registered public accounting firm must attest to 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 consolidated financial statements may be materially misstated. We, or our independent registered public accounting firm (if 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 (if 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, or (ii) 50% or more of our assets produce passive income are held for the production of passive income. Changes in the composition of our active or passive income, passive assets or changes in

our 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 year ended December 31, 2020. 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 the current taxable year or 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 or interpretations thereof in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the IRS and the Irish Revenue Commissioners ("Irish Revenue"), 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, Irish Revenue and other taxing authorities from time to time, and the IRS, Irish Revenue 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, and/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. For example, in 2017 the United States enacted tax reform that contained significant changes to corporate taxation, including a provision that would require capitalization and amortization of research and development costs over five years for tax years beginning after December 31, 2021. In addition, the Irish Government, Irish Revenue, 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," such as 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 Ireland, 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, and/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, as amended (the "Companies Act"), which differs 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.

The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares.

Under the Irish Takeover Rules, if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of the company, the acquirer and, in

certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for the outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30% and 50% of the voting rights in the company if the effect of such acquisition were to increase that person's percentage of the voting rights by 0.05% within a 12 month period. Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of our shares. The application of these presumptions may result in restrictions upon the ability of any of the concert parties and/or members of our board of directors to acquire more of our securities, including under the terms of any executive incentive arrangements. In the future, we may consult with the Irish Takeover Panel with respect to the application of this presumption and the restrictions on the ability to acquire further securities, although we are unable to provide any assurance as to whether the Irish Takeover Panel will overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

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 drug 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 The Depository Trust Company ("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 turn a profit, 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 25%) 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). Non-Irish resident 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	
10.1#	Offer Letter, dated March 18, 2021, between Prothena Biosciences Inc and Hideki Garren					X
10.2#	Seventh Amendment to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan					X
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	XBRL Instance Document - The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					

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.*

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 11, 2021

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 10.1

Hideki Garren
[Address Redacted]

REVISED – March 18, 2021

Dear Hideki:

I am pleased to confirm this offer for you to join Prothena Biosciences Inc ("Prothena" or the "Company"). We are confident in your knowledge, expertise and judgment, and believe your performance will meet our team's high-quality objectives and standards.

Your start date will be **April 5, 2021**, and the Prothena Corporation plc Board of Directors will appoint you as **Chief Medical Officer** effective April 5, 2021, subject to your commencement of employment with the Company that day. In this position, you will report to Gene Kinney (President and CEO), although your duties, title and reporting relationship may change, based on the Company's needs and priorities. This is a full-time, exempt position – which means that you are not eligible for overtime pay under state and federal laws.

Your starting annualized salary will be **$490,000.00** (gross), paid twice per month. Your pay is subject to applicable taxes and withholdings.

We agree to pay you a Retention Bonus of **$50,000.00** (gross) which will be fully earned in the event that you remain employed with Prothena for one year. The entire Retention Bonus will be paid to you with your first paycheck, less applicable taxes and withholdings. This Retention Bonus will be earned on a pro-rata basis for each week worked during your initial one-year period of your employment at Prothena. The unearned portion of this Retention Bonus will be repayable by you to Prothena on a pro-rata basis if you cease employment at Prothena prior to the one-year anniversary of your employment start date, unless your employment ends for a reason that would make you eligible for severance benefits in accordance with the Prothena Biosciences Inc Amended and Restated Severance Plan. The forgoing will be set forth in a Retention Bonus Repayment Agreement, a form of which is attached (Exhibit 1), that we will need you to sign on your start date in order to receive the Retention Bonus.

Prothena embraces a pay-for-performance philosophy. All employees are currently eligible for an annual cash bonus under the terms of the Company's cash incentive plan (the Prothena Corporation plc Amended and Restated Incentive Compensation Plan). The amount of these annual cash bonuses is determined by the Company on the basis of a number of factors, including industry competitiveness, Prothena's business strategy, and the degree to which Company, function and/or individual goals are met. Your targeted cash bonus for our 2021 performance year will be **50%** of your actual salaried earnings during that year.[1] A condition of earning any cash incentive award is that you remain employed through the pay date of an otherwise earned award, which will be paid no later than March 15, 2022. The cash bonus plan is operated at the sole discretion of Prothena, is subject to review on a regular basis and may change from time to time.

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[1] For the 2021 performance year, rather than using your actual salary earned, your annualized base salary of $490,000.00 will be used as your salaried earnings

In connection with your start date and appointment as CMO, you will also be eligible to receive an option to acquire **250,000** shares of Prothena Corporation plc. This stock option award is at the discretion of the Compensation Committee of the Board of Directors of Prothena Corporation plc (the "Committee") and is subject to the approval, and terms and conditions of the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (as amended) and the terms and conditions of the award agreement for such a stock option. The grant date of this stock option will be **April 5, 2021**, the date you start with Prothena and are appointed CMO, or on such other date as determined by the Committee in its sole discretion. The option exercise price will be equal to the closing price of Prothena Corporation plc's ordinary shares on the NASDAQ Global Select Market on that date. Subject to your continued employment, the stock option will vest 25% on the first anniversary of the grant date, and monthly at a rate of 1/48th of the award thereafter, such that the option will fully vest after a four-year period following the grant date.
On the first day of the month following your employment start date, you will be eligible to participate in Prothena's comprehensive health and welfare benefits program. On your start date, you will also be eligible to participate in our retirement benefits plan, as well as the Prothena Biosciences Inc Amended and Restated Severance Plan (**Tier I**). Details about these and other applicable plans will be provided separately.

The Company provides paid vacation time to full-time employees in accordance with the Company's vacation policy in its Employee Handbook, which will be provided to you upon commencement of your employment. You will also be eligible for paid sick time as required by state law. Additional information about paid sick time is contained in the Company's Employee Handbook.

Further information regarding onboarding requirements and/or documents needed on your employment start date (e.g., Employee Proprietary Information and Invention Assignment Agreement, Code of Conduct, Form I-9 completion process, direct deposit information, Form W-4 allowance elections) will be provided separately.

This offer is contingent upon your successful completion of a background check and a pre-employment drug test. More information regarding this process will be provided by Human Resources.

Additionally, your acceptance of this offer of employment and commencement of that employment means that you understand and agree that your employment relationship with the Company is at-will, for no specific period, and neither this letter nor any other oral or written representations may be considered a contract of employment for any specific period of time. As a result, you are free to resign your employment with Prothena at any time, for any reason or no reason. Similarly, Prothena is also free to end your employment at any time, with or without cause or advance notice. At-will employment also means that the Company may make decisions regarding other terms of your employment at any time with or without advance notice or cause, including but not limited to demotion, promotion, transfer, discipline, compensation and duties. Further, all benefits and compensation provided by the Company are contingent upon your continued employment.

To accept our offer, please sign this letter and return it to Kevin Hickey (VP, Human Resources) by **Monday, March 22, 2021**. This offer is valid until then, after which time we will not be able to accommodate an acceptance of this offer. Accordingly, please sign and return this letter before the above-stated expiration date. If you do not intend to accept this offer, we would like to be notified as soon as possible.

This letter, along with the Company's policies and procedures, sets forth the terms of your employment with the Company if you accept this offer and commence that employment, and supersedes any prior representations or agreements, whether written or oral. This letter may be modified only by a written agreement signed by you and an authorized officer of the Company.

We look forward to having you join Prothena as a full-time employee. If you have any questions, or if you would like additional information to help you reach a decision, please feel free to contact Kevin at (650) 278-1762. Please be sure to bring with you on you first day of employment documentation that proves your eligibility to work in the U.S., your bank details and emergency contact information.

Sincerely,

/s/ Gene G. Kinney
Gene Kinney
President and CEO
Prothena Biosciences Inc

ACCEPTANCE:

/s/ Hideki Garren March 19, 2021
Hideki Garren Date

Exhibit 1 – RETENTION BONUS REPAYMENT AGREEMENT

I, Hideki Garren, will receive **$50,000.00** (gross) as a Retention Bonus with my first paycheck, less applicable withholdings and deductions, from Prothena Biosciences Inc ("Prothena" or the "Company"), which will not be fully earned until I have provided 12 months of Active Service as described below.

I understand and agree that a key purpose of the Retention Bonus is my retention as an employee, that the Retention Bonus is being paid to me before it is earned, and that I have not earned the Retention Bonus until I complete 12 months of continuous Active Service. For purposes of this Retention Bonus, "Active Service" includes periods from my employment start date that I am continuously employed by the Company or its affiliates, including time off for approved vacation, holidays, personal time, family & medical leave, and military leave, but not other leaves of absence unless otherwise required by applicable law.

I understand and agree that if I complete 12 months of Active Service from my employment start date, then I have earned this Retention Bonus and have no obligation to repay any portion of it upon termination of my employment.

I further understand and agree that if my employment terminates for any reason (other than if my employment ends for a reason that would make me eligible for severance benefits in accordance with the Prothena Biosciences Inc Amended and Restated Severance Plan) prior to my completion of 12 months of Active Service from my start date, then I must repay a pro-rata amount of the Retention Bonus in one lump sum within 30 days of my termination date. Within 5 days of my employment end date, the Company will notify me in writing of the amount to be repaid.

If I fail to repay the amount due under this Retention Bonus Repayment Agreement (this "Agreement") within 30 days of the termination of my employment, then the Company may bring legal proceedings against me for collection. I further agree that for any claims brought by the Company to enforce the terms of this Agreement, the prevailing party will be entitled to costs and reasonable attorneys' fees.

I agree and understand that nothing in this Agreement alters the at-will nature of my employment with Prothena, meaning that my employment is for no definite period and may be terminated either by me or the Company at any time, with or without cause or advance notice.

I acknowledge that I understand the terms of this Agreement, that I have had an opportunity to consult with counsel or another advisor prior to signing it, and that I agree to abide by its terms. I am voluntarily signing this Agreement.

ACCEPTANCE:

[TO BE SIGNED AND DATED ON DAY 1 OF EMPLOYMENT]

_____ _____

Hideki Garren Date

Exhibit 10.2

SEVENTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN

This Seventh Amendment (this "Seventh Amendment") to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan ("2020 EIIP"), was made and adopted by the Board of Directors ("Board") of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the "Company"), on February 1, 2021 (the "Amendment Date").

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:

"2.28 "***Overall Share Limit***" means 785,000 Shares."

2. This Seventh Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO RULE 13a-14(a)/15d-14(a), AS ADOPTED 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 11, 2021

/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 RULE 13a-14(a)/15d-14(a), AS ADOPTED 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 11, 2021

/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, 2021, 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 11, 2021

/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 Company and will be retained by the Company 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 Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.