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**

For the transition period from _____ to _____

Commission file number: 001-36294

uniQure N.V.
(Exact name of Registrant as specified in its charter)

The Netherlands	**Not applicable**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

Paasheuvelweg 25
1105 BP Amsterdam, The Netherlands
(Address of principal executive offices) (Zip Code)

+31-20-240-6000
(Registrant's telephone number, including area code)

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

Title of each class:	**Trading Symbol(s)**	**Name of each exchange on which registered**
Ordinary Shares, par value €0.05	QURE	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 (§ 232.405 of this chapter) 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, smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer" "accelerated filer" and "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 ☒

As of May 6, 2021, the registrant had 46,017,621 ordinary shares, par value €0.05, outstanding.

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SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains "forward-looking statements" as defined under federal securities laws. Forward-looking statements are based on our current expectations of future events and many of these statements can be identified using terminology such as "believes," "expects," "anticipates," "plans," "may," "will," "projects," "continues," "estimates," "potential," "opportunity" and similar expressions. These forward-looking statements, include, but are not limited to, statements related to the COVID-19 coronavirus pandemic, our collaboration and license agreement with CSL Behring LLC, our cash runway, the advancement of our clinical trials, and the impact of regulatory actions on our regulatory submission timelines.

Forward-looking statements are only predictions based on management's current views and assumptions and involve risks and uncertainties, and actual results could differ materially from those projected or implied. The most significant factors known to us that could materially adversely affect our business, operations, industry, financial position or future financial performance include those discussed in Part II, Item 1A "Risk Factors," as well as those discussed in Part I, Item 2 "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Quarterly Report on Form 10-Q, as well as other factors which may be identified from time to time in our other filings with the Securities and Exchange Commission ("SEC"), including our most recent Annual Report on Form 10-K filed with the SEC on March 1, 2021, or in the documents where such forward-looking statements appear. You should carefully consider that information before you make an investment decision.

You should not place undue reliance on these forward-looking statements, which speak only as of the date that they were made. Our actual results or experience could differ significantly from those anticipated in the forward-looking statements and from historical results, due to the risks and uncertainties described in this Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, and in our Annual Report on Form 10-K for the year ended December 31, 2020, including in "Part I, Item 1A. Risk Factors," as well as others that we may consider immaterial or do not anticipate at this time. These cautionary statements should be considered in connection with any written or oral forward-looking statements that we may make in the future or may file or furnish with the SEC. We do not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of the filing of this Quarterly Report on Form 10-Q to reflect later events or circumstances or to reflect the occurrence of unanticipated events. All forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements.

In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Part I – FINANCIAL INFORMATION

Item 1. Financial Statements

uniQure N.V.

UNAUDITED CONSOLIDATED BALANCE SHEETS

	March 31, 2021	December 31, 2020
	(in thousands, except share and per share amounts)	
Current assets		
Cash and cash equivalents	$ 260,813	$ 244,932
Accounts receivables	5,445	6,618
Prepaid expenses	9,186	4,337
Other current assets	6,886	3,024
Total current assets	**282,330**	**258,911**
Non-current assets		
Property, plant and equipment, net of accumulated depreciation of $35.9 million as of March 31, 2021 and $35.2 million as of December 31, 2020, respectively	33,862	32,328
Operating lease right-of-use assets	25,313	26,086
Intangible assets, net	2,908	3,361
Goodwill	518	542
Restricted cash	2,716	2,748
Deferred tax asset	16,206	16,419
Total non-current assets	**81,523**	**81,484**
Total assets	**$ 363,853**	**$ 340,395**
Current liabilities		
Accounts payable	$ 5,749	$ 3,772
Accrued expenses and other current liabilities	20,896	18,038
Current portion of operating lease liabilities	5,457	5,524
Total current liabilities	**32,102**	**27,334**
Non-current liabilities		
Long-term debt	70,467	35,617
Operating lease liabilities, net of current portion	29,487	30,403
Other non-current liabilities	3,107	3,136
Total non-current liabilities	**103,061**	**69,156**
Total liabilities	**135,163**	**96,490**
Commitments and contingencies		
Shareholders' equity		
Ordinary shares, €0.05 par value: 60,000,000 shares authorized as of March 31, 2021 and December 31, 2020 and 45,924,729 and 44,777,799 ordinary shares issued and outstanding as of March 31, 2021 and December 31, 2020, respectively	2,780	2,711
Additional paid-in-capital	1,049,850	1,016,018
Accumulated other comprehensive income	2,347	9,907
Accumulated deficit	(826,287)	(784,731)
Total shareholders' equity	**228,690**	**243,905**
Total liabilities and shareholders' equity	**$ 363,853**	**$ 340,395**

The accompanying notes are an integral part of these unaudited consolidated financial statements.

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Three months ended March 31,	
	2021	2020
	(in thousands, except share and per share amounts)	
License revenues from related party	—	47
Collaboration revenues	454	—
Collaboration revenues from related party	—	57
Total revenues	**454**	**104**
Operating expenses:		
Research and development expenses	(32,656)	(26,013)
Selling, general and administrative expenses	(12,375)	(9,072)
Total operating expenses	**(45,031)**	**(35,085)**
Other income	352	857
Other expense	(233)	(339)
Loss from operations	**(44,458)**	**(34,463)**
Interest income	40	822
Interest expense	(1,551)	(975)
Foreign currency gains, net	4,626	4,602
Other non-operating gains, net	—	2,015
Loss before income tax expense	**$ (41,343)**	**$ (27,999)**
Income tax expense	(213)	—
Net loss	**$ (41,556)**	**$ (27,999)**
Other comprehensive loss:		
Foreign currency translation adjustments	(7,560)	(5,277)
Total comprehensive loss	**$ (49,116)**	**$ (33,276)**
Basic and diluted net loss per ordinary share	$ (0.91)	$ (0.63)
Weighted average shares used in computing basic and diluted net loss per ordinary share	45,468,485	44,279,456

The accompanying notes are an integral part of these unaudited consolidated financial statements.

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE THREE-MONTH PERIOD ENDED MARCH 31

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive (loss)/income	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
	(in thousands, except share data)					
Balance at December 31, 2019	**43,711,954**	**$ 2,651**	**$ 986,803**	**$ (6,689)**	**$ (659,707)**	**$ 323,058**
Loss for the period	—	—	—	—	(27,999)	(27,999)
Other comprehensive loss	—	—	—	(5,277)	—	(5,277)
Exercise of share options	64,762	3	929	—	—	932
Restricted and performance share units distributed during the period	521,079	29	(29)	—	—	—
Share-based compensation expense	—	—	4,355	—	—	4,355
Issuance of ordinary shares relating to employee stock purchase plan	1,801	—	78	—	—	78
Balance at March 31, 2020	**44,299,596**	**$ 2,683**	**$ 992,136**	**$ (11,966)**	**$ (687,706)**	**$ 295,147**
Balance at December 31, 2020	**44,777,799**	**$ 2,711**	**$ 1,016,018**	**$ 9,907**	**$ (784,731)**	**$ 243,905**
Loss for the period	—	—	—	—	(41,556)	(41,556)
Other comprehensive loss	—	—	—	(7,560)	—	(7,560)
Issuance of ordinary shares	859,885	52	27,647	—	—	27,699
Exercise of share options	16,782	1	391	—	—	392
Restricted and performance share units distributed during the period	269,089	16	(16)	—	—	—
Share-based compensation expense	—	—	5,761	—	—	5,761
Issuance of ordinary shares relating to employee stock purchase plan	1,174	—	49	—	—	49
Balance at March 31, 2021	**45,924,729**	**$ 2,780**	**$ 1,049,850**	**$ 2,347**	**$ (826,287)**	**$ 228,690**

The accompanying notes are an integral part of these unaudited consolidated financial statements.

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF CASH FLOWS

	Three months ended March 31,	
	2021	2020
	(in thousands)	
Cash flows from operating activities		
Net loss	$ (41,556)	$ (27,999)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,862	1,733
Share-based compensation expense	5,761	4,355
Change in fair value of derivative financial instruments	-	(2,015)
Unrealized foreign exchange gains	(5,342)	(4,824)
Deferred tax expense	213	-
Change in deferred revenue	-	270
Changes in operating assets and liabilities:		
Accounts receivable, prepaid expenses, and other current assets	(8,023)	(1,282)
Accounts payable	2,510	(546)
Accrued expenses, other liabilities, and operating leases	3,302	(2,645)
Net cash used in operating activities	(41,273)	(32,953)
Cash flows from investing activities		
Purchases of intangible assets	-	(2,213)
Purchases of property, plant, and equipment	(3,876)	(677)
Net cash used in investing activities	(3,876)	(2,890)
Cash flows from financing activities		
Proceeds from loan increment, net of debt issuance costs	34,603	-
Proceeds from issuance of ordinary shares	28,734	-
Share issuance costs from issuance of ordinary shares	(1,161)	-
Proceeds from issuance of shares related to employee stock option and purchase plans	442	1,010
Net cash generated from financing activities	62,618	1,010
Currency effect on cash, cash equivalents and restricted cash	(1,620)	(943)
Net increase / (decrease) in cash, cash equivalents and restricted cash	15,849	(35,776)
Cash, cash equivalents and restricted cash at beginning of period	247,680	380,726
Cash, cash equivalents and restricted cash at the end of period	**$ 263,529**	**$ 344,950**
Cash and cash equivalents	$ 260,813	$ 342,029
Restricted cash related to leasehold and other deposits	2,716	2,921
Total cash, cash equivalents and restricted cash	**$ 263,529**	**$ 344,950**
Supplemental cash flow disclosures:		
Cash paid for interest	$ (1,410)	$ (780)

The accompanying notes are an integral part of these unaudited consolidated financial statements.

1 General business information

uniQure (the "Company") was incorporated on January 9, 2012 as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) under the laws of the Netherlands. The Company is a leader in the field of gene therapy and seeks to deliver to patients suffering from rare and other devastating diseases single treatments with potentially curative results. The Company's business was founded in 1998 and was initially operated through its predecessor company, Amsterdam Molecular Therapeutics (AMT) Holding N.V ("AMT"). In 2012, AMT undertook a corporate reorganization, pursuant to which uniQure B.V. acquired the entire business and assets of AMT and completed a share-for-share exchange with the shareholders of AMT. Effective February 10, 2014, in connection with its initial public offering, the Company converted into a public company with limited liability (*naamloze vennootschap*) and changed its legal name from uniQure B.V. to uniQure N.V.

The Company is registered in the trade register of the Chamber of Commerce (*Kamer van Koophandel*) in Amsterdam, the Netherlands under number 54385229. The Company's headquarters are in Amsterdam, the Netherlands, and its registered office is located at Paasheuvelweg 25, Amsterdam 1105 BP, the Netherlands and its telephone number is +31 20 240 6000.

The Company's ordinary shares are listed on the Nasdaq Global Select Market and trade under the symbol "QURE".

2 Summary of significant accounting policies

2.1 Basis of preparation

The Company prepared these unaudited consolidated financial statements in compliance with generally accepted accounting principles in the United States of America ("U.S. GAAP") and applicable rules and regulations of the Securities and Exchange Commission ("SEC") regarding interim financial reporting. Any reference in these notes to applicable guidance is meant to refer to authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

The unaudited consolidated financial statements are presented in U.S. dollars, except where otherwise indicated. Transactions denominated in currencies other than U.S. dollars are presented in the transaction currency with the U.S. dollar amount included in parenthesis, converted at the foreign exchange rate as of the transaction date.

2.2 Unaudited interim financial information

The interim financial statements and related disclosures are unaudited, have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for a fair statement of the financial position, results of operations and changes in financial position for the period presented.

Certain information and footnote disclosures normally included in annual financial statements prepared in accordance with U.S. GAAP have been omitted. The results of operations for the three months ended March 31, 2021, are not necessarily indicative of the results to be expected for the full year ending December 31, 2021 or for any other future year or interim period. The accompanying financial statements should be read in conjunction with the audited financial statements and the related notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 1, 2021.

2.3 Use of estimates

The preparation of the financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates.

2.4 Accounting policies

The principal accounting policies applied in the preparation of these unaudited consolidated financial statements are described in the Company's audited financial statements as of and for the year ended December 31, 2020, and the notes thereto, which are included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 1, 2021. There have been no material changes in the Company's significant accounting policies during the three months ended March 31, 2021.

2.5 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 Note 2.3.22 of the Company's Annual Report on Form 10-K for the year ended December 31, 2020, which could be expected to materially impact the Company's unaudited consolidated financial statements.

3 Collaboration arrangements and concentration of credit risk

CSL Behring collaboration

On June 24, 2020, uniQure biopharma B.V., a wholly-owned subsidiary of uniQure N.V., entered into a commercialization and license agreement (the "CSL Behring Agreement") with CSL Behring LLC, ("CSL Behring"), pursuant to which CSL Behring will receive exclusive global rights to etranacogene dezaparvovec, the Company's investigational gene therapy for patients with hemophilia B, (the "Product").

Under the terms of the CSL Behring Agreement, the Company is entitled to receive a $450.0 million upfront cash payment upon the closing of the transaction contemplated by the CSL Behring Agreement and will be eligible to receive up to $1.6 billion in additional payments based on regulatory and commercial milestones. The CSL Behring Agreement also provides that the Company will be eligible to receive tiered double-digit royalties in a range of up to a low-twenties percent of net sales of the Product based on sales thresholds.

Pursuant to the CSL Behring Agreement, the Company will be responsible for the completion of the HOPE-B clinical trial, manufacturing process validation, and the manufacturing supply of the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization. Concurrently with the execution of the CSL Behring Agreement, the Company and CSL Behring entered into a development and commercial supply agreement, pursuant to which, among other things, the Company will supply the Product to CSL Behring at an agreed-upon price. Clinical development and regulatory activities performed by the Company pursuant to the CSL Behring Agreement will be reimbursed by CSL Behring. CSL Behring will be responsible for global regulatory submissions and commercialization requirements for the Product.

The effectiveness of the transaction contemplated by the CSL Behring Agreement was contingent on completion of review under antitrust laws in the United States, Australia, and the United Kingdom. As of March 31, 2021, such regulatory approvals had not been received in the United States. On May 5, 2021 the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (the "HSR Act") expired, and as such the CSL Behring Agreement became fully effective on May 6, 2021.

As of March 31, 2021, the Company concluded it has no enforceable right to the upfront payment, the regulatory and sale milestone payments, or the royalties (together "CSL Behring License Revenue") that the Company will receive in accordance with the CSL Behring Agreement, as all payments were contingent upon the successful completion of reviews, or the expiration of the waiting period, under the HSR Act, which had not occurred as of March 31, 2021. Therefore, the Company determined to not recognize any revenue in relation to the CSL Behring License Revenue, in accordance with ASC 606 during the three-month period ended March 31, 2021.

In accordance with its existing license and other agreements, the Company is contractually required to pay in total a low to high single digit percentage of any upfront payment to its licensors and financial advisor ("License Fees") following the closing of the transaction. The Company did not record any License Fees for the three-month period ended March 31, 2021, as the Company had not recognized the upfront payment as of this date.

The Company incurred $5.0 million of expenses related to the obligations related to the CSL Behring Agreement that had not been satisfied as of March 31, 2021. The Company capitalized these expenses as contract fulfillment costs (presented within Other current assets). As of March 31, 2021, the Company also recognized a $5.0 million receivable (presented within Accounts receivable) from CSL Behring for expenses for which the Company has a right of reimbursement. A contract liability was also recognized for the entire amount of expenses for which the Company has a right to reimbursement (presented within Accrued expenses and other current liabilities). In accordance with ASC 606 it cannot recognize any CSL Behring License Revenue as of this date.

Bristol-Myers Squibb collaboration

In May 2015, the Company and Bristol-Myers Squibb ("BMS") entered into a collaboration and license agreement and various related agreements with BMS ("BMS CLA").

The initial four-year research term under the collaboration terminated on May 21, 2019. On December 1, 2020, the Company and BMS amended the BMS CLA ("amended BMS CLA"). Under the amended BMS CLA, BMS is limited to four Collaboration Targets. BMS may until November 30, 2021 replace up to two of these four Collaboration Targets with up to two new targets in the field of cardiovascular disease. The Company continues to be eligible to receive research, development, and regulatory milestone payments of up to $217.0 million for each Collaboration Target, if defined milestones are achieved.

For as long as any of the four Collaboration Targets are being advanced, BMS may place a purchase order to be supplied with research, clinical and commercial supplies. Subject to the terms of the amended BMS CLA, BMS has the right to terminate the research, clinical and commercial supply relationships, and has certain remedies for failures of supply, up to and including technology transfer for any such failure that otherwise cannot be reasonably resolved. Both BMS and the Company may agree to a technology transfer of manufacturing capabilities pursuant to the terms of the amended BMS CLA.

The amended BMS CLA does not extend the initial four-year research term. BMS may place purchase orders to provide limited services primarily related to analytical and development efforts in respect of the four Collaboration Targets. BMS may request such services for a period not to exceed the earlier of (i) the completion of all activities under a Research Plan and (ii) either (A) three years after the last replacement target has been designated by BMS during the one-year replacement period ending on November 30, 2021, or (B) November 30, 2023 if no replacement targets are designated. BMS continues to reimburse the Company for these services.

The Company evaluated the impact of the amended BMS CLA in relation to its performance obligation to provide access to BMS to its technology and know-how in the field of gene therapy and to participate in joint steering committee and other governing bodies ("License Revenue").

The Company determined that its remaining performance obligation under the amended BMS CLA was immaterial and recognized the remaining balance of unrecognized License Revenue as of November 30, 2020. The Company includes variable consideration related to any research, development, and regulatory milestone payments, in the transaction price once it is considered probable that including these payments in the transaction price would not result in the reversal of cumulative revenue recognized. Due to the significant uncertainty surrounding the development of gene-therapy product candidates and the dependence on BMS's performance and decisions, the Company does not generally consider this probable and did not record any License Revenue during the three months ended March 31, 2021.

4 Fair value measurement

The Company measures certain financial assets and liabilities at fair value, either upon initial recognition or for subsequent accounting or reporting. U.S. GAAP requires disclosure of methodologies used in determining the reported fair values, and establishes a hierarchy of inputs used when available. The three levels of the fair value hierarchy are described below:

- Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company can access at the measurement date.
- Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active or models for which the inputs are observable, either directly or indirectly.
- Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and are unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amount of cash and cash equivalents, accounts receivable, prepaid expenses, other assets, accounts payable, accrued expenses and other current liabilities reflected in the Consolidated balance sheets approximate their fair values due to their short-term maturities.

The following table sets forth the Company's assets and liabilities that are required to be measured at fair value on a recurring basis as of March 31, 2021, and December 31, 2020:

	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total	Classification in Consolidated balance sheets
			(in thousands)		
At December 31, 2020					
Assets:					
Cash, cash equivalents and restricted cash	$ 247,680	$ —	$ —	$ 247,680	Cash and cash equivalents; restricted cash
Total assets	$ 247,680	$ —	$ —	$ 247,680	
Liabilities:					
Derivative financial instruments	—	—	2,645	2,645	Other non-current liabilities
Total liabilities	$ —	$ —	$ 2,645	$ 2,645	
At March 31, 2021					
Assets:					
Cash, cash equivalents and restricted cash	$ 263,529	$ —	$ —	$ 263,529	Cash and cash equivalents; restricted cash
Total assets	$ 263,529	$ —	$ —	$ 263,529	
Liabilities:					
Derivative financial instruments	$ —	$ —	$ 2,645	$ 2,645	Other non-current liabilities
Total liabilities	$ —	$ —	$ 2,645	$ 2,645	

Changes in Level 3 items during the three months ended March 31, 2021, are as follows:

	Derivative financial instruments
	(in thousands)
Balance at December 31, 2020	**$ 2,645**
Net (gains) / losses recognized in profit or loss	—
Balance at March 31, 2021	**$ 2,645**

Derivative financial instruments

The Company issued derivative financial instruments related to its collaboration with BMS.

In 2015, the Company granted BMS two warrants that were subsequently terminated in connection with the amendment to the BMS CLA on December 1, 2020.

On December 1, 2020, the Company and BMS agreed that upon the consummation of a change of control transaction of uniQure that occurs prior to December 1, 2026 or BMS' delivery of a target cessation notice for all four Collaboration Targets, the Company (or its third party acquirer) shall pay to BMS a one-time, non-refundable, non-creditable cash payment of $70.0 million, provided that (x) if $70.0 million is greater than five percent (5.0%) of the net proceeds (as contractually defined) from such change of control transaction, the payment shall be an amount equal to five percent of such net proceeds, and (y) if $70.0 million is less than one percent of such net proceeds, the change of control payment shall be an amount equal to one percent of such net proceeds ("CoC-payment"). The Company has not consummated any change of control transaction as of March 31, 2021 that would obligate it to make a CoC-payment.

The Company determined that the CoC-payment should be recorded as a derivative financial liability as of December 1, 2020 and that subsequent changes in the fair market value of this derivative financial liability should be recorded in profit and loss. The fair market value of the derivative financial liability is materially impacted by probability that market participants assign to the likelihood of the occurrence of a change of control transaction that would give rise to a CoC-payment. This probability represents an unobservable input. The Company determined the fair market value of the derivative financial liability by using a present value model based on expected cash flow. The expected cash flows are materially impacted by the probability that market participants assign to the likelihood of the occurrence of a change of control transaction within the biotechnology industry. The Company estimated this unobservable input using the best information available as of March 31, 2021 and December 31, 2020. The Company obtained reasonably available market information that it believed market participants would use in determining the likelihood of the occurrence of a change-of control transaction within the biotechnology industry. Selecting and evaluating market information involves considerable judgement and uncertainty. Based on all such information and its judgment the Company estimated that the fair market value of the derivative financial liability (presented within "Other non-current liabilities") as of March 31, 2021 and December 31, 2020 was $2.6 million.

5 Accrued expenses and other current liabilities

Accrued expenses and other current liabilities include the following items:

	March 31, 2021	December 31, 2020
	(in thousands)	
Accruals for services provided by vendors-not yet billed	$ 11,180	$ 8,269
Personnel related accruals and liabilities	4,716	7,687
Contract liability (see Note 3. "Collaboration arrangements")	5,000	2,082
Total	**$ 20,896**	**$ 18,038**

6 Long-term debt

On June 14, 2013, the Company entered into a venture debt loan facility with Hercules Capital, Inc. (formerly known as Hercules Technology Growth Capital, Inc.) ("Hercules"), which was amended and restated on June 26, 2014, and again on May 6, 2016 ("2016 Amended Facility"). On December 6, 2018, the Company signed an amendment that both refinanced the then-existing $20.0 million 2016 Amended Facility and allowed the Company to draw down an additional $15.0 million ("2018 Amended Facility"). The 2018 Amended Facility extended the loan's maturity date from May 1, 2020 until June 1, 2023. The interest-only period was initially extended from November 2018 to January 1, 2021 and was further extended to January 1, 2022 as a result of raising more than $90.0 million in equity financing in September 2019. The interest only period was again further extended to June 1, 2023 as a result of the January 2021 amendment (see below). The interest rate is adjustable and is the greater of (i) 8.85% and (ii) 8.85% plus the prime rate less 5.50% per annum. Under the 2018 Amended Facility, the Company owes a back-end fee of 4.95% of the outstanding debt. In addition, in May 2020 the Company paid a back-end fee of $1.0 million in relation to the 2016 Amended Facility.

On January 29, 2021, the Company and Hercules amended the 2018 Amended Facility ("2021 Amended Facility"). Pursuant to the 2021 Amended Facility, Hercules agreed to an additional Facility of $100.0 million ("Tranche B"), increasing the aggregate principal amount of the term loan facilities from $35.0 million to up to $135.0 million. On January 29, 2021, the Company drew down $35.0 million of the Tranche B. The Company may draw down the remaining $65.0 million under the Tranche B in a series of one or more advances of not less than $20.0 million each until December 15, 2021. Advances under Tranche B bear interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance and all accrued but unpaid interest on advances under Tranche B is due on June 1, 2023, which date may be extended by the Company by up to two twelve-month periods. Advances under Tranche B may not be prepaid prior to July 29, 2021, following which the Company may prepay all such advances without charge. The Company owes a back-end fee of 4.85% of amounts outstanding under Tranche B. The back-end fee is reduced if prepayment occurs at an earlier date.

The amortized cost (including interest due presented as part of accrued expenses and other current liabilities) of the 2018 Amended Facility and 2021 Amended Facility was $71.0 million as of March 31, 2021, compared to $35.9 million amortized cost for the 2018 Amended Facility as of December 31, 2020, and is recorded net of discount and debt issuance costs. The foreign currency loss on the facilities in the three months ended March 31, 2021, was $3.2 million compared to a foreign currency loss of $0.7 million during the same period in 2020 for the 2018 Amended Facility.

Interest expense associated with the 2018 Amended Facility and 2021 Amended Facility during the three months ended March 31, 2021 was $1.5 million, compared to $0.9 million during the same periods in 2020 for the 2018 Amended Facility.

As a covenant in the 2018 Amended Facility and 2021 Amended Facility, the Company has periodic reporting requirements and is required to keep a minimum cash balance deposited in bank accounts in the United States, equivalent to the lesser of (i) 65% of the outstanding balance of principal due or (ii) 100% of worldwide cash and cash equivalents. This restriction on cash and cash equivalents only relates to the location of the cash and cash equivalents, and such cash and cash equivalents can be used at the discretion of the Company. In combination with other covenants, the 2018 Amended Facility and 2021 Amended Facility restricts the Company's ability to, among other things, incur future indebtedness and obtain additional debt financing, to make investments in securities or in other companies, to transfer assets, to perform certain corporate changes, to make loans to employees, officers, and directors, and to make dividend payments and other distributions to its shareholders. The Company secured the facilities by directly or indirectly pledging its total assets of $363.9 million with the exception of $97.6 million of cash and cash equivalents and other current assets held by uniQure N.V.

The 2018 Amended Facility and 2021 Amended Facility contain provisions that include the occurrence of a material adverse effect, as defined therein, which would entitle Hercules to declare all principal, interest and other amounts owed by the Company immediately due and payable. As of March 31, 2021, the Company was in material compliance with all covenants and provisions.

7 Shareholders' Equity

On March 1, 2021, the Company entered into a Sales Agreement with SVB Leerink LLC ("SVB Leerink") with respect to an at-the-market ("ATM") offering program, under which the Company may, from time to time in its sole discretion, offer and sell through SVB Leerink, acting as agent, its ordinary shares, up to an aggregate offering price of $200.0 million. The Company will pay SVB Leerink a commission equal to 3% of the gross proceeds of the sales price of all ordinary shares sold through it as sales agent under the Sales Agreement. Through March 31, 2021 the Company issued 859,885 ordinary shares at a weighted average price of $33.42 per share, with net proceeds of $27.6 million, after deducting underwriting discounts and net of offering expenses. The Company defers direct, incremental costs associated to this offering, except for the commission costs to SVB Leerink, which are a reduction to additional paid-in capital, and will deduct these costs from additional paid-in capital in the consolidated balance sheets proportionately to the amount of proceeds raised. As of March 31, 2021, $1.0 million of direct, incremental costs were deducted from additional paid-in capital.

8 Share-based compensation

The Company's share-based compensation plans include the 2014 Amended and Restated Share Option Plan (the "2014 Plan") and inducement grants under Rule 5653(c)(4) of the Nasdaq Global Select Market with terms similar to the 2014 Plan (together the "2014 Plans"). At the annual general meeting of shareholders in June 2018, the Company's shareholders approved amendments of the 2014 Plan, increasing the shares authorized for issuance by 3,000,000 to a total of 8,601,471.

a) 2014 Plans

Share-based compensation expense recognized by classification included in the Consolidated statements of operations and comprehensive loss in relation to the 2014 Plans for the periods indicated below was as follows:

	Three months ended March 31,	
	2021	2020
	(in thousands)	
Research and development	$ 2,674	$ 2,382
Selling, general and administrative	3,080	1,958
Total	**$ 5,754**	**$ 4,340**

Share-based compensation expense recognized by award type was as follows:

	Three months ended March 31,	
	2021	2020
	(in thousands)	
Award type		
Share options	$ 2,840	$ 2,208
Restricted share units	2,560	1,444
Performance share units	354	688
Total	**$ 5,754**	**$ 4,340**

As of March 31, 2021, the unrecognized share-based compensation expense related to unvested awards under the 2014 Plans were:

	Unrecognized share-based compensation expense	Weighted average remaining period for recognition
	(in thousands)	(in years)
Award type		
Share options	$ 35,517	3.09
Restricted share units	26,227	2.40
Performance share units	1,241	0.83
Total	**$ 62,985**	**2.76**

The Company satisfies the exercise of share options and vesting of Restricted Share Units ("RSUs") and Performance Share Units ("PSUs") through newly issued ordinary shares.

Share options

Share options are priced on the date of grant and, except for certain grants made to non-executive directors, vest over a period of four years. The first 25% vests after one year from the initial grant date and the remainder vests in equal quarterly installments over years two, three and four. Certain grants to non-executive directors vest in full after one year. Any options that vest must be exercised by the tenth anniversary of the initial grant date.

The following tables summarize option activity under the Company's 2014 Plans for the three months ended March 31, 2021:

	Options	
	Number of ordinary shares	Weighted average exercise price
Outstanding at December 31, 2020	**2,659,279**	**$ 28.13**
Granted	734,683	$ 36.95
Forfeited	(40,440)	$ 43.85
Expired	(5,094)	$ 37.85
Exercised	(16,782)	$ 23.34
Outstanding at March 31, 2021	**3,331,646**	**$ 29.90**
Thereof, fully vested and exercisable at March 31, 2021	1,718,923	$ 20.19
Thereof, outstanding and expected to vest after March 31, 2021	1,612,723	$ 40.24

Total weighted average grant date fair value of options issued during the period (in $ millions)	$ 15.8
Proceeds from option sales during the period (in $ millions)	$ 0.4

The fair value of each option issued is estimated at the respective grant date using the Hull & White option pricing model with the following weighted-average assumptions:

	Three months ended March 31,	
Assumptions	**2021**	**2020**
Expected volatility	75%	70%
Expected terms	10 years	10 years
Risk free interest rate	1.21% - 1.71%	1.44%
Expected dividend yield	0%	0%

Restricted share units ("RSUs")

The following table summarizes the RSUs activity for the three months ended March 31, 2021:

	RSU	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2020	**467,344**	**$ 43.56**
Granted	404,967	$ 36.96
Vested	(136,721)	$ 38.63
Forfeited	(15,938)	$ 43.46
Non-vested at March 31, 2021	**719,652**	**$ 40.79**

Total weighted average grant date fair value of RSUs granted during the period (in $ millions)	$ 15.0

RSUs vest over one to three years. RSUs granted to non-executive directors vest one year from the date of grant.

Performance share units ("PSUs")

The following table summarizes the PSUs activity for the three months ended March 31, 2021:

	PSU	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2020	**212,614**	**$ 42.32**
Vested	(132,368)	$ 33.09
Forfeited	(2,916)	$ 57.56
Non-vested at March 31, 2021	**77,330**	**$ 57.56**

The PSUs will vest on the third anniversary of the grant, subject to the grantee's continued employment.

b) Employee Share Purchase Plan ("ESPP")

In June 2018, the Company's shareholders adopted and approved an ESPP allowing the Company to issue up to 150,000 ordinary shares. The ESPP is intended to qualify under Section 423 of the Internal Revenue Code of 1986. Under the ESPP, employees are eligible to purchase ordinary shares through payroll deductions, subject to any plan limitations. The purchase price of the ordinary shares on each purchase date is equal to 85% of the lower of the closing market price on the offering date and the closing market price on the purchase date of each three-month offering period. During the three months ended March 31, 2021, 1,174 ordinary shares were issued under the ESPP compared to 1,801 during the same period in 2020. As of March 31, 2021, a total of 130,852 ordinary shares remain available for issuance under the ESPP plan compared to a total of 136,406 as of March 31, 2020.

9 Income taxes

The Company released its valuation allowance against the Company's deferred tax assets in the United States as of December 31, 2020. The Company recorded $0.2 million deferred tax expense in relation to its operations in the United States during the three month period ended March 31, 2021. The Company recorded a nil net deferred tax expense in the prior year as it had recorded a valuation allowance against its net deferred tax assets in the United States as of March 31, 2020.

The effective income tax rate of 0.5% during the three months ended March 31, 2021 is substantially lower than the enacted rated of 25% in the Netherlands as the Company recorded a valuation allowance against its net deferred tax assets in the Netherlands. Refer to Note 3 "Collaboration arrangements and concentration of credit risk" for discussion on the effectiveness of the CSL Behring Agreement. The effective income tax rate during the three months ended March 31, 2020 was 0% as the Company had recorded a valuation allowance against all its net deferred tax assets.

The closing of the transaction contemplated by the CSL Behring agreement on May 6, 2021 is expected to materially impact the Company's operating result as well as the taxable income for the year ended December 31, 2021 as well as in future periods. The Company expects to utilize a material portion of its net operating loss carryforwards in the Netherlands during 2021 as a result of closing the transaction. As of March 31, 2021 the Company expects to continue incurring tax losses in the years thereafter and expects to record a valuation allowance against all its Dutch net deferred tax assets as of December 31, 2021. The Company determined the impact which recognition of CSL Behring License Revenue is estimated to have, with regards to the expected effective tax rate of 0% that was applied with respect to the Company's Dutch operations as of March 31, 2021, is immaterial.

10 Basic and diluted earnings per share

Diluted earnings per share are calculated by adjusting the weighted average number of ordinary shares outstanding, assuming conversion of all potentially dilutive ordinary shares. As the Company has incurred a loss, all potentially dilutive ordinary shares would have an antidilutive effect, if converted, and thus have been excluded from the computation of loss per share. The shares are presented without giving effect to the application of the treasury method or exercise prices that would be above the share price as of March 31, 2021 and March 31, 2020, respectively. In addition, the BMS warrants were not exercisable as of March 31, 2020 since this would have required the prior designation of Collaboration Targets by BMS. This would generally result in a lower number of potentially dilutive ordinary shares as some stock option grants as well as the BMS warrants would have been excluded.

The potentially dilutive ordinary shares are summarized below:

	March 31,	
	2021	2020
	(ordinary shares)	
BMS warrants (derecognized as of December 1, 2020 - see Note 4, "Fair value measurement")	—	10,262,500
Stock options under 2014 Plans	3,331,646	3,003,430
Non-vested RSUs and earned PSUs	796,982	635,390
Stock options under previous option plan	14,000	14,000
Employee share purchase plan	729	681
Total potential dilutive ordinary shares	**4,143,357**	**13,916,001**

11 Subsequent events

Appointment of Chief Operating Officer

Effective May 17, 2021, Pierre Caloz will be appointed as Chief Operating Officer and will be based out of the Amsterdam facility. Mr. Caloz will be responsible for all Manufacturing Operations, Global Chemistry, Manufacturing and Controls development and innovation, and Supply Chain and Facilities. As a result, Alex Kuta, Ph.D., will transition from Executive Vice President, Operations to Executive Vice President, Quality and Regulatory.

Closing of Collaboration and Licensing transaction with CSL Behring (see also note 3)

On May 5, 2021, the waiting period under the HSR Act expired, and on May 6, 2021 the CSL Behring Agreement became fully effective. Under the CSL Behring Agreement, the upfront payment of $450.0 million was paid to the Company on May 7, 2021. Additionally, the Company is eligible to receive more than $300 million in regulatory and first commercial sale milestones, up to an additional $1.3 billion in commercial milestones, and tiered double-digit royalties of up to a low-twenties percentage of net sales of the Product arising from the collaboration. The Company contractually owes a single-digit percentage of revenue from the collaboration to its licensors. The Company expects to utilize a material portion of its net operating loss carryforwards in the Netherlands during 2021 as a result of closing the transaction contemplated by the CSL Behring Agreement.

The Company will be responsible for the completion of the HOPE-B clinical trial, manufacturing process validation, and the manufacturing supply of the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization. Clinical development and regulatory activities performed by the Company pursuant to the CSL Behring Agreement will be reimbursed by CSL Behring. CSL Behring will be responsible for global regulatory submissions and commercialization requirements for the Product.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following Management's Discussion and Analysis of Financial Condition and Results of Operations ("MD&A") is intended to help the reader understand our results of operations and financial condition. This MD&A is provided as a supplement to, and should be read in conjunction with, our unaudited consolidated financial statements and the accompanying notes thereto and other disclosures included in this Quarterly Report on Form 10-Q, including the disclosures under Part II, Item 1A "Risk Factors," and our audited financial information and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the Securities and Exchange Commission (the "SEC") on March 1, 2021. Our unaudited consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the U.S. ("U.S. GAAP") and unless otherwise indicated are presented in U.S. dollars.

Overview

We are a leader in the field of gene therapy and seek to deliver to patients suffering from rare and other devastating diseases single treatments with potentially curative results. We are advancing a focused pipeline of innovative gene therapies, including product candidates for the treatment of hemophilia B, which effective May 6, 2021, we licensed to CSL Behring pursuant to the CSL Behring Agreement (as defined below), and Huntington's disease. We believe our validated technology platform and manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost, and time to market. We produce our Adeno-associated virus ("AAV") -based gene therapies in our own facilities with a proprietary, commercial-scale, current good manufacturing practices ("cGMP")-compliant, manufacturing process. We believe our Lexington, Massachusetts-based facility is one of the world's most versatile gene therapy manufacturing facilities.

Business Developments

Below is a summary of our recent significant business developments:

Financing

As of December 31, 2020, a $35.0 million term loan was outstanding in accordance with the Second Amended and Restated Loan and Security Agreement (the "2018 Amended Facility") between us and Hercules.

On January 29, 2021, we and Hercules amended the 2018 Amended Facility ("2021 Amended Facility"). Pursuant to the 2021 Amended Facility, Hercules agreed to an additional Facility of $100.0 million ("Tranche B") increasing the aggregate principal amount of the term loan facilities from $35.0 million to up to $135.0 million. On January 29, 2021, we drew down $35.0 million of the Tranche B. We may draw down the remaining $65.0 million under the Tranche B in a series of one or more advances of not less than $20.0 million each until December 15, 2021. Advances under Tranche B bear interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance and all accrued but unpaid interest on advances under Tranche B is due on June 1, 2023, which date may be extended by us by up to two twelve-month periods. Advances under the 2021 Amended Facility may not be prepaid until July 29, 2021, following which we may prepay all such advances without charge.

In addition to Tranche B, the 2021 Amended Facility also extends the interest only payment period of the previously funded $35.0 million term loan from January 1, 2022 to June l, 2023. End of term charges in respect of advances under the 2021 Amended Facility range from 1.65% to 6.85%, depending on the maturity date.

The 2021 Amended Facility extended the funding of our operations until the second half of 2022.

On March 1, 2021, we entered into a Sales Agreement with SVB Leerink LLC ("SVB Leerink") with respect to an at-the-market ("ATM") offering program, under which we may, from time to time in our sole discretion, offer and sell through SVB Leerink, acting as agent, our ordinary shares, up to an aggregate offering price of $200.0 million. We will pay SVB Leerink a commission equal to 3% of the gross proceeds of the sales price of all ordinary shares sold through it as a sales agent under the Sales Agreement.

In March 2021, we issued 0.9 million ordinary shares at a weighted average price of $33.42 per share, with net proceeds of $27.6 million, after deducting underwriting discounts and net of offering expenses. This further extended the funding of our operations until the end of 2022.

CSL Behring commercialization and license agreement

On June 24, 2020, uniQure biopharma B.V., a wholly-owned subsidiary of uniQure N.V., entered into a commercialization and license agreement (as amended, the "CSL Behring Agreement") with CSL Behring LLC ("CSL Behring") pursuant to which CSL Behring will receive exclusive global rights to etranacogene dezaparvovec, our investigational gene therapy for patients with hemophilia B (the "Product").

Under the terms of the CSL Behring Agreement, we are entitled to receive a $450.0 million upfront cash payment upon the closing of the CSL Behring Agreement and will be eligible to receive up to $1.6 billion in additional payments based on regulatory and commercial milestones. The CSL Behring agreement also provides that we will be eligible to receive tiered double-digit royalties in a range of up to a low-twenties percent of net sales of the Product based on sales thresholds.

Pursuant to the CSL Behring Agreement, we will be responsible for the completion of the HOPE-B clinical trial, manufacturing process validation, and the manufacturing supply of the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization. Concurrently with the execution of the CSL Behring Agreement, we and CSL Behring entered into a development and commercial supply agreement, pursuant to which, among other things, we will supply the Product to CSL Behring at an agreed-upon price. Clinical development and regulatory activities performed by us pursuant to the CSL Behring Agreement will be reimbursed by CSL Behring. CSL Behring will be responsible for global regulatory submissions and commercialization requirements for the Product.

The effectiveness of the transaction contemplated by the CSL Behring Agreement was contingent on completion of review under antitrust laws in the United States, Australia, and the United Kingdom. As of March 31, 2021, the transaction had been cleared by the Australian and United Kingdom antitrust authorities and on May 6, 2021, the CSL Behring Agreement became fully effective after the expiration of the waiting period under the HSR Act on May 5, 2021.

Under the CSL Behring Agreement, the upfront payment of $450.0 million was paid to us on May 7, 2021. We are also eligible to receive up to more than $300 million in regulatory and first commercial sale milestones, $1.3 billion in additional commercial milestones, and tiered double-digit royalties of up to a low-twenties percentage of net product sales arising from the collaboration. We contractually owe a single-digit percentage of revenue from the collaboration to our licensors. We expect to utilize a material portion of our net operating loss carryforwards in the Netherlands during 2021 as a result of closing the transaction. The upfront payment, net of payments owed to licensors and other parties, is expected to extend the funding of our operations into the second half of 2024 (assuming a full repayment of funds borrowed from Hercules Growth Capital, Inc. under our term loan facilities by 2023). The receipt of the near-term milestones would further expand the funding of our operations. However, we expect to continue to incur losses and to generate negative cash flows beyond 2021, the fiscal year in which we closed the transaction.

Hemophilia B program – Etranacogene dezaparvovec (AMT-061)

Etranacogene dezaparvovec is our lead gene therapy candidate and includes an AAV serotype 5 (together "AAV-5") vector incorporating the functional human Factor IX ("FIX") Padua variant. We are currently conducting a pivotal study in patients with severe and moderately-severe hemophilia B.

In December 2020, we announced top-line data from the HOPE-B trial. The 26-week follow-up date from the trial showed that FIX activity in the 54 patients increased after dosing from ≤ 2% to a mean of 37.2% at 26 weeks, meeting a first primary endpoint of the HOPE-B trial. No correlation between pre-existing neutralizing antibodies and FIX activity was found in patients with neutralizing antibody titers up to 678.2, a range expected to include more than 95% of the general population; one patient with a neutralizing antibody titer of 3,212.3 did not show an increase in FIX activity. Less than 1% of the general population is expected to have neutralizing antibody titers of greater than 3,000.

During the 26-week period after dosing, 15 patients (28%) reported a total of 21 bleeding events, representing a reduction of 83% compared to the 123 bleeding events reported by 38 patients (70%) during the observational lead-in phase of the trial. Total bleeds include any bleeding event reported after the treatment of etranacogene dezaparvovec, including spontaneous, traumatic, and those associated with unrelated medical procedures, whether or not FIX treatment was required. Of the total bleeding events reported during the 26-week period after dosing, only three were classified as spontaneous bleeds requiring treatment, representing a reduction of 92% compared to the 37 such bleeding events reported during the observational lead-in phase. Mean annualized usage of FIX replacement therapy, a secondary endpoint in the clinical trial, declined by 96% during the 26-week period after dosing compared to the observational lead-in phase. Etranacogene dezaparvovec was generally well-tolerated. As of the November 2020 cut-off date, most adverse events were classified as mild (81.5%). The most common events included transaminase elevation treated with steroids per protocol (9 patients; 17%), infusion-related reactions (7 patients; 13%), headache (7 patients; 13%) and influenza-like symptoms (7 patients; 13%). Liver enzyme elevations resolved with a tapering course of corticosteroids and FIX activity remained in the mild range in the steroid treated patients. No relationship between safety and neutralizing antibody titers was observed. Based on interactions with the U.S. Food and Drug Administration ("FDA") and the European Medicines Agency ("EMA"), we plan to incorporate FIX activity and bleeding rates at 52 weeks as additional co-primary endpoints in the study.

On December 21, 2020, our clinical trials of etranacogene dezaparvovec, including our HOPE-B trial were placed on clinical hold by the FDA. The clinical hold was initiated following the submission of a safety report in mid-December relating to a possibly related serious adverse event associated with a preliminary diagnosis of hepatocellular carcinoma ("HCC"), a form of liver cancer, in one patient in the HOPE-B trial that was treated with etranacogene dezaparvovec in October 2019. The patient has multiple risk factors associated with HCC, including a twenty-five-year history of hepatitis C, hepatitis B, evidence of non-alcoholic fatty liver disease and advanced age. Chronic infections with hepatitis B and C have been associated with approximately 80% of HCC cases. No other cases of HCC have been reported in our clinical trials conducted in more than 67 patients in hemophilia B, with some patients dosed more than 5 years ago.

On March 26, 2021, we submitted the results of a comprehensive investigation into the case of HCC to the FDA. The investigation found that it is highly unlikely the HCC was caused by etranacogene dezaparvovec. Multiple analyses conducted by an independent laboratory and reviewed by leading external experts in the field show that AAV vector integration in the patient's tissue sample was extremely rare and accounted for 0.027% of the cells in the sample. The integration events were distributed randomly across the genome, and there was no evidence of clonal expansion or any dominant integration event. Additionally, whole genome sequencing of the tumor confirmed that the patient had several genetic mutations that are characteristic of HCC and are independent of vector integration. Finally, gene expression analysis of the tumor and adjacent tissue suggested a precancerous state in the liver consistent with several risk factors that predispose this patient to HCC. On April 23, 2021, the FDA informed us that the clinical hold on our hemophilia B gene therapy program is removed after determining that we had satisfactorily addressed all issues identified.

Etranacogene dezaparvovec has been granted Breakthrough Therapy Designation by the FDA and access to the current priority medicines ("PRIME") initiative by the EMA.

Huntington's disease program (AMT-130)

AMT-130 is our novel gene therapy candidate for the treatment of Huntington's disease. AMT-130 utilizes our proprietary, gene-silencing miQURE platform and incorporates an AAV vector carrying a miRNA specifically designed to silence the huntingtin gene and the potentially highly toxic exon 1 protein fragment. AMT-130 has received orphan drug and Fast Track designations from the FDA and Orphan Medicinal Product Designation from the EMA.

In June 2020, we announced the completion of the first two patient procedures in the Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease. In October 2020 we completed the third and fourth patients' procedures. In February 2021, the independent Data Safety Monitoring Board ("DSMB") overseeing the Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease met. No significant safety concerns were noted to prevent further dosing. On April 5, 2021 we announced that we completed the procedures for the fifth to tenth patients completing the treatment of the first cohort.

On April 5, 2021 we also announced the initiation of a Phase 1b/II clinical trial in Europe. The planned Phase Ib/II study is expected to begin enrolling patients in the second half of 2021. This open-label study will enroll 15 patients with early manifest Huntington's disease across two dose cohorts. Together with the U.S. study, the European study is intended to establish safety, proof of concept, and the optimal dose of AMT-130 to take forward into Phase III development or into a confirmatory study should an accelerated registration pathway be feasible.

COVID-19 measures

The coronavirus disease ("COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 ("Sars-CoV 2 virus") was characterized as a pandemic by the World Health Organization ("WHO") on March 11, 2020. During late 2020 various, potentially more infectious, variants of the Sars-CoV 2 virus causing COVID-19 were identified.

Starting March 2020, we implemented measures to address the impact of COVID-19 on our business. We mandated a work-from-home policy for all non-essential employees at our Amsterdam and Lexington facilities when the pandemic began. We implemented a series of protocols governing the operations of our Lexington facility to comply with the requirements of the various orders and guidance from the Commonwealth of Massachusetts and other related orders, guidance, laws, and regulations. We continue to monitor local government rules and recommendations and office protocols will be aligned with these rules and recommendations.

To align with the Dutch government's measures, we implemented a mandatory work-from-home policy in Amsterdam. Employees based in Amsterdam who cannot perform their duties outside of our Amsterdam facility will continue to work at our Amsterdam facility. We adapted to operate our laboratories at our Amsterdam site to comply with social distancing rules and to ensure the health and wellbeing of our employees under the current circumstances. All other employees in Amsterdam will work from home through at least the end of August 2021, partly in conjunction with the ongoing expansion of our laboratory space.

As a biopharma research and development company, we were deemed to provide essential services under the "stay at home" advisory that was issued by the Governor of Massachusetts on March 23, 2020 and we therefore have maintained our manufacturing operations at our Lexington site. To ensure adequate social distancing in our Lexington facility, our COVID-19 protocols generally have limited occupancy to numbers below those allowed by the Massachusetts COVID-19 guidelines. In our Lexington facility, we currently have implemented an occupancy limitation of approximately 25%. Our employees that cannot perform their duties outside of our Lexington facility continue to work at our Lexington facility. All other employees are required to work remotely to the extent possible through at least the end of the second quarter of 2021. Our actual occupancy at the Lexington facility has been less than approximately 25% of our permitted occupancy during all phases of the Massachusetts reopening plan. We have also implemented a mandatory COVID-19 PCR testing protocol effective February 11, 2021 that requires employees to have tested negative for COVID-19 prior to entering the Lexington facility.

We have adapted our ongoing clinical research activities based on the directions and flexibility provided by the "FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic" issued on March 18, 2020 and updated throughout the pandemic to minimize any risk, disruption, or delay in either patient dosing or follow-up visits. These procedures occurred after a postponement that resulted from the COVID-19 pandemic and the associated states of emergency declarations in the United States.

The broader implications of COVID-19 on our results of operations and overall financial performance remain uncertain. The COVID-19 pandemic and its adverse effects have become more prevalent in the locations where we, and our third-party business partners conduct business. While we have experienced disruptions in our operations as a result of COVID-19, we are adapting to the current environment to minimize the effect to our business. However, we may experience more pronounced disruptions in our operations in the future.

Facility

In February 2021 we commenced the expansion of our Amsterdam site to build additional laboratories to support the expansions of our research and development activities as well the construction of a cleanroom designed to be capable of manufacturing cGMP materials at a 500-liter scale. In May 2021 we entered into a sublease agreement to let an additional approximately 1,080 square meters of office space to accommodate the hiring of additional full-time employees. The lease expires in October 2028 and includes a break option until October 2023.

Financial Overview

Key components of our results of operations include the following:

	Three months ended March 31,	
	2021	2020
	(in thousands)	
Total revenues	$ 454	$ 104
Research and development expenses	(32,656)	(26,013)
Selling, general and administrative expenses	(12,375)	(9,072)
Net loss	(41,556)	(27,999)

As of March 31, 2021, and December 31, 2020, we had cash and cash equivalents of $260.8 million and $244.9 million, respectively. We had a net loss of $41.6 million in the three months ended March 31, 2021, compared to $28.0 million for the same period in 2020. As of March 31, 2021, and December 31, 2020, we had accumulated deficits of $826.3 million and $784.7 million, respectively. Our losses will be materially impacted by the amount of license revenue that we will recognize in accordance with ASC 606 as a result of the closing of the transaction contemplated under the CSL Behring Agreement, which became fully effective on May 6, 2021.

We anticipate that our expenses will increase substantially as we:

- Advance the clinical development of AMT-130 for our Huntington's disease gene therapy program;
- Advance multiple research programs related to gene therapy candidates targeting liver-directed and central nervous system ("CNS") diseases;
- Acquire or in-license rights to new therapeutic targets or product candidates;
- Continue to expand, enhance and optimize our technology platform, including our manufacturing capabilities, next-generation viral vectors and promoters, and other enabling technologies;
- Continue to expand our employee base to support research and development, as well as general and administrative functions;
- Maintain, expand, and protect our intellectual property portfolio, including in-licensing additional intellectual property rights from third parties; and
- Build out our commercial and medical affairs infrastructure and seek marketing approval for any product candidates.

See "Results of Operations" below for a discussion of the detailed components and analysis of the amounts above.

Critical Accounting Policies and Estimates

In preparing our consolidated financial statements in accordance with U.S. GAAP and pursuant to the rules and regulations promulgated by the SEC we make assumptions, judgments and estimates that can have a significant impact on our net income/loss and affect the reported amounts of certain assets, liabilities, revenue and expenses, and related disclosures. On an ongoing basis, we evaluate our estimates and judgments, including those related to the treatment of the CSL Behring Agreement, our arrangements with Bristol-Myers Squibb ("BMS"), including the amended collaboration and license agreement that we entered into with BMS in December 2020 (the "amended BMS CLA"), share-based payments, corporate income taxes related to valuation allowance and accounting for operating leases under ASC 842. We base our assumptions, judgments and estimates on historical experience and various other factors that we believe 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 clear from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies. During the three months ended March 31, 2021, there were no material changes to our critical accounting policies as reported in our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on March 1, 2021.

We believe that the assumptions, judgments, and estimates related to the treatment of the CSL Behring Agreement, the amended BMS CLA, share-based payments, corporate income taxes related to valuation allowance and accounting for operating leases under ASC 842 to be our critical accounting policies.

The preparation of our consolidated financial statements for the three-month period ended March 31, 2021, required us to analyze the accounting treatment of the CSL Behring Agreement.

The effectiveness of the transaction contemplated by the CSL Behring Agreement was contingent on completion of review under antitrust laws in the United States, Australia, and the United Kingdom. The review processes in Australia and the United Kingdom were completed prior to January 6, 2021. As of March 31, 2021, regulatory approval in the United Sates had not occurred. On May 5, 2021, the waiting period under the HSR Act expired and the transaction became fully effective on May 6, 2021.

As of March 31, 2021, we concluded that we had no enforceable right to receive the $450.0 million upfront payment, in accordance with the CSL Behring Agreement as payment was contingent upon the successful completion of reviews under the HSR Act and the reviews were not completed by March 31, 2021. Therefore, we determined we would not recognize any revenue in relation to the upfront payment, the regulatory and sale milestone payments, or the royalties (together "CSL Behring License Revenue") in accordance with ASC 606 during the three-month period ended March 31, 2021.

We recognize deferred tax assets to the extent that we determine that these assets are more likely than not to be realized. We determined that recognition of the CSL Behring License Revenue in 2021 will consume a material portion of our net operating loss carryforwards in the Netherlands. However, we expect to continue to record operating losses in the years thereafter. Accordingly, we expect to continue to record a full valuation allowance in relation to our net operating loss carryforwards in the Netherlands as of the end of the current fiscal year. We determined the impact which recognition of CSL Behring License Revenue is estimated to have, with regards to the expected effective tax rate of 0% that was applied with respect to our Dutch operations as of March 31, 2021, is immaterial. Accordingly, we continued to record a full valuation allowance as of March 31, 2021, in relation to our net operating loss carryforwards in the Netherlands.

Revenues

We recognize collaboration revenues associated with Collaboration Target-specific pre-clinical analytical development and process development activities that are reimbursable by BMS under the BMS CLA (as defined below) and the amended BMS CLA as well as other related agreements. Collaboration Revenue related to these contracted services is recognized when performance obligations are satisfied.

We recognized license revenues associated with the amortization of the non-refundable upfront payment and target designation fees we received from BMS in 2015. We evaluated our outstanding performance obligation following the amendment of the BMS CLA on December 1, 2020 and determined that our remaining performance obligation is immaterial. We updated our measure of progress accordingly and amortized the remaining balance of unrecognized revenue as of December 1, 2020. In accordance with the amended BMS CLA, we continue to be eligible to receive research, development, and regulatory milestone payments as well as sales milestone payments and royalties for each of the four active Collaboration Targets if defined milestones are achieved in relation to the license to our technology and know-how. We will recognize revenue from these payments when earned or as sales occur.

Research and development expenses

We expense research and development ("R&D") expenses as incurred. Our R&D expenses generally consist of costs incurred for the development of our target candidates, which include:

- Employee-related expenses, including salaries, benefits, travel and share-based compensation expense;
- Costs incurred for laboratory research, preclinical and nonclinical studies, clinical trials, statistical analysis and report writing, and regulatory compliance costs incurred with clinical research organizations and other third-party vendors;
- Costs incurred to conduct consistency and comparability studies;
- Costs incurred for the development and improvement of our manufacturing processes and methods;
- Costs associated with our research activities for our next-generation vector and promoter platform; and
- Facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies.

Our research and development expenses may vary substantially from period to period based on the timing of our research and development activities, including manufacturing campaigns, regulatory submissions and enrollment of patients in clinical trials. The successful development of our product candidates is highly uncertain. Estimating the nature, timing or cost of the development of any of our product candidates involves considerable judgement due to numerous risks and uncertainties associated with developing gene therapies, including the uncertainty of:

- the scope, rate of progress and expense of our research and development activities;
- our ability to successfully manufacture and scale-up production;
- clinical trial protocols, speed of enrollment and resulting data;
- the effectiveness and safety of our product candidates;
- the timing of regulatory approvals; and
- our ability to agree to ongoing development budgets with collaborators who share the costs of our development programs.

A change in the outcome of any of these variables with respect to our product candidates that we may develop, including as a result of the COVID-19 pandemic, could mean a significant change in the expenses and timing associated with the development of such product candidate.

Selling, general and administrative expenses

Our general and administrative expenses consist principally of employee, office, consulting, legal and other professional and administrative expenses. We incur expenses associated with operating as a public company, including expenses for personnel, legal, accounting and audit fees, board of directors’ costs, directors' and officers' liability insurance premiums, Nasdaq listing fees, expenses related to investor relations and fees related to business development and maintaining our patent and license portfolio. Our selling costs include employee expenses as well as professional fees related to the preparation of a commercial launch of etranacogene dezaparvovec.

Other items, net

Our other income primarily consists of payments to subsidize our research and development efforts as well as income from the subleasing of our Amsterdam facility.

Our other expense primarily consists of expenses we incur in relation to our subleasing income.

Results of Operations

Comparison of the three months ended March 31, 2021 and 2020

The following table presents a comparison of our results of operations for the three months ended March 31, 2021 and 2020.

	Three months ended March 31,		
	2021	2020	2021 vs 2020
		(in thousands)	
Total revenues	$ 454	$ 104	$ 350
Operating expenses:			
Research and development expenses	(32,656)	(26,013)	(6,643)
Selling, general and administrative expenses	(12,375)	(9,072)	(3,303)
Total operating expenses	**(45,031)**	**(35,085)**	**(9,946)**
Other income	352	857	(505)
Other expense	(233)	(339)	106
Loss from operations	**(44,458)**	**(34,463)**	**(9,995)**
Other non-operating items, net	3,115	6,464	(3,349)
Net loss before income tax expense	**$ (41,343)**	**$ (27,999)**	**$ (13,344)**
Income tax expense	(213)	-	(213)
Net loss	**$ (41,556)**	**$ (27,999)**	**$ (13,557)**

Revenue

Our revenue for the three months ended March 31, 2021 and 2020 was as follows:

	Three months ended March 31,		
	2021	2020	2021 vs 2020
		(in thousands)	
License Revenue	$ —	$ 47	$ (47)
Collaboration Revenue	454	57	397
Total revenues	**$ 454**	**$ 104**	**$ 350**

We recognized $0.0 million License Revenue related to upfront payments and target designation fees received from BMS in 2015 under the BMS CLA for the period ended March 31, 2020. We did not recognize any License Revenue from the December 1, 2020 amended BMS CLA for the period ended March 31, 2021.

We recognized $0.5 million Collaboration Revenue in the three months ended March 31, 2021, compared to $0.1 million for the same period in 2020.

Research and development expenses

Research and development expenses for the three months ended March 31, 2021 were $32.7 million, compared to $26.0 million for the same period in 2020. Other research and development expenses are separately classified in the table below. These are not allocated as they are deployed across multiple projects under development.

	Three months ended March 31,		
	2021	2020	2021 vs 2020
	(in thousands)		
Etranacogene dezaparvovec (AMT-060/061)	$ 3,647	$ 4,540	$ (893)
Huntington's disease (AMT-130)	1,971	1,060	911
Programs in preclinical development and platform related expenses	2,289	1,455	834
Total direct research and development expenses	**$ 7,907**	**$ 7,055**	**$ 852**
Employee and contractor-related expenses	11,595	9,348	2,247
Facility expenses	4,624	4,016	608
Disposables	3,344	2,410	934
Share-based compensation expense	2,679	2,395	284
Other expenses	2,507	789	1,718
Total other research and development expenses	**$ 24,749**	**$ 18,958**	**$ 5,791**
Total research and development expenses	**$ 32,656**	**$ 26,013**	**$ 6,643**

Direct research and development expenses

Etranacogene dezaparvovec (AMT-060/061)

In the three months ended March 31, 2021 and 2020, the external costs for our hemophilia B program were primarily related to the execution of our Phase III clinical trial. Following the completion of patient enrollment into our HOPE-B trial we also started incurring costs related to preparation of a Biologics License Application (“BLA”) and marketing authorization application (“MAA”) and for commercialization of etranacogene dezaparvovec.

We enrolled patients into a six-month lead in phase between January 2018 and September 2019 and dosed a total of 54 patients between January 2019 and March 2020. Our expenses related to etranacogene dezaparvovec were largely unaffected by the COVID-19 pandemic as we completed enrollment prior to the lockdowns in those countries that we enroll patients.

In addition, we continue to incur costs for the long-term follow-up of patients in our Phase I/II clinical trial of AMT-060 and our Phase IIb clinical trial of etranacogene dezaparvovec.

Huntington disease (AMT-130)

In the three months ended March 31, 2021 and March 31, 2020, our external costs for the development of Huntington’s disease were primarily related to the execution of our Phase I/II clinical trial.

Preclinical programs & platform development

In the three months ended March 31, 2021, we incurred $2.3 million of costs primarily related to our preclinical activities primarily associated with product candidates, SCA3 (AMT-150) and Fabry disease (AMT-190), as well as various other research programs and technology innovation projects, compared to costs of $1.5 million in the same period in 2020, which included costs related to our product candidate for Hemophilia A (AMT-180) that was subsequently deprioritized in June 2020.

Other research & development expenses

- We incurred $11.6 million in personnel and contractor related expenses in the three months ended March 31, 2021, compared to $9.3 million for the same period in 2020. Our costs during the three months ended March 31, 2021 increased by $2.3 million as a result of the recruitment of personnel to support the development of our product candidates;
- We incurred $2.7 million in share-based compensation expenses in the three months ended March 31, 2021, compared to $2.4 million for the same period in 2020 primarily driven by increase in awards granted, including those to newly recruited personnel;
- We incurred $4.6 million in operating expenses and depreciation expenses related to our rented facilities in the three months ended March 31, 2021, compared to $4.0 million in the same period in 2020; and
- We incurred $2.5 million in other costs in the three months ended March 31, 2021, compared to $0.8 million for the same period in 2020 related to miscellaneous other costs we incur as a result of expanding our organization.

Selling, general and administrative expenses

Selling, general and administrative expenses for the three months ended March 31, 2021 were $12.4 million, compared to $9.1 million for the same period in 2020.

- We incurred $3.9 million in personnel and contractor related expenses in the three months ended March 31, 2021, compared to $3.2 million in the same period in 2020. The increase in the three months ended March 31, 2021, relates to the recruitment of personnel;
- We incurred $3.1 million in share-based compensation expenses in the three months ended March 31, 2021, compared to $1.9 million in the same period in 2020 primarily driven by increase in awards granted, including those to newly recruited personnel; and
- We incurred $2.9 million in professional fees in the three months ended March 31, 2021, compared to $1.2 million in the same period in 2020. We regularly incur accounting, audit and legal fees associated with operating as a public company. Additionally, in the three months ended March 31, 2021, we incurred professional fees in relation to our licensing transaction with CSL Behring.

Other items, net

We recognized $0.0 million in income from payments received from European authorities to subsidize our research and development efforts in the Netherlands in the three months ended March 31, 2021, compared $0.2 million for the same period in 2020.

Other non-operating items, net

We recognize interest income associated with our cash and cash equivalents.

We hold monetary items and enter into transactions in foreign currencies, predominantly in euros and U.S. dollars. We recognize foreign exchange results related to changes in these foreign currencies.

We issued warrants to BMS in 2015. We recognize changes in the fair value of these warrants within other non-operating income / (expense). Following the termination of the BMS warrants on December 1, 2020, we no longer recognize changes in the fair value of these warrants within other non-operating (expense) / income. As of the same date, we recognized a derivative financial liability related to a contingent payment due to BMS upon the consummation of a change of control transaction (“CoC-payment”) as described elsewhere in the Quarterly Report on Form 10-Q.

Our other non-operating items, net, for the three months ended March 31, 2021 and 2020 were as follows:

	Three months ended March 31,		
	2021	2020	2021 vs 2020
		(in thousands)	
Interest income	$ 40	$ 822	$ (782)
Interest expense - Hercules long-term debt	(1,551)	(975)	(576)
Foreign currency gains, net	4,626	4,602	24
Other non-operating gains	—	2,015	(2,015)
Total other non-operating income, net	**$ 3,115**	**$ 6,464**	**$ (3,349)**

We recognized a net foreign currency gain, related to our borrowings from Hercules and our cash and cash equivalents as well as loans between entities within the uniQure group, of $4.6 million during the three months ended March 31, 2021, compared to a net gain of $4.6 million during the same period in 2020.

In the three months ended March 31, 2021, we recognized income of nil as there was no change in the fair value of the BMS derivative financial liability for the CoC-payment, compared to income of $2.0 million during the same period in 2020 related to changes in the fair value of the BMS warrants from the BMS CLA.

Income tax

We recognized $0.2 million of deferred tax expense for the period ended March 31, 2021 and nil in the same period ended 2020.

Financial Position, Liquidity and Capital Resources

As of March 31, 2021, we had cash, cash equivalents and restricted cash of $263.5 million. We believe our cash and cash equivalents as of March 31, 2021, combined with the $100.0 million 2021 Amended Facility, will enable us to fund our operating expenses, including our debt repayment obligations, as they become due and capital expenditure requirements until the end of 2022. Following the receipt of the $450.0 million upfront payment, which was paid to us on May 7, 2021, we expect that our cash and cash equivalents will be sufficient to fund operations into the second half of 2024 (assuming a full repayment of funds borrowed from Hercules under our term loan facility by 2023). We are also eligible to receive up to $1.6 billion of milestones and tiered double-digit royalties in a range of up to a low-twenties percent of net sales of the Product based on sales thresholds, both of which are not included in the above guidance.

	Three months ended March 31,	
	2021	2020
	(in thousands)	
Cash, cash equivalents and restricted cash at the beginning of the period	$ 247,680	$ 380,726
Net cash used in operating activities	(41,273)	(32,953)
Net cash used in investing activities	(3,876)	(2,890)
Net cash generated from financing activities	62,618	1,010
Foreign exchange impact	(1,620)	(943)
Cash, cash equivalents and restricted cash at the end of period	**$ 263,529**	**$ 344,950**

We have incurred losses and cumulative negative cash flows from operations since our business was founded by our predecessor entity AMT Therapeutics (“AMT”) Holding N.V. in 1998. We had a net loss of $41.6 million during the three months ended March 31, 2021, compared to a net loss of $28.0 million during the same period in 2020. As of March 31, 2021, we had an accumulated deficit of $826.3 million.

Sources of liquidity

From our first institutional venture capital financing in 2006 through March 31, 2021, we funded our operations primarily through private and public placements of equity securities and convertible and other debt securities as well as payments from our collaboration partners.

On March 1, 2021, we entered into a Sales Agreement with SVB Leerink with respect to an ATM offering program, under which we may, from time to time in our sole discretion, offer and sell through SVB Leerink, acting as agent, our ordinary shares, up to an aggregate offering price of $200.0 million. We will pay SVB Leerink a commission equal to 3% of the gross proceeds of the sales price of all ordinary shares sold through it as a sales agent under the Sales Agreement. In March 2021 we issued 0.9 million ordinary shares for net proceeds of $27.6 million.

On December 6, 2018, we signed the 2018 Amended Facility with Hercules that both refinanced our then-existing $20.0 million credit facility and provided us with an additional unconditional commitment of $15.0 million as well as a conditional commitment of $15 million that expired on June 30, 2020. At signing, we drew down an additional $15.0 million, for a total outstanding amount of $35.0 million.

The 2018 Amended Facility extended the loan's maturity date until June 1, 2023. The interest-only period was initially extended from November 2018 to January 1, 2021. The interest-only period was further extended to January 1, 2022 as a result of raising more than $90.0 million in equity financing in September 2019. The interest-only period was again further extended to June 1, 2023 as a result of the 2021 Amended Facility. The variable interest rate of the 2018 Amended Facility is equal to the greater of (i) 8.85% or (ii) 8.85% plus the prime rate less 5.50%. Under the 2018 Amended Facility, we paid a facility fee equal to 0.50% at signing of the $35.0 million loan outstanding and will owe a back-end fee of 4.95% of the outstanding debt. In addition, in May 2020, we paid a back-end fee of $1.0 million in relation to the 2016 Amended Facility.

On January 29, 2021, we and Hercules entered into the 2021 Amended Facility. Pursuant to the 2021 Amended Facility, Hercules agreed to an additional Facility of $100.0 million ("Tranche B"), increasing the aggregate principal amount of the term loan facilities from $35.0 million to up to $135.0 million. On January 29, 2021, we drew down $35.0 million of the Tranche B. We may draw down the remaining $65.0 million under the Tranche B in a series of one or more advances of not less than $20.0 million each until December 15, 2021. Advances under the Tranche B bear interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance and all accrued but unpaid interest on advances under the Tranche B is due on June 1, 2023, which date may be extended by us by up to two twelve-month periods. Advances under the Tranche B may not be prepaid until six-months after the Closing Date, following which we may prepay all such advances without charge. As of March 31, 2021, $70.0 million was outstanding under the 2018 Amended Facility and the 2021 Amended Facility (December 31, 2020: $35.0 million under the 2018 Amended Facility).

We are subject to the same covenants under our 2018 Amended Facility and 2021 Amended Facility and may become subject to covenants under any future indebtedness that could limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends, which could adversely impact our ability to conduct our business. In addition, our pledge of assets as collateral to secure our obligations under the 2018 Amended Facility and 2021 Amended Facility may limit our ability to obtain debt financing. To the extent we need to finance our cash needs through equity offerings or debt financings, such financing may be subject to unfavorable terms including without limitation, the negotiation and execution of definitive documentation, as well as credit and debt market conditions, and we may not be able to obtain such financing on terms acceptable to us or at all. If financing is not available when needed, including through debt or equity financings, or is available only on unfavorable terms, we may be unable to meet our cash needs. If we raise additional funds through collaborations, strategic alliances or marketing, distribution, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, which could have a material adverse effect on our business, financial conditions, results of operations and cash flows.

Net Cash used in operating activities

Net cash used in operating activities was $41.3 million for the three months ended March 31, 2021 and consisted of a net loss of $41.6 million adjusted for non-cash items, including depreciation and amortization expense of $1.9 million, share-based compensation expense of $5.8 million, unrealized foreign exchange gains of $5.3 million and deferred tax expense of $0.2 million. Net cash used in operating activities also included unfavorable changes in operating assets and liabilities of $3.9 million. These changes primarily related to a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $8.0 million primarily related to the increase in a contract asset and receivable recorded for CSL expenses to be reimbursed as well as an increase in various prepayments for the year and a net increase in accounts payable, accrued expenses, other liabilities, and operating leases of $5.8 million primarily related to an increase in contract liability for CSL expenses to be reimbursed and an increase in accruals for services provided by vendors not yet billed offset by the pay-out of employee bonuses.

Net cash used in operating activities was $33.0 million for the three months ended March 31, 2020 and consisted of a net loss of $28.0 million adjusted for non-cash items, including depreciation and amortization expense of $1.7 million, share-based compensation expense of $4.4 million, fair value gains on derivative financial instruments of $2.0 million, unrealized foreign exchange gain of $4.8 million, and an increase in unamortized deferred revenue of $0.3 million. Net cash used in operating activities also included unfavorable changes in operating assets and liabilities of $4.5 million. These changes primarily related to a net increase in accounts receivable, prepaid expenses, and other current assets of $1.3 million primarily as a result of increase in prepayments for the year and a net decrease in accounts payable, accrued expenses and other liabilities of $3.2 million primarily related to pay-out of employee bonuses.

Net cash used in investing activities

In the three months ended March 31, 2021, we used $3.9 million in our investing activities compared to $2.9 million for the same period in 2020.

	Three months ended March 31,	
	2021	2020
	(in thousands)	
Build out of Amsterdam site	$ (2,416)	$ (355)
Build out of Lexington site	(1,460)	(322)
Acquisition of licenses, patents, and other rights	—	(2,213)
Total investments	**$ (3,876)**	**$ (2,890)**

The build out of the Amsterdam site was $2.4 million for the three months ended March 31, 2021, compared to $0.4 million for the same period in 2020. The increase is a result of the construction of additional laboratories to support the expansions of our research and development activities as well as the construction of a cleanroom designed to be capable of manufacturing cGMP materials at a 500-liter scale.

Net cash generated from financing activities

In the three months ended March 31, 2021, we generated $62.6 million in our financing activities compared to $1.0 million for the same period in 2020.

	Three months ended March 31,	
	2021	2020
	(in thousands)	
Cash flows from financing activities		
Proceeds from loan increment, net of debt issuance costs	$ 34,603	$ -
Proceeds from issuance of ordinary shares	28,734	-
Share issuance costs from issuance of ordinary shares	(1,161)	-
Proceeds from issuance of shares related to employee stock option and purchase plans	442	1,010
Net cash generated from financing activities	**$ 62,618**	**$ 1,010**

We received proceeds of $28.7 million associated with our ATM offering in March 2021, offset by fees of $1.2 million.

In January 2021, we received $34.6 million net proceeds from the Hercules 2021 Amended Facility.

During the three months ended March 31, 2021, we received $0.4 million from the exercise of options to purchase ordinary shares in relation to our share incentive plans compared to $1.0 million for the same period in 2020.

Funding requirements

We believe our cash and cash equivalents as of March 31, 2021, combined with the $100.0 million 2021 Amended Facility as well as the upfront payment of $450.0 million that we became entitled to receive following the closing of our transaction with CSL Behring on May 6, 2021, will enable us to fund our operating expenses, including our debt repayment obligations, as they become due and capital expenditure requirements into the second half of 2024 (assuming a full repayment of funds borrowed from Hercules under our term loan facility by 2023). Our future capital requirements will depend on many factors, including but not limited to:

- achieving the milestones and royalties as defined within the CSL Behring Agreement;
- the extent to which we acquire or in-license other businesses, products, product candidates or technologies;
- the amount and timing of revenue, if any, we receive from commercial sales of any product candidates for which we, or our collaboration partner, receives marketing approval in the future;
- the amount and timing of revenue, if any, we receive from manufacturing products from CSL Behring.
- the scope, timing, results, and costs of our current and planned clinical trials, including those for AMT-130 in Huntington's disease;
- the scope, timing, results and costs of preclinical development and laboratory testing of our additional product candidates;
- the need for additional resources and related recruitment costs to support the preclinical and clinical development of our product candidates;
- the need for any additional tests, studies, or trials beyond those originally anticipated to confirm the safety or efficacy of our product candidates and technologies;
- the cost, timing and outcome of regulatory reviews associated with our product candidates;
- our ability to enter into collaboration arrangements in the future;
- the costs and timing of preparing, filing, expanding, acquiring, licensing, maintaining, enforcing, and prosecuting patents and patent applications, as well as defending any intellectual property-related claims;
- the repayments of the principal and other fees associated with our venture debt loan with Hercules, which following the January 29, 2021 amendment will be due in June 2023;
- the costs associated with maintaining quality compliance and optimizing our manufacturing processes, including the operating costs associated with our Lexington, Massachusetts manufacturing facility;
- the costs associated with increasing the scale and capacity of our manufacturing capabilities; and
- the costs associated with process validation and inspection readiness of etranacogene dezaparvovec.

Contractual obligations and commitments

The table below sets forth our contractual obligations and commercial commitments as of March 31, 2021, that are expected to have an impact on liquidity and cash flows in future periods.

	Less than 1 year	Between 1 and 3 years	Between 3 and 5 years	Over 5 years	Total
			(in thousands)		
Debt obligations (including $17.1 million interest payments)	$ 6,068	$ 81,028	$ —	$ —	$ 87,096
Operating lease obligations	5,566	11,424	12,992	26,977	56,959
Total	**$ 11,634**	**$ 92,452**	**$ 12,992**	**$ 26,977**	**$ 144,055**

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones (such as the start of a clinical trial, filing of a BLA, approval by the FDA or product launch). We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these milestones is not fixed and determinable. We also have obligations to make future payments that become due and payable upon the collection of the upfront payment or milestone payments from CSL Behring. We have not included these commitments on our balance sheet or in the table above because these payments only become due and payable after the CSL Behring Agreement became fully effective on May 6, 2021.

We enter into contracts in the normal course of business with clinical research organizations ("CROs") for preclinical research studies and clinical trials, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Off-Balance Sheet Arrangements

As of March 31, 2021, we did not have any off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to a variety of financial risks in the normal course of our business, including market risk (including currency, price and interest rate risk), credit risk and liquidity risk. Our overall risk management program focuses on preservation of capital and the unpredictability of financial markets and has sought to minimize potential adverse effects on our financial performance and position.

Our market risks and exposures to such market risks during the three months ended March 31, 2021, have not materially changed from our market risks and our exposure to market risk discussed in Part II, Item 7A of our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on March 1, 2021.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive and chief financial officer ("CEO"), evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) as of March 31, 2021. Based on such evaluation, our CEO has concluded that as of March 31, 2021, our disclosure controls and procedures were effective to ensure that information required to be disclosed by it in reports the Company files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that such material information is accumulated and communicated to the Company's management, including its Principal Executive Officer and Principal Financial Officer, to allow timely decisions regarding required disclosure. Because of the inherent limitations in all control systems, any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management necessarily is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Furthermore, the Company's controls and procedures can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of such control, and misstatements due to error or fraud may occur and not be detected on a timely basis.

Changes in Internal Control over Financial Reporting

During the first quarter of 2021, there were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. We have not experienced any material impact to our internal controls over financial reporting despite the fact that a large group of our employees are working remotely due to the COVID-19 pandemic. We are continually monitoring and assessing the impact the COVID-19 situation has on the operating effectiveness of our internal controls.

Part II – OTHER INFORMATION

Item 1. Legal Proceedings

During 2020, VectorY B.V., a Netherlands-based gene therapy company founded in August 2020 by Forbion International Management B.V., hired Pavlina Konstantinova and several other former uniQure employees, which we believed was in violation of the employment agreements of those employees and involved the misappropriation of our proprietary resources. On or about February 22, 2021, Dr. Konstantinova, VectorY B.V., and Forbion International Management B.V. commenced a summary proceeding in the Netherlands primarily seeking an order: (i) allowing VectorY and Dr. Konstantinova to continue their employment relationship; (ii) suspending the non-competition agreement between uniQure biopharma B.V. and Dr. Konstantinova; and (iii) precluding any monetary penalties pursuant to that non-competition agreement. The complaint also sought payment of the costs of legal proceedings and a monetary monthly payment to Dr. Konstantinova in lieu of a promise by uniQure biopharma B.V. to release Dr. Konstantinova from her obligations under the non-competition agreement.

On April 16, 2021, we settled all matters related to the dispute described above (the "Settlement"). In connection with the Settlement, we will receive preference shares in VectorY representing 5% of the fully diluted share capital in VectorY. In addition, we and certain Forbion entities entered into the Cooperation Agreement described below.

Under the terms of the Cooperation Agreement, the Forbion Entities have agreed, among other things, for a period of two years from April 16, 2021:

1. To vote all of their ordinary shares in uniQure N.V. (1) in favor of the re-election of any persons serving on the Board of Directors of the Company (the "Board") as of the date of the Cooperation Agreement and nominated by the Board for re-election; (2) against any nominees to serve on the Board who have not been recommended by the Board, and (3) with respect to all other matters, other than a Voting Exempt Matter, in accordance with the Board's recommendations as identified in our notice of general meeting or any supplement thereto. For purposes of the Cooperation Agreement, a "Voting Exempt Matter" means, with respect to the Company, any shareholder vote taken to approve or ratify any merger, acquisition, recapitalization, restructuring, financing, disposition, distribution, spin-off, sale or transfer of all or substantially all of our or any of its affiliates' assets in one or a series of transactions, joint venture or other business combination of uniQure N.V. or any of its affiliates with a third party or certain other similar transactions.
2. Not to make any announcement or proposal with respect to, or offer, seek, propose or indicate an interest in (A) any form of business combination or acquisition or other transaction relating to assets or securities of the uniQure N.V. or any of its subsidiaries, (B) any form of restructuring, recapitalization or similar transaction with respect to the uniQure N.V. or any of its subsidiaries or (C) any form of tender or exchange offer for the ordinary shares of the uniQure N.V.
3. Not to make, engage in, assist with, or in any way participate in, directly or indirectly, any solicitation of proxies or written consents to vote (or withhold the vote of) any voting securities of uniQure N.V.
4. Not to take certain other specified actions aimed at changing or influencing the Board, management or control of the uniQure N.V.

We and the Forbion Entities have also agreed to certain non-disparagement provisions. Based on a Schedule 13G/A filed by For UniQure B.V. and Forbion I Management B.V. on February 16, 2021, ForUniQure held 4,386,742 ordinary shares of uniQure N.V. or approximately 9.5% of our issued outstanding ordinary shares.

Item 1A. Risk Factors

An investment in our ordinary shares involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Quarterly Report on Form 10-Q, including our financial statements and related notes thereto, and the risk factors discussed in Part I, Item 1A "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 1, 2021, before deciding to invest in our ordinary shares. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the value of our securities to decline, and you may lose all or part of your investment.

Summary Risk Factors

The following is a summary of the principal risks associated with an investment in our ordinary shares:

- We may encounter substantial delays in, and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates.
- Our business and operations have been, and may continue to be, materially and adversely affected by the ongoing COVID-19 pandemic.
- We may not be successful in our efforts to use our gene therapy technology platform to build a pipeline of additional product candidates.
- We may not be successful in our efforts to in-license or acquire product candidates that align with our research and development strategy.
- Our manufacturing facility is subject to significant government regulations and approvals. If we fail to comply with these regulations or to maintain these approvals our business could be materially harmed.
- Our resources might be adversely affected if we are unable to meet our product development and supply needs and obligations, including our ability to complete the validation of our existing manufacturing processes as well as to develop larger scale manufacturing processes, which could adversely affect our ability to sufficiently meet our future production needs or regulatory filing timelines.
- We cannot predict when or if we will obtain marketing approval to commercialize a product candidate.
- We are exposed to a number of external factors such as competition, insurance coverage of and pricing and reimbursement for our product candidates that may adversely affect our product revenue and that may cause our business to suffer.
- We rely on licenses of intellectual property from third parties, and such licenses may not provide adequate rights or may not be available in the future on commercially reasonable terms or at all, and our licensors may be unable to obtain and maintain patent protection for the technology or products that we license from them.
- If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our ability to successfully commercialize our products may be impaired.
- Our reliance on third parties may require us to share our trade secrets, which could increase the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.
- We will likely need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations which could have a material adverse effect on our business, financial condition, results of operations, and cash flows.
- Our relationships with customers and third-party payers will be subject to applicable anti-kickback, anti-bribery, fraud and abuse and other laws and regulations, which, if we are found in violation thereof, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

- We are subject to laws governing data protection in the different jurisdictions in which we operate. The implementation of such data protection regimes is complex, and should we fail to fully comply, we may be subject to penalties that may have an adverse effect on our business, financial condition, and results of operations.
- Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.
- If we fail to maintain an effective system of internal controls, we may be unable to accurately report our results of operations or prevent fraud or fail to meet our reporting obligations, and investor confidence and the market price of our ordinary shares may be materially and adversely affected.

Risks Related to the Current COVID-19 Pandemic

Our business and operations have been, and may continue to be, materially and adversely affected by the ongoing COVID-19 pandemic.

The ongoing outbreak of COVID-19 originated in Wuhan, China, in December 2019 and has since spread to multiple countries, including the United States and the Netherlands. On March 11, 2020, the WHO declared the outbreak a pandemic. The COVID-19 pandemic is affecting the United States and global economies and has affected and may continue to affect our operations and those of third parties on which we rely. The COVID-19 pandemic has caused and may continue to cause disruptions in our raw material supply, our commercial-scale manufacturing capabilities for AAV-based gene therapies, the development of our product candidates, employee productivity and the conduct of current and future clinical trials. In addition, the COVID-19 pandemic has affected and may continue to affect the operations of the FDA, EMA, and other health authorities, which could result in delays of reviews and approvals, including with respect to our product candidates.

As evidenced by the postponement of procedures for two patients in our Phase I/II clinical study of AMT-130, the evolving COVID-19 pandemic has impacted the pace of enrollment and procedures in our clinical trials, as well as caused challenges in scheduling follow-up visits and managing other aspects of our clinical trials. We may be affected by similar delays as patients may avoid or may not be able to travel to healthcare facilities and physicians' offices unless due to a health emergency and clinical trial staff can no longer get to the clinic. Such facilities and offices have been and may continue to be required to focus limited resources on non-clinical trial matters, including treatment of COVID-19 patients, thereby decreasing availability, in whole or in part, for clinical trial services. In addition, employee disruptions and remote working environments related to the COVID-19 pandemic, and federal, state, and local public health measures designed to mitigate the spread of the virus, have impacted and could continue to negatively impact the efficiency and pace with which we work and develop our product candidates and our manufacturing capabilities. Further, while the potential economic impact brought by, and the duration of, the COVID-19 pandemic is difficult to assess or predict, the impact of the COVID-19 pandemic on global financial markets may reduce our ability to access capital, which could negatively impact our short-term and long-term liquidity. The ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, financing, or clinical trial activities or on healthcare systems or the global economy as a whole. However, these negative effects could have a material impact on our liquidity, capital resources, operations, and business and those of the third parties on whom we rely.

Risks Related to the Development of Our Product Candidates

None of our product candidates have been approved for commercial sale and they might never receive regulatory approval or become commercially viable. We have never generated any significant revenue from product sales and may never be profitable.

All our product candidates are in research or development. We have not generated any revenues from the sale of products or manufacturing of our product for a licensee and do not expect to generate any such revenue before 2022. Our product candidates, including AMT-130 and any of our other potential product candidates, will require extensive preclinical and/or clinical testing, manufacture development and regulatory approval prior to commercial use. Our research and development efforts may not be successful. Even if our clinical development efforts result in positive data, our product candidates may not receive regulatory approval or be successfully introduced and marketed at prices that would permit us to operate profitably.

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates.

Clinical and non-clinical development is expensive, time-consuming, and uncertain as to outcome. Our product candidates are in different stages of clinical or preclinical development, and there is a significant risk of failure or delay in each of these programs. We cannot guarantee that any preclinical tests or clinical trials will be completed as planned or completed on schedule, if at all. A failure of one or more preclinical tests or clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development, as well as product candidate approval, include, but are not limited to:

- occurrence of serious adverse events associated with a product candidate that are viewed to outweigh its potential benefits;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations ("CROs") and clinical trial sites;
- delays in receiving regulatory authorization to conduct the clinical trials or a regulatory authority decision that the clinical trial should not proceed;
- delays in obtaining or failure to obtain required IRB and IBC approval at each clinical trial site;
- requirements of regulatory authorities, IRBs, or IBCs to modify a study in such a way that it makes the study impracticable to conduct;
- regulatory authority requirements to perform additional or unanticipated clinical trials;
- regulatory authority refusal to accept data from foreign clinical study sites;
- disagreements with regulatory authorities regarding our study design, including endpoints, our chosen indication, or our interpretation of data from preclinical studies and clinical trials or a finding that a product candidate's benefits do not outweigh its safety risks;
- delays in obtaining or failure to obtain required approvals from a DSMB or other required approvals;
- imposition of a clinical hold by regulatory agencies after an inspection of our clinical trial operations or trial sites;
- suspension or termination of clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects, or other unexpected characteristics (alone or in combination with other products) of the product candidate, or due to findings of undesirable effects caused by a chemically or mechanistically similar therapeutic or therapeutic candidate;
- failure by CROs, other third parties or us to adhere to clinical trial requirements or otherwise properly manage the clinical trial process, including meeting applicable timelines, properly documenting case files, including the retention of proper case files, and properly monitoring and auditing clinical sites;
- failure of sites or clinical investigators to perform in accordance with Good Clinical Practice or applicable regulatory guidelines in other countries;
- failure of patients to abide by clinical trial requirements;
- difficulty or delays in patient recruiting into clinical trials or in the addition of new investigators;
- the impact of the COVID-19 pandemic on the healthcare system or any clinical trial sites;
- delays or deviations in the testing, validation, manufacturing, and delivery of our product candidates to the clinical sites;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a study;
- the number of patients required for clinical trials of our product candidates being larger than we anticipate;
- clinical trials producing negative or inconclusive results, or our studies failing to reach the necessary level of statistical significance, requiring that we conduct additional clinical trials or abandon product development programs;
- interruptions in manufacturing clinical supply of our product candidates or issues with manufacturing product candidates that meet the necessary quality requirements;
- unanticipated clinical trial costs or insufficient funding, including to pay substantial application user fees;
- occurrence of serious adverse events or other undesirable side effects associated with a product candidate that are viewed to outweigh its potential benefits;
- disagreements with regulatory authorities regarding the interpretation of our clinical trial data and results, or the emergency of new information about or impacting our product candidates;

- determinations that there are issues with our manufacturing facility or process; or
- changes in regulatory requirements and guidance, as well as new, revised, postponed, or frozen regulatory requirements, especially in light of the change in the United States administration, that require amending or submitting new clinical protocols, undertaking additional new tests or analyses, or submitting new types or amounts of clinical data.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Such trials and regulatory review and approval take many years. It is impossible to predict when or if any of our clinical trials will demonstrate that product candidates are effective or safe in humans.

If the results of our clinical trials are inconclusive, or fail to meet the level of statistical significance required for approval or if there are safety concerns or adverse events associated with our product candidates, we may:

- be delayed in or altogether prevented from obtaining marketing approval for our product candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes with the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Because of the nature of the gene therapies we are developing, regulators may also require us to demonstrate long-term gene expression, clinical efficacy and safety, which may require additional or longer clinical trials, and which may not be able to be demonstrated to the regulatory authorities' standards.

Our ability to recruit patients for our trials is often reliant on third parties, such as clinical trial sites. Clinical trial sites may not have the adequate infrastructure established to handle gene therapy products or may have difficulty finding eligible patients to enroll into a trial.

In addition, we, or any collaborators we may have may not be able to locate and enroll enough eligible patients to participate in these trials as required by the FDA, the EMA or similar regulatory authorities outside the United States and the European Union. This may result in our failure to initiate or continue clinical trials for our product candidates or may cause us to abandon one or more clinical trials altogether. Because our programs are focused on the treatment of patients with rare or orphan or ultra-orphan diseases, our ability to enroll eligible patients in these trials may be limited or slower than we anticipate considering the small patient populations involved and the specific age range required for treatment eligibility in some indications. In addition, our potential competitors, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, may seek to develop competing therapies, which would further limit the small patient pool available for our studies. Also, patients may be reluctant to enroll in gene therapy trials where there are other therapeutic alternatives available or that may become available, which may be for various reasons including uncertainty about the safety or effectiveness of a new therapeutic such as a gene therapy and the possibility that treatment with a gene therapy therapeutic could preclude future gene therapy treatments due to the formation of antibodies following and in response to the treatment.

Any inability to successfully initiate or complete preclinical and clinical development could result in additional costs to us or impair our ability to receive marketing approval, to generate revenues from product sales or obtain regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, including changes in the vector or manufacturing process used, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. It is also possible that any such manufacturing of formulation changes may have an adverse impact on the performance of the product candidate. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may materially harm our business, financial condition, and results of operations.

Our progress in early-stage clinical trials may not be indicative of long-term efficacy in late-stage clinical trials, and our progress in trials for one product candidate may not be indicative of progress in trials for other product candidates.

Study designs and results from previous studies are not necessarily predictive of our future clinical study designs or results, and initial, top-line, or interim results may not be confirmed upon full analysis of the complete study data. Our product candidates may fail to show the required level of safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. Changes to product candidates may also impact their performance in subsequent studies.

By example, our initial clinical trials in hemophilia B were conducted with AMT-060. Following these studies, we made modifications to AMT-060, substituting two nucleotides in the coding sequence for FIX. This modified product candidate is etranacogene dezaparvovec. In 2017, we announced our plans to advance etranacogene dezaparvovec, which includes an AAV5 vector carrying the FIX-Padua transgene, into a pivotal study. While we believe etranacogene dezaparvovec and AMT-060, our product candidate that was previously studied in a Phase I/II study, have been demonstrated to be materially comparable in nonclinical studies and manufacturing quality assessments, it is possible that ongoing or future clinical studies of etranacogene dezaparvovec may show unexpected differences from AMT-060. Should these differences have an unfavorable impact on clinical outcomes, or should they not have their intended effect of increasing the product candidate's FIX activity, they may adversely impact our ability to achieve regulatory approval or market acceptance of etranacogene dezaparvovec. We may also need to conduct additional or longer-term studies, which may delay regulatory submissions or approvals and which the regulatory authorities may ultimately not accept or approve.

In our Phase I/II clinical study of AMT-060, we screened patients for pre-existing anti-AAV5 antibodies to determine their eligibility for the trial. Three of the ten patients screened for the study tested positive for anti-AAV5 antibodies on reanalysis using a more sensitive antibody assay. Since we did not observe any ill-effects or correlation between the level of anti-AAV5 antibodies and clinical outcomes, patients who have anti-AAV5 antibodies are permitted to enroll in our planned pivotal study of etranacogene dezaparvovec. Since we only have been able to test a limited number of patients and have limited clinical and pre-clinical data, it is possible that ongoing or future clinical studies may not confirm these results, and if so, negatively impact the outcome of our study.

In advance of treating patients in the pivotal study of etranacogene dezaparvovec, we conducted a short study to confirm the dose expected to be used in the pivotal trial. The dose-confirmation study enrolled three patients, who were administered a single dose of $2x10^{13}$ gc/kg. We have relied on the short-term data from this study, including FIX activity and safety outcomes during the weeks following administration of etranacogene dezaparvovec, to confirm the dose to be used in the pivotal study. Following the results of this study, our Data Monitoring Committee confirmed the dose of $2x10^{13}$ gc/kg for administration in the pivotal study. Given the limited number of patients and short follow-up period, data from this study may differ materially from the future results of our planned pivotal study of etranacogene dezaparvovec.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials even after achieving promising results in early-stage clinical trials. If a larger population of patients does not experience positive results during clinical trials, if these results are not reproducible or if our products show diminishing activity over time, our product candidates may not receive approval from the FDA or EMA. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections because of many factors, including changes in regulatory policy during the period of product development. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our products in later-stage clinical trials with larger patient populations could have a material adverse effect on our business, financial condition, and results of operations.

Additionally, where there are differences in the early-stage and late-stage trials, such as the differences between AMT-060 and AMT-061, regulatory authorities may require additional or longer-term data in late-stage trials, which may delay regulatory submissions or approvals and which the regulatory authorities may ultimately not accept or approve.

Fast track product, breakthrough therapy, priority review, or Regenerative Medicine Advanced Therapy ("RMAT") designation by the FDA, or access to the PRIME scheme by the EMA, for our product candidates may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We have obtained and may in the future seek one or more of fast track designation, breakthrough therapy designation, RMAT designation, PRIME scheme access or priority review designation for our product candidates. A fast track product designation is designed to facilitate the clinical development and expedite the review of drugs intended to treat a serious or life-threatening condition and which demonstrate the potential to address an unmet medical need. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to speed the FDA marketing application review timeframe for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. PRIME is a scheme provided by the EMA, similar to the FDA's breakthrough therapy designation, to enhance support for the development of medicines that target an unmet medical need.

For drugs and biologics that have been designated as fast track products, RMAT, or breakthrough therapies, or granted access to the PRIME scheme, interaction and communication between the regulatory agency and the sponsor of the trial can help to identify the most efficient path for clinical development. Sponsors of fast track products, RMAT products, or breakthrough therapies may also be able to submit marketing applications on a rolling basis, meaning that the FDA may review portions of a marketing application before the sponsor submits the complete application to the FDA, if the sponsor pays the user fee upon submission of the first portion of the marketing application and the FDA approves a schedule for the submission of the remaining sections. For products that receive a priority review designation, the FDA's marketing application review goal is shortened to six months, as opposed to ten months under standard review.

Designation as a fast track product, breakthrough therapy, RMAT, PRIME, or priority review product is within the discretion of the regulatory agency. Accordingly, even if we believe one of our product candidates meets the relevant criteria, the agency may disagree and instead determine not to make such designation. In any event, the receipt of such a designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional regulatory procedures and does not assure ultimate marketing approval by the agency. In addition, the FDA may later decide that the products no longer meet the applicable conditions for qualification as either a fast track product, RMAT, or a breakthrough therapy or, for priority review products, decide that the period for FDA review or approval will not be shortened.

We may not be successful in our efforts to use our gene therapy technology platform to build a pipeline of additional product candidates.

An element of our strategy is to use our gene therapy technology platform to expand our product pipeline and to progress these candidates through preclinical and clinical development ourselves or together with collaborators. Although we currently have a pipeline of programs at various stages of development, we may not be able to identify or develop product candidates that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. Research programs to identify new product candidates require substantial technical, financial, and human resources. We or any collaborators may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. If we do not continue to successfully develop and commercialize product candidates based upon our technology, we may face difficulty in obtaining product revenues in future periods, which could result in significant harm to our business, results of operations and financial position and materially adversely affect our share price.

Our strategy of obtaining rights to key technologies through in-licenses may not be successful.

We seek to expand our product pipeline from time to time in part by in-licensing the rights to key technologies, including those related to gene delivery, genes, and gene cassettes. The future growth of our business will depend in significant part on our ability to in-license or otherwise acquire the rights to additional product candidates or technologies, particularly through our collaborations with academic research institutions. However, we may be unable to in-license or acquire the rights to any such product candidates or technologies from third parties on acceptable terms or at all. The in-licensing and acquisition of these technologies is a competitive area, and many more established companies are also pursuing strategies to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be competitors may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our areas of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition, and prospects could suffer.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain marketing approvals for our product candidates.

Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. The risk of cancer remains a concern for gene therapy, and we cannot assure that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material.

A small number of patients have experienced serious adverse events during our clinical trials of either AMT-060 (our first-generation hemophilia B gene therapy) or etranacogene dezaparvovec. In each instance of a serious adverse event, whether or not attributed to one of our product candidates, the issues resolved without delay in the respective clinical trial. However, adverse events in our clinical trials or those conducted by other parties (even if not ultimately attributable to our product candidates), and the resulting publicity, could result in delay, a hold or termination of our clinical trials, increased governmental regulation, unfavorable public perception, failure of the medical community to accept and prescribe gene therapy treatments, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. If any of these events should occur, it may have a material adverse effect on our business, financial condition and results of operations.

Certain of our product candidates may require medical devices for product administration and/or diagnostics, resulting in our product candidates being deemed combination products. This may result in the need to comply with additional regulatory requirements. If we are unable to meet these regulatory requirements, we may be delayed or not be able to obtain product approval.

Certain of our product candidates, such as AMT-130, require medical devices, such as a stereotactic, magnetic resonance imaging guided catheter, for product administration. Other of our product candidates may also require the use of a companion diagnostic device to confirm the presence of specific genetic or other biomarkers. This may result in our product candidates being deemed to be combination products, potentially necessitating compliance with the FDA's investigational device regulations, separate marketing application submissions for the medical device component, a demonstration that our product candidates are safe and effective when used in combination with the medical devices, cross labeling with the medical device, and compliance with certain of the FDA's device regulations. If we are not able to comply with the FDA's device regulations, if we are not able to effectively partner with the applicable medical device manufacturers, if we or any partners are not able to obtain any required FDA clearances or approvals of the applicable medical devices, or if we are not able to demonstrate that our product candidates are safe and efficacious when used with the applicable medical devices, we may be delayed in or may never obtain FDA approval for our product candidates, which would materially harm our business.

Moreover, certain of our delivery modalities, such as direct delivery of product candidates to the brain, may require significant physician ability and skill. If physicians are not able to effectively deliver our product candidates to the applicable site of action or if delivery modalities are too difficult, we may never be able to obtain approval for our product candidates, may be delayed in obtaining approval, or, following approval, physicians may not adopt our product candidates, any of which may materially harm our business.

Risks Related to Our Manufacturing

Our manufacturing facility is subject to significant government regulations and approvals. If we fail to comply with these regulations or maintain these approvals our business will be materially harmed.

Our manufacturing facility in Lexington is subject to ongoing regulation and periodic inspection by the FDA, EMA, and other regulatory bodies to ensure compliance with current cGMP. Moreover, before approving a BLA for any product candidate, the FDA will inspect our manufacturing facility and processes. Any failure to follow and document our adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical study, may result in the termination of or a hold on a clinical study, or may delay or prevent filing or approval of marketing applications for our products.

Failure to comply with applicable regulations could also result in the FDA, EMA, or other applicable authorities taking various actions, including levying fines and other civil penalties; imposing consent decrees or injunctions; requiring us to suspend or put on hold one or more of our clinical trials; suspending or withdrawing regulatory approvals; delaying or refusing to approve pending applications or supplements to approved applications; requiring us to suspend manufacturing activities or product sales, imports or exports; requiring us to communicate with physicians and other customers about concerns related to actual or potential safety, efficacy, and other issues involving our products; mandating or recommending product recalls or seizing products; imposing operating restrictions; and seeking criminal prosecutions, among other outcomes. Poor control of production processes can also lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of a product candidate that may not be detectable in final product testing and that could have an adverse effect on clinical studies, or patient safety or efficacy. Moreover, if our manufacturing facility is not able to follow regulatory requirements, we may need to implement costly and time-consuming remedial actions. Any of the foregoing could materially harm our business, financial condition, and results of operations.

Moreover, if we are not able to manufacture a sufficient amount of our product candidates for clinical studies or eventual commercialization, our development program and eventual commercial prospects will be harmed. If we cannot produce an adequate amount of our product candidates in compliance with the applicable regulatory requirements, we may need to contract with a third party to do so, in which case third party manufacturers may not be available or available on favorable terms. The addition of a new manufacturer may also require FDA approvals, which we may not be able to obtain.

Gene therapies are complex and difficult to manufacture. We could experience capacity, production or technology transfer problems that result in delays in our development or commercialization schedules or otherwise adversely affect our business.

The insect-cell based manufacturing process we use to produce our products and product candidates is highly complex and in the normal course is subject to variation or production difficulties. Issues with any of our manufacturing processes, even minor deviations from the normal process, could result in insufficient yield, product deficiencies or manufacturing failures that result in adverse patient reactions, lot failures, insufficient inventory, product recalls and product liability claims. Additionally, we may not be able to scale up some or all of our manufacturing processes that may result in delays in regulatory approvals or otherwise adversely affect our ability to manufacture sufficient amounts of our products.

Many factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or cases of force majeure and acts of god (including the effects of the COVID-19 pandemic) beyond our control. We also may encounter problems in hiring and retaining the experienced specialized personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing processes or facilities could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs, result in delays in our clinical development or marketing schedules and materially harm our business.

Our use of viruses, chemicals and other hazardous materials requires us to comply with regulatory requirements and exposes us to significant potential liabilities.

Our development and manufacturing processes involve the use of viruses, chemicals, other (potentially) hazardous materials and produce waste products. Accordingly, we are subject to national, federal, state, and local laws and regulations in the United States and the Netherlands governing the use, manufacture, distribution, storage, handling, treatment, and disposal of these materials. In addition to ensuring the safe handling of these materials, applicable requirements require increased safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for damages that result, and any such liability could exceed our assets and resources, and could result in material harm to our business, financial condition, and results of operations.

Our resources might be adversely affected if we are unable to validate our manufacturing processes or develop new processes to meet our product supply needs and obligations.

The manufacture of our AAV gene therapies, including etranacogene dezaparvovec, is complex and requires significant expertise. Even with the relevant experience and expertise, manufacturers of gene therapy products often encounter difficulties in production, particularly in scaling out and validating initial production, and ensuring that the product meets required specifications. These problems include difficulties with production costs and yields, quality control, including stability and potency of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. In the past, we have manufactured certain batches of etranacogene dezaparvovec, and other product candidates, intended for nonclinical, clinical and process validation purposes that have not met all of our pre-specified quality parameters. To meet our expected future production needs and our regulatory filing timelines for etranacogene dezaparvovec, as well as other gene therapy product candidates, we will need to complete the validation of our existing manufacturing processes as well as to develop larger scale manufacturing processes. If we are unable to consistently manufacture etranacogene dezaparvovec, or other gene therapy product candidates, in accordance with our pre-specified quality parameters and applicable regulatory standards, it could adversely impact our ability to validate our manufacturing processes, to meet our production needs, to file our BLA or other regulatory submissions, to develop our other proprietary programs, to conserve our cash, or to receive financial payments pursuant to our agreements with third parties, including with CSL Behring in return for supplying etranacogene dezaparvovec following regulatory approval.

Risks Related to Regulatory Approval of Our Products

We cannot predict when or if we will obtain marketing approval to commercialize a product candidate.

The development and commercialization of our product candidates, including their design, testing, manufacture, safety, efficacy, purity, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States, the EMA, and other regulatory agencies of the member states of the European Union, and similar regulatory authorities in other jurisdictions. Failure to obtain marketing approval for a product candidate in a specific jurisdiction will prevent us from commercializing the product candidate in that jurisdiction.

The process of obtaining marketing approval for our product candidates in the United States, the European Union, and other countries is expensive and may take many years, if approval is obtained at all. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application, may decide that our data are insufficient for approval, may require additional preclinical, clinical, or other studies and may not complete their review in a timely manner. Further, any marketing approval we ultimately obtain may be for only limited indications or be subject to stringent labeling or other restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining marketing approval for any of our product candidates in the United States, the European Union, or other countries, the commercial prospects of our other product candidates may be harmed and our ability to generate revenues will be materially impaired.

The risks associated with the marketing approval process are heightened by the status of our products as gene therapies.

We believe that all our current product candidates will be viewed as gene therapy products by the applicable regulatory authorities. While there are a number of gene therapy product candidates under development, in the United States, the FDA has only approved a limited number of gene therapy products, to date. Accordingly, regulators, like the FDA, may have limited experience with the review and approval of marketing applications for gene therapy products.

Both the FDA and the EMA have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates that are difficult to predict. The FDA and the EMA have issued various guidance documents pertaining to gene therapy products, with which we likely must comply to gain regulatory approval of any of our product candidates in the United States or European Union, respectively. The close regulatory scrutiny of gene therapy products may result in delays and increased costs and may ultimately lead to the failure to obtain approval for any gene therapy product.

Regulatory requirements affecting gene therapy have changed frequently and continue to evolve, and agencies at both the U.S. federal and state level, as well as congressional committees and foreign governments, have sometimes expressed interest in further regulating biotechnology. In the United States, there have been a number of recent changes relating to gene therapy development. By example, FDA issued a number of new guidance documents on human gene therapy development, one of which was specific to human gene therapy for hemophilia and another of which was specific to rare diseases. Moreover, the European Commission conducted a public consultation in early 2013 on the application of EU legislation that governs advanced therapy medicinal products, including gene therapy products, which could result in changes in the data we need to submit to the EMA for our product candidates to gain regulatory approval or change the requirements for tracking, handling and distribution of the products which may be associated with increased costs. In addition, divergent scientific opinions among the various bodies involved in the review process may result in delays, require additional resources, and ultimately result in rejection. The FDA, EMA, and other regulatory authorities will likely continue to revise and further update their approaches to gene therapies in the coming years. These regulatory agencies, committees and advisory groups and the new regulations and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenues to maintain our business.

Our failure to obtain or maintain orphan product exclusivity for any of our product candidates for which we seek this status could limit our commercial opportunity, and if our competitors are able to obtain orphan product exclusivity before we do, we may not be able to obtain approval for our competing products for a significant period.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. While certain of our product candidates have received orphan drug designation, there is no guarantee that we will be able to receive such designations in the future. The FDA may grant orphan designation to multiple sponsors for the same compound or active molecule and for the same indication. If another sponsor receives FDA approval for such product before we do, we would be prevented from launching our product in the United States for the orphan indication for a period of at least seven years unless we can demonstrate clinical superiority.

Moreover, while orphan drug designation neither shortens the development or regulatory review time, nor gives the product candidate advantages in the regulatory review or approval process, generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the relevant indication, the product is entitled to a period of market exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication for that period. The FDA and the EMA, however, may subsequently approve a similar drug or same drug, in the case of the United States, for the same indication during the first product's market exclusivity period if the FDA or the EMA concludes that the later drug is clinically superior in that it is shown to be safer or more effective or makes a major contribution to patient care. Orphan exclusivity in the United States also does not prevent the FDA from approving another product that is considered to be the same as our product candidates for a different indication or a different product for the same orphan indication. If another product that is the same as ours is approved for a different indication, it is possible that third-party payors will reimburse for products off-label even if not indicated for the orphan condition.

Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if the incidence and prevalence of patients who are eligible to receive the drug in these markets materially increase. The inability to obtain or failure to maintain adequate product exclusivity for our product candidates could have a material adverse effect on our business prospects, results of operations and financial condition.

Additionally, regulatory criteria with respect to orphan products is evolving, especially in the area of gene therapy. By example, in the United States, whether two gene therapies are considered to be the same for the purpose of determining clinical superiority is subject to change, and depends on a number of factors, including the expressed transgene, the vector, and other product or product candidate features. Accordingly, whether any of our product candidates will be deemed to be the same as another product or product candidate is uncertain.

As appropriate, we intend to seek all available periods of regulatory exclusivity for our product candidates. However, there is no guarantee that we will be granted these periods of regulatory exclusivity or that we will be able to maintain these periods of exclusivity.

The FDA grants product sponsors certain periods of regulatory exclusivity, during which the agency may not approve, and in certain instances, may not accept, certain marketing applications for competing drugs. For example, biologic product sponsors may be eligible for twelve years of exclusivity from the date of approval, seven years of exclusivity for drugs that are designated to be orphan drugs, and/or a six-month period of exclusivity added to any existing exclusivity period for the submission of FDA requested pediatric data. While we intend to apply for all periods of market exclusivity that we may be eligible for, there is no guarantee that we will be granted any such periods of market exclusivity. By example, regulatory authorities may determine that our product candidates are not eligible for periods of regulatory exclusivity for various reasons, including a determination by the FDA that a BLA approval does not constitute a first licensure of the product. Additionally, under certain circumstances, the FDA may revoke the period of market exclusivity. Thus, there is no guarantee that we will be able to maintain a period of market exclusivity, even if granted. In the case of orphan designation, other benefits, such as tax credits and exemption from user fees may be available. If we are not able to obtain or maintain orphan drug designation or any period of market exclusivity to which we may be entitled, we could be materially harmed, as we will potentially be subject to greater market competition and may lose the benefits associated with programs. It is also possible that periods of exclusivity will not adequately protect our product candidates from competition. For instance, even if we receive twelve years of exclusivity from the FDA, other applicants will still be able to submit and receive approvals for versions of our product candidates through a full BLA.

If we do not obtain or maintain periods of market exclusivity, we may face competition sooner than otherwise anticipated. For instance, in the United States, this could mean that a competing biosimilar product may be able to submit an application to the FDA and obtain approval. This may require that we undertake costly and time-consuming patent litigation, to the extent available, or defend actions brought by the biosimilar applicant for declaratory judgement. If a biosimilar product does enter the market, it is possible that it could be substituted for one of our product candidates, especially if it is available at a lower price.

It is also possible that, at the time we obtain approval of our product candidates, regulatory laws and policies around exclusivities may have changed. For instance, there have been efforts to decrease the United States period of exclusivity to a shorter timeframe. Future proposed budgets, international trade agreements and other arrangements or proposals may affect periods of exclusivity.

Risks Related to Commercialization

If we are unable to successfully commercialize our product candidates or experience significant delays in doing so, our business could be materially harmed.

Our ability to generate product revenues will depend on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on many factors, including:

- successful execution of our contractual relationship with CSL Behring for the commercialization of etranacogene dezaparvovec;
- successful completion of preclinical studies and clinical trials, and other work required by regulators;
- receipt and maintenance of marketing approvals from applicable regulatory authorities;
- our ability to timely manufacture sufficient quantities of our products according to required quality specifications;

- obtaining and maintaining patent and trade secret protection and non-patent, orphan drug exclusivity for our product candidates;
- obtaining and maintaining regulatory approvals using our manufacturing facility in Lexington, Massachusetts;
- launch and commercialization of our products, if approved, whether alone or in collaboration with others;
- identifying and engaging effective distributors or resellers on acceptable terms in jurisdictions where we plan to utilize third parties for the marketing and sales of our product candidates;
- acceptance of our products, if approved, by patients, the medical community, and third-party payers;
- effectively competing with existing therapies and gene therapies based on safety and efficacy profiles;
- the strength of our marketing and distribution;
- achieve optimal pricing based on durability of expression, safety, and efficacy;
- the ultimate content of the regulatory authority approved label, including the approved clinical indications, and any limitations or warnings;
- any distribution or use restrictions imposed by regulatory authorities;
- the interaction of our products with any other medicines that patients may be taking or the restriction on the use of our products with other medicines;
- the standard of care at the time of product approval;
- the relative convenience and ease of administration of our products;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- any price concessions, rebates, or discounts we may need to provide;
- complying with any applicable post-approval requirements and maintaining a continued acceptable overall safety profile; and
- obtaining adequate reimbursement for the total patient population and each subgroup to sustain a viable commercial business model in U.S. and EU markets.

By example, even if our product candidates are approved, they may be subject to limitations that make commercialization difficult. There may be limitations on the indicated uses and populations for which the products may be marketed. They may also be subject to other conditions of approval, may contain significant safety warnings, including boxed warnings, contraindications, and precautions, may not be approved with label statements necessary or desirable for successful commercialization, or may contain requirements for costly post-market testing and surveillance, or other requirements, including the submission of a risk evaluation and mitigation strategy, or REMS, to monitor the safety or efficacy of the products. Failure to achieve or implement any of the above elements could result in significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business.

The affected populations for our gene therapies may be smaller than we or third parties currently project, which may affect the size of our addressable markets.

Our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our therapies, are estimates based on our knowledge and understanding of these diseases. The total addressable market opportunities for these therapies will ultimately depend upon many factors, including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient consent, patient access and product pricing and reimbursement.

Prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative. The use of such data involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of the diseases we seek to address. The number of patients with the diseases we are targeting may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, reimbursement may not be sufficient to sustain a viable business for all sub populations being studied, or new patients may become increasingly difficult to identify or access, any of which could adversely affect our results of operations and our business.

The addressable markets for AAV-based gene therapies may be impacted by the prevalence of neutralizing antibodies to the capsids, which are an integral component of our gene therapy constructs. Patients that have pre-existing antibodies to a particular capsid may not be eligible for administration of a gene therapy that includes this particular capsid. For example, etranacogene dezaparvovec, our gene therapy candidate for hemophilia B patients, incorporates an AAV5 capsid. In our Phase I/II clinical study of AMT-060, we screened patients for pre-existing anti-AAV5 antibodies to determine their eligibility for the trial. Three of the ten patients screened for the study tested positive for anti-AAV5 antibodies on reanalysis. Although we did not observe any ill-effects or correlation between the level of anti-AAV5 antibodies and clinical outcomes in these three patients, suggesting that patients who have anti-AAV5 antibodies may still be eligible for AAV5-based gene therapies, since we only have been able to test a limited number of patients and have limited clinical and pre-clinical data, we do not know if future clinical studies will confirm these results. This may limit the addressable market for etranacogene dezaparvovec and any future revenues derived from the sale of the product, if approved.

Any approved gene therapy we seek to offer may fail to achieve the degree of market acceptance by physicians, patients, third party payers and others in the medical community necessary for commercial success.

Doctors may be reluctant to accept a gene therapy as a treatment option or, where available, choose to continue to rely on existing treatments. The degree of market acceptance of any of our product candidates that receive marketing approval in the future will depend on many factors, including:

- the efficacy and potential advantages of our therapies compared with alternative treatments;
- our ability to convince payers of the long-term cost-effectiveness of our therapies and, consequently, the availability of third-party coverage and adequate reimbursement;
- the cost of treatment with gene therapies, including ours, in comparison to traditional chemical and small-molecule treatments;
- the limitations on use and label requirements imposed by regulators;
- the convenience and ease of administration of our gene therapies compared with alternative treatments;
- the willingness of the target patient population to try new therapies, especially a gene therapy, and of physicians to administer these therapies;
- the strength of marketing and distribution support;
- the prevalence and severity of any side effects;
- limited access to site of service that can perform the product preparation and administer the infusion; and
- any restrictions by regulators on the use of our products.

A failure to gain market acceptance for any of the above reasons, or any reasons at all, by a gene therapy for which we receive regulatory approval would likely hinder our ability to recapture our substantial investments in that and other gene therapies and could have a material adverse effect on our business, financial condition, and results of operation.

If we are unable to expand our commercialization capabilities or enter into agreements with third parties to market and sell any of our product candidates for which we obtain marketing approval, we may be unable to generate any product revenue.

To successfully commercialize any products that may result from our development programs, we need to continue to expand our commercialization capabilities, either on our own or with others. The development of our own market development effort is, and will continue to be, expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability.

We may enter into collaborations regarding our other product candidates with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current or future collaborators do not commit sufficient resources to commercialize our products, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded medical affairs, marketing, and sales operations to recruit, hire, train and retain marketing and sales personnel. We also may face competition in any search for third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected, and our business may suffer.

We focus our research and product development on treatments for severe genetic and orphan diseases. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, the EU and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, any of which could adversely affect our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive other potential products less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets. Further, the severity of the progression of a disease up to the time of treatment, especially in certain degenerative conditions, could diminish the therapeutic benefit conferred by a gene therapy. Lastly, certain patients' immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes.

Our gene therapy approach utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product and product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product and product candidates, if approved, prescribing treatments that involve the use of our product and product candidates, if approved, in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in other trials using other vectors. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any products for which we obtain marketing approval.

Ethical, legal, and social issues may reduce demand for any gene therapy products for which we obtain marketing approval.

Prior to receiving certain gene therapies, patients may be required to undergo genetic testing. Genetic testing has raised concerns regarding the appropriate utilization and the confidentiality of information provided by genetic testing. Genetic tests for assessing a person's likelihood of developing a chronic disease have focused public attention on the need to protect the privacy of genetic information. For example, concerns have been expressed that insurance carriers and employers may use these tests to discriminate on the basis of genetic information, resulting in barriers to the acceptance of genetic tests by consumers. This could lead to governmental authorities restricting genetic testing or calling for limits on or regulating the use of genetic testing, particularly for diseases for which there is no known cure. Any of these scenarios could decrease demand for any products for which we obtain marketing approval.

If we obtain approval to commercialize any of our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates outside the United States, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements which may make it more difficult or expensive to export or import products and supplies to or from the United States;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods, and fires.

We face substantial competition, and others may discover, develop, or commercialize competing products before or more successfully than we do.

The development and commercialization of new biotechnology and biopharmaceutical products, including gene therapies, is highly competitive. We may face intense competition with respect to our product candidates, as well as with respect to any product candidates that we may seek to develop or commercialize in the future, from large and specialty pharmaceutical companies and biotechnology companies worldwide, who currently market and sell products or are pursuing the development of products for the treatment of many of the disease indications for which we are developing our product candidates. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. In recent years, there has been a significant increase in commercial and scientific interest and financial investment in gene therapy as a therapeutic approach, which has intensified the competition in this area.

We are aware of numerous companies focused on developing gene therapies in various indications, including Applied Genetic Technologies Corp., Abbvie, Abeona Therapeutics, Adverum Biotechnologies, Ally Therapeutics, Apic Bio, Asklepios BioPharmaceutical, Astellas, AVROBIO, Bayer, Biogen, BioMarin, bluebird bio, CRISPR Therapeutics, Editas Medicine, Expression Therapeutics, Fate, Freeline Therapeutics, Generation Bio, Genethon, GlaxoSmithKline, Homology Medicines, Intellia Therapeutics, Johnson & Johnson, Krystal Biotech, Lexeo Therapeutics, LogicBio Therapeutics, Lysogene, MeiraGTx, Milo Biotechnology, Mustang Bio, Novartis, Orchard Therapeutics, Oxford Biomedica, Passage Bio, Pfizer, REGENXBIO, Renova Therapeutics, Roche, Rocket Pharmaceuticals, Sangamo Therapeutics, Sanofi, Selecta Biosciences, Sarepta Therapeutics, Sio Therapeutics, Solid Biosciences, SwanBio, Takeda, Taysha Gene Therapies, Ultragenyx, Vivet Therapeutics, and Voyager Therapeutics, as well as several companies addressing other methods for modifying genes and regulating gene expression. We may also face competition with respect to the treatment of some of the diseases that we are seeking to target with our gene therapies from protein, nucleic acid, antisense, RNAi and other pharmaceuticals under development or commercialized at pharmaceutical and biotechnology companies such as Alnylam Pharmaceuticals, Bayer, BioMarin, CSL Behring, Dicerna Pharmaceuticals, Ionis Pharmaceuticals, Novartis, Novo Nordisk, Pfizer, Translate Bio, Roche, Sanofi, Sobi, Takeda, WaVe Life Sciences, and numerous other pharmaceutical and biotechnology firms.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than the products that we develop. Our competitors also may obtain FDA, EMA, or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market. A competitor approval may also prevent us from entering the market if the competitor receives any regulatory exclusivities that block our product candidates. Because we expect that gene therapy patients may generally require only a single administration, we believe that the first gene therapy product to enter the market for a particular indication will likely enjoy a significant commercial advantage and may also obtain market exclusivity under applicable orphan drug regimes.

Many of the companies with which we are competing or may compete in the future have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed and, as a result, our stock price may decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, or development milestones. These development milestones may include the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings, and approval for commercial sale. From time to time, we publicly announce the expected timing of some of these milestones. All these milestones are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones, including those that are publicly announced, the commercialization of our products may be delayed and, as a result, our stock price may decline.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct, supervise, and monitor our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or failing to comply with regulatory requirements.

We rely on third parties, study sites, and others to conduct, supervise, and monitor our preclinical and clinical trials for our product candidates and do not currently plan to independently conduct clinical or preclinical trials of any other potential product candidates. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical and scientific institutions, and clinical and preclinical investigators, to conduct our preclinical studies and clinical trials.

While we have agreements governing the activities of such third parties, we have limited influence and control over their actual performance and activities. For instance, our third-party service providers are not our employees, and except for remedies available to us under our agreements with such third parties we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non-clinical, and preclinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, our trials may be repeated, extended, delayed, or terminated, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates, we may not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates, or we or they may be subject to regulatory enforcement actions. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be materially and adversely affected. Our third-party service providers may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting trials or other therapeutic development activities that could harm our competitive position.

Our reliance on these third-parties for development activities will reduce our control over these activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our trials is conducted in accordance with the general investigational plan and protocols for the trial. We must also ensure that our preclinical trials are conducted in accordance with GLPs, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with GCPs for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical and preclinical investigators, and trial sites. If we or any of our third-party service providers fail to comply with applicable GCPs or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the data generated in our trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional studies.

In addition, we will be required to report certain financial interests of our third-party investigators if these relationships exceed certain financial thresholds or meet other criteria. The FDA or comparable foreign regulatory authorities may question the integrity of the data from those clinical trials conducted by investigators who may have conflicts of interest.

We cannot assure that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our trials complies with the applicable regulatory requirements. In addition, our clinical trials must be conducted with product candidates that were produced under GMP conditions. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register certain clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in enforcement actions and adverse publicity.

Agreements with third parties conducting or otherwise assisting with our clinical or preclinical studies might terminate for a variety of reasons, including a failure to perform by the third parties. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative providers or to do so on commercially reasonable terms. Switching or adding additional third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, if we need to enter into alternative arrangements, it could delay our product development activities and adversely affect our business. Though we carefully manage our relationships with our third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects, and results of operations.

We also rely on other third parties to store and distribute our products for the clinical and preclinical trials that we conduct. Any performance failure on the part of our distributors could delay development, marketing approval, or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue.

We rely on third parties for important aspects of our development programs. If these parties do not perform successfully or if we are unable to enter into or maintain key collaboration or other contractual arrangements, our business could be adversely affected.

We have in the past entered into, and expect in the future to enter into, collaborations with other companies and academic research institutions with respect to important elements of our development programs.

Any collaboration may pose several risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- we may have limited or no control over the design or conduct of clinical trials sponsored by collaborators;
- we may be hampered from entering into collaboration arrangements if we are unable to obtain consent from our licensors to enter into sublicensing arrangements of technology we have in-licensed;
- if any collaborator does not conduct the clinical trials they sponsor in accordance with regulatory requirements or stated protocols, we will not be able to rely on the data produced in such trials in our further development efforts;
- collaborators may not perform their obligations as expected;
- collaborators may also have relationships with other entities, some of which may be our competitors;

- collaborators may not pursue development and commercialization of any product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could develop, independently or with third parties, products that compete directly or indirectly with our products or product candidates, if, for instance, the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- our collaboration arrangements may impose restrictions on our ability to undertake other development efforts that may appear to be attractive to us;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights that achieves regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including over proprietary rights, contract interpretation or the preferred course of development, could cause delays or termination of the research, development or commercialization of product candidates, lead to additional responsibilities for us, delay or impede reimbursement of certain expenses or result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our rights or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may in some cases be terminated for the convenience of the collaborator and, if terminated, we could be required to expend additional funds to pursue further development or commercialization of the applicable product or product candidates.

If any collaboration does not result in the successful development and commercialization of products or if a collaborator were to terminate an agreement with us, we may not receive future research funding or milestone or royalty payments under that collaboration, and we may lose access to important technologies and capabilities of the collaboration. All the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of any development collaborators.

Risks Related to Our Intellectual Property

We rely on licenses of intellectual property from third parties, and such licenses may not provide adequate rights or may not be available in the future on commercially reasonable terms or at all, and our licensors may be unable to obtain and maintain patent protection for the technology or products that we license from them.

We currently are heavily reliant upon licenses of proprietary technology from third parties that is important or necessary to the development of our technology and products, including technology related to our manufacturing process, our vector platform, our gene cassettes and the therapeutic genes of interest we are using. These and other licenses may not provide adequate rights to use such technology in all relevant fields of use. Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

The agreements under which we license intellectual property or technology 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 and financial condition.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose rights that are important to our business.

Our licensing arrangements with third parties may impose diligence, development and commercialization timelines, milestone payment, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, our counterparties may have the right to terminate these agreements either in part or in whole, in which case we might not be able to develop, manufacture or market any product that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or amended agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our ability to successfully commercialize our products may be impaired.

We rely, in part, upon a combination of forms of intellectual property, including in-licensed and owned patents to protect our intellectual property. Our success depends in a large part on our ability to obtain and maintain this protection in the United States, the European Union, and other countries, in part by filing patent applications related to our novel technologies and product candidates. Our patents may not provide us with any meaningful commercial protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. For example, patents we own currently are and may become subject to future patent opposition or similar proceedings, which may result in loss of scope of some claims or the entire patent. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

Successful challenges to our patents may result in loss of exclusivity or freedom to operate 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.

The patent prosecution process is expensive, time-consuming, and uncertain, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Additionally, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, EU patent law with respect to the patentability of methods of treatment of the human body is more limited than U.S. law. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after their priority date, or in some cases at all. Therefore, we cannot know with certainty whether we were the first to make the inventions or that we were the first to file for patent protection of the inventions claimed in our owned or licensed patents or pending patent applications. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the European Union, the United States or other countries may diminish the value of our patents or narrow the scope of our patent protection. Our inability to obtain and maintain appropriate patent protection for any one of our products could have a material adverse effect on our business, financial condition, and results of operations.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, or third parties may assert their intellectual property rights against us, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our owned or licensed patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, maintained in more narrowly amended form or interpreted narrowly.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, increase our operating losses, reduce available resources, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have an adverse effect on the price of our ordinary shares.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. For example, outside of the United States two of the patents we own are subject to patent opposition. If these or future oppositions are successful or if we are found to otherwise infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. We may not be able to obtain the required license on commercially reasonable terms or at all. Even if we could obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product or otherwise to cease using the relevant intellectual property. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease or materially modify some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

For example, we are aware of patents owned by third parties that relate to some aspects of our programs that are still in development. In some cases, because we have not determined the final methods of manufacture, the method of administration or the therapeutic compositions for these programs, we cannot determine whether rights under such third-party patents will be needed. In addition, in some cases, we believe that the claims of these patents are invalid or not infringed or will expire before commercialization. However, if such patents are needed and found to be valid and infringed, we could be required to obtain licenses, which might not be available on commercially reasonable terms, or to cease or delay commercializing certain product candidates, or to change our programs to avoid infringement.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.

In addition to seeking patent protection, we also rely on other proprietary rights, including protection of trade secrets, know-how and confidential and proprietary information. To maintain the confidentiality of our trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, collaborators and other third parties who have access to our trade secrets. Our agreements with employees also provide that any inventions conceived by the individual while rendering services to us will be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. 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. In addition, in the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants, or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our confidential information including a breach of our confidentiality agreements. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable. In addition, some courts in and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. The disclosure of our trade secrets or the independent development of our trade secrets by a competitor or other third party would impair our competitive position and may materially harm our business, financial condition, results of operations, stock price and prospects.

Our reliance on third parties may require us to share our trade secrets, which could increase the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we collaborate from time to time with various organizations and academic research institutions on the advancement of our gene therapy platform, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, materials transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, if we are notified in advance and may delay publication for a specified time to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements.

Some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those with whom they communicate, from using that technology or information to compete with us.

Risks Related to Pricing and Reimbursement

We face uncertainty related to insurance coverage of, and pricing and reimbursement for product candidates for which we may receive marketing approval.

We anticipate that the cost of treatment using our product candidates will be significant. We expect that most patients and their families will not be capable of paying for our products themselves. There will be no commercially viable market for our product candidates without reimbursement from third party payers, such as government health administration authorities, private health insurers and other organizations. Even if there is a commercially viable market, if the level of third-party reimbursement is below our expectations, most patients may not be able to afford treatment with our products and our revenues and gross margins will be adversely affected, and our business will be harmed.

Government authorities and other third-party payers, such as private health insurers and health maintenance organizations, decide for which medications they will pay and, subsequently, establish reimbursement levels. Reimbursement systems vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. Government authorities and third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and procedures and negotiating or requiring payment of manufacturer rebates. Increasingly, third party payers require drug companies to provide them with predetermined discounts from list prices, are exerting influence on decisions regarding the use of particular treatments and are limiting covered indications. Additionally, in the United States and some foreign jurisdictions, pending or potential legislative and regulatory changes regarding the healthcare system and insurance coverage could result in more rigorous coverage criteria and downward pressure on drug prices, and may affect our ability to profitably sell any products for which we obtain marketing approval. For example, on November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation payment model under which reimbursement for certain Medicare Part B drugs and biologicals will be based on a price that reflects the lowest per capita GDP-adjusted price of any non-U.S. member country of the OECD with a GDP per capita that is at least sixty percent of the U.S. GDP per capita.

The pricing review period and pricing negotiations for new medicines take considerable time and have uncertain results. Pricing review and negotiation usually begins only after the receipt of regulatory marketing approval, and some authorities require approval of the sale price of a product before it can be marketed. In some markets, particularly the countries of the European Union, prescription pharmaceutical pricing remains subject to continuing direct governmental control and to drug reimbursement programs even after initial approval is granted and price reductions may be imposed. Prices of medical products may also be subject to varying price control mechanisms or limitations as part of national health systems if products are considered not cost-effective or where a drug company's profits are deemed excessive. In addition, pricing and reimbursement decisions in certain countries can lead to mandatory price reductions or additional reimbursement restrictions in other countries. Because of these restrictions, any product candidates for which we may obtain marketing approval may be subject to price regulations that delay or prohibit our or our partners' commercial launch of the product in a particular jurisdiction. In addition, we or any collaborator may elect to reduce the price of our products to increase the likelihood of obtaining reimbursement approvals. If countries impose prices, which are not sufficient to allow us or any collaborator to generate a profit, we or any collaborator may refuse to launch the product in such countries or withdraw the product from the market. If pricing is set at unsatisfactory levels, or if the price decreases, our business could be harmed, possibly materially. If we fail to obtain and sustain an adequate level of coverage and reimbursement for our products by third party payers, our ability to market and sell our products could be adversely affected and our business could be harmed.

Due to the generally limited addressable market for our target orphan indications and the potential for our therapies to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

The relatively small market size for orphan indications and the potential for long-term therapeutic benefit from a single administration present challenges to pricing review and negotiation of our product candidates for which we may obtain marketing authorization. Most of our product candidates target rare diseases with relatively small patient populations. If we are unable to obtain adequate levels of reimbursement relative to these small markets, our ability to support our development and commercial infrastructure and to successfully market and sell our product candidates for which we may obtain marketing approval could be adversely affected.

We also anticipate that many or all our gene therapy product candidates may provide long-term, and potentially curative benefit, with a single administration. This is a different paradigm than that of other pharmaceutical therapies, which often require an extended course of treatment or frequent administration. As a result, governments and other payers may be reluctant to provide the significant level of reimbursement that we seek at the time of administration of our gene therapies or may seek to tie reimbursement to clinical evidence of continuing therapeutic benefit over time. Additionally, there may be situations in which our product candidates will need to be administered more than once, which may further complicate the pricing and reimbursement for these treatments. In addition, considering the anticipated cost of these therapies, governments and other payers may be particularly restrictive in making coverage decisions. These factors could limit our commercial success and materially harm our business.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses to date, expect to incur losses over the next several years and may never achieve or maintain profitability.

We had a net loss of $41.6 million in the three months ended March 31, 2021, $125.0 in the full year 2020 and $124.2 million in the full year 2019. As of March 31, 2021, we had an accumulated deficit of $826.3 million. To date, we have financed our operations primarily through the sale of equity securities and convertible debt, venture loans, upfront payments from our collaboration partners and, to a lesser extent, subsidies and grants from governmental agencies and fees for services. We have devoted substantially all our financial resources and efforts to research and development, including preclinical studies and clinical trials. We expect to continue to incur significant expenses and losses over the next several years, and our net losses may fluctuate significantly from quarter to quarter and year to year. Our losses will be materially impacted by the amount of license revenue that we will recognize in accordance with ASC 606 as a result of the closing of the transaction under the CSL Behring Agreement, which became fully effective on May 6, 2021.

We anticipate that our expenses will increase substantially as we:

- Advance the clinical development of AMT-130, our Huntington's disease gene therapy program;
- Advance multiple research programs related to gene therapy candidates targeting liver-directed and CNS diseases;
- Acquire or in-license rights to new therapeutic targets or product candidates;
- Continue to expand, enhance, and optimize our technology platform, including our manufacturing capabilities, next-generation viral vectors and promoters, and other enabling technologies;
- Continue to expand our employee base to support research and development, as well as general and administrative functions;
- Maintain, expand, and protect our intellectual property portfolio, including in-licensing additional intellectual property rights from third parties; and
- Build out our commercial and medical affairs infrastructure and seek marketing approval for any product candidates.

We may never succeed in these activities and, even if we do, may never generate revenues that are sufficient to achieve or sustain profitability. Our failure to become and remain profitable would depress the value of our company and could impair our ability to expand our business, maintain our research and development efforts, diversify our product offerings, or even continue our operations.

We will likely need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations which could have a material adverse effect on our business, financial condition, results of operations and cash flows.

We expect to incur significant expenses in connection with our on-going activities and that we will likely need to obtain substantial additional funding in connection with our continuing operations. In addition, we have based our estimate of our financing requirements on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Adequate capital may not be available to us when needed or may not be available on acceptable terms. Our ability to obtain debt financing may be limited by covenants we have made the 2018 Amended Facility and our 2021 Amended Facility with Hercules and our pledge to Hercules of substantially all our assets as collateral. If we raise additional capital through the sale of equity or convertible debt securities, our shareholders' ownership interest could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our ordinary shares.

If we raise additional funds through collaborations, strategic alliances, or marketing, distribution, or licensing arrangements with third parties, we may have to issue additional equity, relinquish valuable rights to our technologies, future revenue streams, products, or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce, or eliminate our research and development programs or any future commercialization efforts, which would have a negative impact on our financial condition, results of operations and cash flows.

Our existing and any future indebtedness could adversely affect our ability to operate our business.

As of March 31, 2020, we had $70.0 million of outstanding principal of borrowings under the 2018 Amended Facility and 2021 Amended Facility, which following our January 2021 amendment we are required to repay in June 2023. We could in the future incur additional debt obligations beyond our borrowings from Hercules. Our existing loan obligations, together with other similar obligations that we may incur in the future, could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, research and development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a disadvantage compared to our competitors that have less debt or better debt servicing options.

We may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under our existing loan obligations. Failure to make payments or comply with other covenants under our existing debt could result in an event of default and acceleration of amounts due. Under the 2018 Amended Facility as well as the 2021 Amended Facility, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets, or condition is an event of default. If an event of default occurs and the lender accelerates the amounts due, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all our assets.

Risks Related to Other Legal Compliance Matters

Our relationships with customers and third-party payers will be subject to applicable anti-kickback, anti-bribery, fraud and abuse and other laws and regulations, which, if we are found in violation thereof, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payers will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third party payers and customers may expose us to broadly applicable anti-bribery laws, including the Foreign Corrupt Practices Act, as well as fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we would be able to market, sell and distribute any products for which we obtain marketing approval.

Efforts to ensure that our business arrangements with third parties will comply with applicable laws and regulations could involve substantial costs. If our operations, or the activities of our collaborators, distributors or other third-party agents are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs and the curtailment or restructuring of our operations. The costs associated with any of these actions could be substantial and could cause irreparable harm to our reputation or otherwise have a material adverse effect on our business, financial condition, and results of operations.

We are subject to laws governing data protection in the different jurisdictions in which we operate. The implementation of such data protection regimes is complex, and should we fail to fully comply, we may be subject to penalties that may have an adverse effect on our business, financial condition, and results of operations.

Many national and state laws govern the privacy and security of health information and other personal and private information. They often differ from each other in significant ways. For instance, the EU has adopted a comprehensive data protection law called the General Data Protection Regulation ("GDPR") that took effect in May 2018. The GDPR, together with the national legislation of the EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EU, security breach notifications, security and confidentiality of the personal data, and imposition of substantial potential fines for breaches of the data protection obligations. The GDPR imposes penalties for non-compliance of up to the greater of EUR 20.0 million or 4% of worldwide revenue. Data protection authorities from the different EU member states may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the EU. Guidance on implementation and compliance practices are often updated or otherwise revised. The significant costs of compliance with, risk of regulatory enforcement actions under, and other burdens imposed by the GDPR as well as under other regulatory schemes throughout the world related to privacy and security of health information and other personal and private data could have an adverse impact on our business, financial condition, and results of operations.

Product liability lawsuits could cause us to incur substantial liabilities and to limit commercialization of our therapies.

We face an inherent risk of product liability related to the testing of our product candidates in human clinical trials and in connection with product sales. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we develop or sell;
- injury to our reputation and significant negative media attention;
- negative publicity or public opinion surrounding gene therapy;
- withdrawal of clinical trial participants or sites, or discontinuation of development programs;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- initiation of investigations, and enforcement actions by regulators; and product recalls, withdrawals, revocation of approvals, or labeling, marketing, or promotional restrictions;
- reduced resources of our management to pursue our business strategy; and
- the inability to further develop or commercialize any products that we develop.

Dependent upon the country where the clinical trial is conducted, we currently hold coverages ranging from EUR 500,000 to EUR 6,500,000 per occurrence and per clinical trial. Such coverage may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials. In addition, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. In the event insurance coverage is insufficient to cover liabilities that we may incur, it could have a material adverse effect on our business, financial condition, and results of operations.

Healthcare legislative and regulatory reform measures may have a material adverse effect on our financial operations.

Our industry is highly regulated and changes in law may adversely impact our business, operations, or financial results. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, is a sweeping measure intended to, among other things, expand healthcare coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. Several provisions of the law may affect us and increase certain of our costs.

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, following passage of the Bipartisan Budget Act of 2018, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the reimbursement our customers may receive for our products. Further, there have been, and there may continue to be, judicial and Congressional challenges to certain aspects of the PPACA. For example, the U.S. Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additional legislative and regulatory changes to the PPACA, its implementing regulations and guidance and its policies, remain possible in the 117th U.S. Congress and under the Biden Administration. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government 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 products.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The size and complexity of our information technology systems, and those of our collaborators, contractors and consultants, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication, and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. The increased number of employees working remotely due to COVID-19 might increase our vulnerability to the above risk.

While we have not experienced a system failure, accident, cyber-attack, or security breach that has resulted in a material interruption in our operations to date, we have experienced and addressed recent system failures, cyber-attacks, and security breaches. In the future, such events could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets, data, or other proprietary information or other similar disruptions. Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal and/or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business and the further development and commercialization of our product and product candidates could be delayed.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on hiring, training, retaining and motivating key personnel to lead our research and development, clinical operations and manufacturing efforts. Although we have entered into employment agreements with our key personnel, each of them may terminate their employment on short notice. We do not maintain key person insurance for any of our senior management or employees.

The loss of the services of our key employees could impede the achievement of our research and development objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing senior management and key employees may be difficult and may take an extended period because of the limited number of individuals in our industry with the breadth and depth of skills and experience required to successfully develop gene therapy products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms.

If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks Related to Our Ordinary Shares

The price of our ordinary shares has been and may in the future be volatile and fluctuate substantially.

Our share price has been and may in the future be volatile. From the start of trading of our ordinary shares on the Nasdaq Global Select Market on February 4, 2014 through May 6, 2021, the sale price of our ordinary shares ranged from a high of $82.49 to a low of $4.72. The closing price on May 6, 2021, was $32.86 per ordinary share. The stock market in general and the market for smaller biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our ordinary shares may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- public perception of gene therapy;
- regulatory delays and greater government regulation of potential products due to adverse events;
- regulatory or legal developments in the European Union, the United States, and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- mergers, acquisitions, licensing, and collaboration activity among our peer companies in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

Our directors, executive officers and major shareholders, if they choose to act together, will continue to have a significant degree of control with respect to matters submitted to shareholders for approval.

Our directors, executive officers and major shareholders holding more than 5% of our outstanding ordinary shares, in the aggregate, beneficially own approximately 49.0% of our issued shares (including such shares to be issued in relation to exercisable options to purchase ordinary shares) as at March 31, 2021. As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to control many matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could control the election of the board directors and the approval of any merger, consolidation or sale of all or substantially all our assets. These shareholders may have interests that differ from those of other of our shareholders and conflicts of interest may arise.

Provisions of our articles of association or Dutch corporate law might deter acquisition bids for us that might be considered favorable and prevent or frustrate any attempt to replace our board.

Certain provisions of our articles of association may make it more difficult for a third party to acquire control of us or effect a change in our board. These provisions include:

- staggered terms of our directors;
- a provision that our directors may only be removed at a general meeting of shareholders by a two-thirds majority of votes cast representing more than half of the issued share capital of the Company; and
- a requirement that certain matters, including an amendment of our articles of association, may only be brought to our shareholders for a vote upon a proposal by our board.

We do not expect to pay dividends in the foreseeable future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that earnings, if any, will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. Accordingly, shareholders cannot rely on dividend income from our ordinary shares and any returns on an investment in our ordinary shares will likely depend entirely upon any future appreciation in the price of our ordinary shares.

If we fail to maintain an effective system of internal controls, we may be unable to accurately report our results of operations or prevent fraud or fail to meet our reporting obligations, and investor confidence and the market price of our ordinary shares may be materially and adversely affected.

If we fail to maintain the adequacy of our internal control over financial reporting, we may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting. If we fail to maintain effective internal control over financial reporting, we could experience material misstatements in our financial statements and fail to meet our reporting obligations, which would likely cause investors to lose confidence in our reported financial information. This could in turn limit our access to capital markets, harm our results of operations, and lead to a decline in the trading price of our ordinary shares. Additionally, ineffective internal control over financial reporting could expose us to increased risk of fraud or misuse of corporate assets and subject us to potential delisting from The Nasdaq Global Select Market, regulatory investigations and civil or criminal sanctions. Our reporting and compliance obligations may place a significant strain on our management, operational and financial resources and systems for the foreseeable future.

Risks for U.S. Holders

We have in the past qualified and in the future may qualify as a passive foreign investment company, which may result in adverse U.S. federal income tax consequence to U.S. holders.

Based on our average value of our gross assets, our cash and cash equivalents as well as the price of our shares we qualified as a passive foreign investment company ("PFIC") for U.S. federal income tax for 2016 but not in 2017, 2018, 2019 or 2020. A corporation organized outside the United States generally will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which at least 75% of its gross income is passive income or on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held to produce passive income. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions. Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will continue to qualify as a PFIC in future taxable years. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate, and may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were considered a PFIC for the current taxable year or any future taxable year, a U.S. holder would be required to file annual information returns for such year, whether the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year. In certain circumstances a U.S. holder may be able to make certain tax elections that would lessen the adverse impact of PFIC status; however, to make such elections the U.S. holder will usually have to have been provided information about the company by us, and we do not intend to provide such information.

The U.S. federal income tax rules relating to PFICs are complex. U.S. holders are urged to consult their tax advisors with respect to the purchase, ownership and disposition of our shares, the possible implications to them of us being treated as a PFIC (including the availability of applicable election, whether making any such election would be advisable in their particular circumstances) as well as the federal, state, local and foreign tax considerations applicable to such holders in connection with the purchase, ownership, and disposition of our shares.

Any U.S. or other foreign judgments may be difficult to enforce against us in the Netherlands.

Although we now report as a U.S. domestic filer for SEC reporting purposes, we are incorporated under the laws of the Netherlands. Some of the members of our board and senior management reside outside the United States. As a result, it may not be possible for shareholders to effect service of process within the United States upon such persons or to enforce judgments against them or us in U.S. courts, including judgments predicated upon the civil liability provisions of the federal securities laws of the United States. In addition, it is not clear whether a Dutch court would impose civil liability on us or any of our Board members in an original action based solely upon the federal securities laws of the United States brought in a court of competent jurisdiction in the Netherlands.

The United States and the Netherlands currently do not have a treaty providing for the reciprocal recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in the Netherlands. To obtain a judgment which is enforceable in the Netherlands, the party in whose favor a final and conclusive judgment of the U.S. court has been rendered will be required to file its claim with a court of competent jurisdiction in the Netherlands. Such party may submit to the Dutch court the final judgment rendered by the U.S. court. If and to the extent that the Dutch court finds that the jurisdiction of the U.S. court has been based on grounds which are internationally acceptable and that proper legal procedures have been observed, the Dutch court will, in principle, give binding effect to the judgment of the U.S. court, unless such judgment contravenes principles of public policy of the Netherlands. Dutch courts may deny the recognition and enforcement of punitive damages or other awards. Moreover, a Dutch court may reduce the amount of damages granted by a U.S. court and recognize damages only to the extent that they are necessary to compensate actual losses or damages. Enforcement and recognition of judgments of U.S. courts in the Netherlands are solely governed by the provisions of the Dutch Civil Procedure Code.

Therefore U.S. shareholders may not be able to enforce against us or our board members or senior management who are residents of the Netherlands or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

The rights and responsibilities of our shareholders and directors are governed by Dutch law and differ in some important respects from the rights and responsibilities of shareholders under U.S. law.

Although we now report as a U.S. domestic filer for SEC purposes, our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in the Netherlands. The rights of our shareholders and the responsibilities of members of our board under Dutch law are different than under the laws of some U.S. jurisdictions. In the performance of their duties, our board members are required by Dutch law to consider the interests of uniQure, its shareholders, its employees, and other stakeholders and not only those of our shareholders (as would be required under the law of most U.S. jurisdictions). As a result of these considerations our directors may take action that would be different than those that would be taken by a company organized under the law of some U.S. jurisdictions

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

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

EXHIBIT INDEX

101* The following financial information from our Quarterly Report on Form 10-Q for the period ended March 31, 2021, filed with the Securities and Exchange Commission on May 10, 2021, is formatted in Inline Extensible Business Reporting Language ("iXBRL"): (i) Consolidated Balance Sheets; (ii) Consolidated Statements of Operations and Comprehensive Loss; (iii) Consolidated Statements of Shareholders' Equity; (iv) Consolidated Statements of Cash Flows; and (v) Notes to Consolidated Financial Statements (tagged as blocks of text)

104* The cover page from our Quarterly Report on Form 10-Q for the period ended March 31, 2021, filed with the Securities and Exchange Commission on May 10, 2021, is formatted in Inline Extensible Business Reporting Language ("iXBRL")

† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the Securities and Exchange Commission.

* Filed herewith.

± Furnished herewith.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

UNIQURE, N.V.

By: /s/ Matthew Kapusta
Matthew Kapusta
Chief Executive Officer
(Principal Executive and Financial Officer)

By: /s/ Christian Klemt
Christian Klemt
Chief Accounting Officer

Dated May 10, 2021

Exhibit 10.1

COOPERATION AGREEMENT

between

UNIQURE N.V.

and

FORUNIQURE B.V.

and

FORBION 1 MANAGEMENT B.V.

and

FORBION INTERNATIONAL MANAGEMENT B.V.

and

FORBION CAPITAL PARTNERS MANAGEMENT HOLDING B.V.

16 April 2021

This cooperation agreement (this "Agreement") is dated 16 April 2021 and entered into between:

(1) **uniQure N.V.**, a public company with limited liability *(naamloze vennootschap*) incorporated under the laws of the Netherlands, having its seat (*statutaire zetel*) at Amsterdam, the Netherlands and its registered office at Paasheuvelweg 25, 1105 BP Amsterdam, registered with the Dutch commercial register under number 54385229 (the "Company");

(2) **ForUniqure B.V.** a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) incorporated under the laws of the Netherlands, having its seat (*statutaire zetel*) at Naarden, the Netherlands and its registered office at Gooimeer 2-35, 1411 DC Naarden, registered with the Dutch commercial register under number 71514341;

(3) **Forbion 1 Management B.V.** a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) incorporated under the laws of the Netherlands, having its seat (*statutaire zetel*) at Naarden, the Netherlands and its registered office at Gooimeer 2-35, 1411 DC Naarden, registered with the Dutch commercial register under number 34249898, in its capacity as director of ForUniqure B.V.;

(4) **Forbion International Management B.V.** a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) incorporated under the laws of the Netherlands, having its seat (*statutaire zetel*) at Naarden, the Netherlands and its registered office at Gooimeer 2-35, 1411 DC Naarden, registered with the Dutch commercial register under number 61982865, in its capacity as director of VectorY B.V., and

(5) **Forbion Capital Partners Management Holding B.V.** a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) incorporated under the laws of the Netherlands, having its seat (*statutaire zetel*) at Naarden, the Netherlands and its registered office at Gooimeer 2-35, 1411 DC Naarden, registered with the Dutch commercial register under number 34259994, in its capacity as shareholder of Forbion 1 Management B.V. and Forbion International Management B.V.

(the parties hereinafter collectively referred to as "Parties" and each a "Party" and parties 2 through 5 collectively referred to as "Investor").

WHEREAS

(A) In light of the exploration of good faith future opportunities between the Parties, the Investor as shareholder of the Company will refrain from certain activist activities from the date hereof ending two years after the signing date of this Agreement (the "Cooperation Period"), subject to the terms and conditions of this Agreement.

IT IS AGREED AS FOLLOWS

1. VOTING

1.1 At each annual general meeting and extraordinary meeting of the Company's shareholders held prior to the expiration of the Cooperation Period, the Investor agrees to (A) vote, or cause to be voted, all shares of the Company (the "Ordinary Shares") beneficially owned by the Investor and its Affiliates on the Company's power of attorney, proxy card or voting instruction form (1) in favor of the re-election of any director serving on the board as of the date of this Agreement who is nominated by the Board and recommended for re-election, and against any proposals to remove any such members of the Board, (2) against any nominees to serve on the Board that have not been recommended by the Board, and (3) with respect to all other matters, other than a Voting Exempt Matter, in accordance with the Board's recommendations as identified in the Company's notice of general meeting or any supplement thereto; and (B) not execute any power or attorney, proxy card or voting instruction form in respect of such shareholders' meeting other than the power of attorney or proxy card and related voting instruction form being solicited by or on behalf of the Board (such voting document, the "Company's card"); provided, however, that with respect to any Voting Exempt Matter, the Investor shall have the ability to vote freely on the Company's card so long as the Investor does not publicly disclose such vote. For purposes of this Clause 1.1, a "Voting Exempt Matter" means, with respect to the Company, any shareholder vote taken to approve or ratify any merger, acquisition, recapitalization, restructuring, financing, disposition, distribution, spin-off, sale or transfer of all or substantially all of the Company's or any of its Affiliates' assets in one or a series of transactions, joint venture or other business combination of the Company or any of its Affiliates with a third party or any other transaction or decision constituting a 2:107A Dutch Civil Code matter. During the Cooperation Period, not later than five (5) business days prior to each of the Company's meetings of shareholders, each Investor shall vote in accordance with this Clause 1.1 and shall not revoke or change any such vote.

2. CONDUCT

2.1 From the date of this Agreement until the expiration of the Cooperation Period, the Investor shall not, and shall cause its Affiliates (as defined below), directors, general partners, officers, employees and, to the extent acting on its behalf or at its direction, agents (collectively, the "Related Persons"), not to, directly or indirectly, alone or with others, in any manner:

(a) make any announcement or proposal with respect to, or offer, seek, propose or indicate an interest in (A) any form of business combination or acquisition or other transaction relating to assets or securities of the Company or any of its subsidiaries, (B) any form of restructuring, recapitalization or similar transaction with respect to the Company or any of its subsidiaries or (C) any form of tender or exchange offer for the Ordinary Shares;

(b) make, engage in, assist with, or in any way participate in, directly or indirectly, any solicitation of proxies or written consents to vote (or withhold the vote of) any voting securities of the Company, or conduct any binding or non-binding referendum with respect to any voting securities of the Company, or engage in any solicitation activities on behalf of any person, or conduct any exempt solicitation, including under Rule 14a-2(b)(1) under the Exchange Act, with respect to the voting of any securities of the Company, or any securities convertible or exchangeable into or exercisable for any such securities, or otherwise take any action that could cause the Investor to be deemed a "participant" in a "solicitation," as such terms are defined in Instruction 3 of Item 4 of Schedule 14A and Rule 14a-1 of Regulation 14A,

respectively, under the Exchange Act, to vote (or withhold the vote of) any securities of the Company;

(c) pursuant to Rule 14a-1(l)(2)(iv) under the Exchange Act communicate with shareholders of the Company or others;

(d) acquire, or propose (publicly or otherwise) to acquire, or agree to acquire, beneficial ownership directly or indirectly, and acting alone or in concert with others, whether by purchase, tender or exchange offer, through the acquisition of control of another person, by joining a partnership, limited partnership, syndicate or other group, or through swap or hedging transactions or otherwise, any securities (including ordinary and preferred equity interests and debt that is convertible into any equity interests) of the Company, any direct or indirect rights or options to acquire any such securities, any derivative securities or contracts or instruments in any way related to the price of the Ordinary Shares, or any assets or liabilities of the Company;

(e) advise, encourage, or influence, or seek to advise, encourage, or influence, any person with respect to the voting of (or execution of a proxy or written consent in respect of), acquisition of, or disposition of any securities of the Company, other than in relation to a disposition of Ordinary Shares held by the Investor;

(f) provide investment advice with respect to the Company's securities to any person, or provide logistical advice or assistance to any person engaged in a contested solicitation of proxies from the Company's shareholders in connection with a meeting of shareholders of the Company or the solicitation of written consents from the Company's shareholders;

(g) take any action in support of or make any proposal or request that constitutes (or would constitute if taken): (A) advising, controlling, changing or influencing the Board or management of the Company, including any plans or proposals to change the voting standard with respect to director elections, number or term of directors or to fill any vacancies on the Board, except as set forth in this Agreement; (B) other where such action, in order to comply with Investor's fiduciary duties, is reasonably considered to be in the best interest of the Investor and its stakeholders, any change in the capitalization, share repurchase programs and practices, capital allocation programs and practices, or dividend policy of the Company; (C) any other change in the Company's management, governance, compensation programs, policies, or business or corporate structure; (D) seeking to have the Company waive or make amendments or modifications to the Company's articles of association, or other actions that may impede or facilitate the acquisition of control of the Company by any person; (E) causing a class of securities of the Company to be delisted from, or to cease to be authorized to be quoted on, any securities exchange; or (F) causing a class of securities of the Company to become eligible for termination of registration pursuant to Section 12(g)(4) of the Exchange Act;

(h) engage in any course of conduct with the purpose of causing shareholders of the Company to vote contrary to the recommendation of the Board on any matter presented to the Company's shareholders for their vote at any meeting of the Company's shareholders or by written consent;

(i) call, seek to call, or request the call of (publicly or otherwise), alone or in concert with others, any meeting of shareholders, whether or not such a meeting is permitted by the Company's articles of association, including, but not limited to, a "town hall meeting;"

(j) seek, alone or in concert with others, representation on the Board;

(k) demand a copy of the Company's list of shareholders or its other books and records;

(l) initiate, encourage or participate in any "vote no," "withhold" or similar campaign relating to the Company;

(m) act, seek, facilitate, or encourage any person, to submit nominations or proposals, whether in furtherance of a "contested solicitation" or otherwise, for the appointment, election or removal of directors or otherwise with respect to the Company or seek, facilitate, encourage, or take any other action with respect to the appointment, election or removal of any directors of the Company;

(n) submit, participate in, or be the proponent of, or seek, or encourage any person, to submit, any shareholder proposal to the Company (including, but not limited to, any submission of shareholder proposals pursuant to Rule 14a-8 under the Exchange Act);

(o) institute, solicit, encourage, assist, or join, as a party, or assist any Third Party in asserting, commencing, or maintaining, any litigation, arbitration or other proceeding (including any derivative action) against or involving the Company or any of its future, current or former directors or senior managers; *provided, however*, that the foregoing shall not prevent the Investor from (A) bringing litigation against the Company to enforce the provisions of this Agreement; (B) making counterclaims with respect to any proceeding initiated by, or on behalf of, the Company against the Investor; or (C) providing non-confidential information, participating in, responding to or complying with a validly issued legal process that neither the Investor nor any of its Related Persons initiated, encouraged or facilitated;

(p) take any action, directly or indirectly, to interfere with any employment, consulting, compensation, indemnification, separation or other agreements, arrangements or understandings, whether written or oral, formal or informal, between the Company and any current or former director or senior manager of the Company, or which are intended to benefit any current or former director or senior manager of the Company, including, but not limited to, any provisions of the Company's articles of association intended to indemnify, provide advancement of expenses or limit the liability of, any current or former director or senior manager of the Company;

(q) disclose publicly or privately, in a manner that could reasonably be expected to become public, any intent, purpose, plan, or proposal with respect to the Board, the Company, its management, business or corporate structure, policies, or affairs, any of its securities or assets or this Agreement that is inconsistent with the provisions of this Agreement;

(r) enter into any discussions, negotiations, understandings, or agreements (whether written or oral) with any person or entity to take any action the Investor is prohibited from taking pursuant to this Clause 1, or make any statement with respect to any such action, or advise, assist, encourage or seek to persuade any person or entity to take any action or make any

statement with respect to any such action, or otherwise take or cause any action or make any statement inconsistent with any of the foregoing;

(s) take any action triggering the Company to make a public disclosure (including, without limitation, the filing of any document with the SEC), other than reporting on percentage ownership;

(t) otherwise take, or solicit, cause or encourage any Third Party to take, any action inconsistent with the foregoing.

2.2 The foregoing provisions of this Clause 2 shall not (i) prohibit the Investor or its Related Persons from engaging in private discussions with the Board or any director or senior manager of the Company regarding any matter so long as such private discussions are not intended to trigger any public disclosure obligations subject to the confidentiality obligations; (ii) impose any restriction on the directors (or any director nominee) from discharging her or his fiduciary duties or exercising her or his rights as a director of the Company; (iii) prohibit the Investor from making any disclosure required by applicable law, regulation, or legal process or as otherwise legally required by a regulatory or judicial authority with jurisdiction over the Investor; (iv) prohibit or limit the ability of the Investor to enforce this Agreement or (v) prohibit the Investor from entering into confidential discussions or agreements (such as irrevocable commitments) with a third party on the Investor's support to tender shares in a tender offer or for any shareholder vote taken to approve or ratify any merger, acquisition, recapitalization, restructuring, financing, disposition, distribution, spin-off, sale or transfer of all or substantially all of the Company's or any of its Affiliates' assets in one or a series of transactions, joint venture or other business combination of the Company or any of its Affiliates with a third party, or (vi) prohibit the Investor or its Related Persons from (a) selling any Ordinary Shares on the open market, (b) distributing any Ordinary Shares to its limited partners or (c) making any block trades of Ordinary Shares through a bank in the ordinary course (for the avoidance of doubt excluding where Investor or its Related Persons are aware that the buyer of such Ordinary Shares is an activist or otherwise has no good faith intentions in relation to the Company) .

2.3 As of the date of this Agreement, the Investor and, to the extent the Investor is aware, its Related Persons have no intention of taking any actions that if taken by the Investor would violate any of the terms of this Agreement.

2.4 As used in this Agreement, the terms "Affiliate" and "Associate" shall have the respective meanings set forth in Rule 12b-2 promulgated by the SEC under the Exchange Act; the terms "beneficial owner" and "beneficial ownership" shall have the same meanings as set forth in Rule 13d-3 promulgated by the SEC under the Exchange Act; the terms "economic owner" and "economically own" shall have the same meanings as "beneficial owner" and "beneficially own,"; the terms "person" or "persons" shall mean any individual, corporation (including not-for-profit), general or limited partnership, limited liability company, joint venture, estate, trust, association, organization, or other entity of any kind or nature; and the term "business day" shall mean any day that is not a Saturday, Sunday or other day on which commercial banks in the Netherlands are authorized or obligated to be closed by applicable law or regulations. For the avoidance of doubt, "Affiliate" will not be deemed to include (A) direct or indirect holders of an interest, shares or limited partners of the Investor or (B) any portfolio company of the Investor.

3. FUTURE OPPORTUNITIES

3.1 The Company and the Investor shall in good faith explore future opportunities to cooperate between themselves and/or their Affiliates, including the possibility to out-license de-prioritized programmes/assets of the Company to the Investor and/or its Affiliates.

3.2 The Parties agree that the Company may immediately terminate, or cause its relevant Affiliate to immediately terminate, any discussions, arrangements or agreements regarding any cooperation opportunities between the Parties and/or their Affiliates in the event of a breach of this Agreement by the Investor, without any form of compensation being due by the Company and/or its relevant Affiliate.

4. MUTUAL NON-DISPARAGEMENT AND NON-INVESTIGATION

4.1 The Investor agrees that, until the earlier of (i) the expiration of the Cooperation Period and (ii) any material breach of this Agreement by the Company (provided that the Company shall have ten business days following written notice from the Investor of any material breach to remedy such material breach if capable of remedy), neither it nor any of its Affiliates will, and it will cause each of its Affiliates and Related Persons not to, directly or indirectly, without the prior written consent of the Company, make, express, transmit, speak, write, verbalize, or otherwise communicate in any way (or cause, further, assist, solicit, encourage, support, or participate in any of the foregoing), any remark, comment, message, information, declaration, communication or other statement of any kind, whether verbal or in writing, that might reasonably be construed to be derogatory, critical or negative toward, the Company or any of its directors, senior managers, Affiliates, subsidiaries, employees, or agents in their capacity as such (collectively, the "Company Agents"), or that might reasonably be construed to malign, harm, disparage, defame, or damage the reputation or good name of the Company, any of its businesses, products, or services, or any of the Company Agents in their capacity as such, including, without limitation: (x) in any document or report filed with or furnished to the SEC or any other governmental agency, (y) in any press release or other publicly available format, or (z) to any journalist or member of the media (including without limitation, in a television, radio, newspaper or magazine interview).

4.2 The Company hereby agrees that, until the earlier of (i) the expiration of the Cooperation Period, and (ii) any material breach of this Agreement by the Investor (provided that the Investor shall have ten business days following written notice from the Company of any material breach to remedy such material breach if capable of remedy), neither it nor any of its Affiliates will, and it will cause each of its Affiliates not to, directly or indirectly, without the prior written consent of the Investor, make, express, transmit, speak, write, verbalize, or otherwise communicate in any way (or cause, further, assist, solicit, encourage, support, or participate in any of the foregoing), any remark, comment, message, information, declaration, communication, or other statement of any kind, whether verbal or in writing, that might reasonably be construed to be derogatory, critical or negative toward, the Investor or any of its principals, officers, Affiliates, employees, or agents in their capacity as such (collectively, the "Investor Agents"), or that might reasonably be construed to malign, harm, disparage, defame, or damage the reputation or good name of the Investor, any of its businesses, products, or services, or any of the Investor Agents in their capacity as such, including, without limitation: (x) in any document or report filed with or furnished to the SEC or any other governmental agency, (y) in any press release or other publicly available format, or (z) to any journalist or member of the media (including without limitation, in a television, radio, newspaper or magazine interview).

4.3 During the Cooperation Period, (i) The Investor shall not engage, encourage or cooperate in any private investigations firm or other person to investigate any of the Company's directors or senior managers;

and (ii) the Company shall not engage any private investigations firm or other person to investigate any member of the Investor or any of its Related Persons. For the avoidance of doubt, nothing contained in this Clause 3.3, shall prevent the Company or the Board from engaging a private investigations firm or other person to conduct a customary background review of any proposed director nominee prior to his or her appointment or election to the Board during the Cooperation Period.

4.4 Notwithstanding the foregoing, nothing in Clauses 4.1, 4.2, and 4.3. or elsewhere in this Agreement shall prohibit any person from (i) reporting possible violations of federal law or regulation to any governmental authority pursuant to Section 21F of the Exchange Act or Rule 21F promulgated thereunder, or (ii) making any other statement or disclosure required under the federal securities laws or other applicable law or regulations, including, but not limited to, the listing standards and other rules and regulations of the Nasdaq Stock Market.

5. CONFIDENTIALITY / PUBLICITY

5.1 Each Party (including its individual directors and senior managers) will hold in complete confidence any information on the negotiations which led up to this Agreement, the existence of this Agreement and the terms of this Agreement, and will not disclose this Agreement or any documents related to this Agreement, in any form whatsoever to third parties, except as expressly provided herein. This confidentiality also relates to the information contained in any of the Schedules to this Agreement, as these may be updated from time to time.

5.2 The confidentiality obligations set out in Clause 5.1 do not apply if and to the extent that:

(i) all other Parties consent in writing to the disclosure, such consent not to be unreasonably withheld;

(ii) there is a legal or governance related obligation to disclose information regarding this Agreement or a legal obligation to submit (a copy of) this Agreement;

(iii) such disclosure is reasonably determined by the disclosing party to be required by the rules and regulations of the SEC or Nasdaq, including, without limitation, pursuant to Section 5.1;

(iv) proceedings are pending between any of the Parties before the regular courts or in arbitration, in which submission of this Agreement is necessary for the settlement of the dispute;

(v) (information regarding) this Agreement is already in the public domain, unless such is a result of a breach of this Agreement by the party to whom the confidentiality obligations set out in Clause 5.1 extend; and/or

(vi) communication with a Party's shareholders and its or their directors, employees, agents, its professional legal and financial advisers, auditors and underwriters is required. The Parties agree to ensure that these persons are aware of the confidentiality provisions in Clause 5.1 and require them to agree to those terms.

6. MISCELLANEOUS

6.1 No later than four (4) business days following the execution of this Agreement, the Company shall file a Current Report on Form 8-K with the SEC reporting the entry into this Agreement and appending or incorporating by reference this Agreement as an exhibit thereto.

6.2 If either party alleges that the other party has materially breached this Agreement, the alleging party (the "Alleging Party") shall promptly provide written notice to the other party (the "Non-Alleging Party") reasonably detailing the alleged breach. The rights and obligations of each party shall continue under this Agreement until a court of competent jurisdiction determines that the Non-Alleging Party has breached this Agreement.

6.3 No right or obligation stemming from this Agreement may be assigned or transferred in any way (including without limitation by way of *cessie*, *schuldoverneming* and *contractsoverneming*) by a Party without the prior written consent of the other Parties.

6.4 Each Party undertakes towards each other Party to perform additional legal acts and/or sign additional documents, if required under law or upon a reasonable request by another Party, in order to perfect the execution of this Agreement and/or establish and protect such other Party's rights under this Agreement.

6.5 The provisions of this Agreement may only be amended by a written agreement signed by all Parties.

6.6 Each Party will bear its own costs in connection with the execution of this Agreement.

6.7 Each of the Parties warrants that this Agreement constitutes its legal, valid and binding obligations and that it has full power and authority to enter into and perform, and has taken all necessary action to authorise entry into and performance of this Agreement.

6.8 If and insofar provisions of this Agreement are inconsistent with any prior agreement, understanding, written or oral, between any of the Parties on the same subject matter, the provisions of this Agreement shall prevail.

6.9 Nothing in this Agreement shall limit the rights of a Party in case of fraud, gross negligence or wilful misconduct of any other Party.

7. EXCLUSION OF RESCISSION, AMENDMENT AND NULLIFICATION

The Parties mutually waive the right to claim full or partial rescission (*ontbinding*) or nullification (*vernietiging*) of this Agreement, or to invoke invalidity (*nietigheid*) on any ground whatsoever and whether or not by way of defence, or to request amendment (*wijziging*) of this Agreement under Section 6:230 of the Dutch Civil Code.

8. NOTICES AND OTHER ANNOUNCEMENTS TO THE PARTIES

8.1 Except as otherwise required by law, all notices, announcements, summons and/or communications pursuant to or in connection with this Agreement shall be in the English language and be delivered to the below addresses (or to such other address as a Party has after the date hereof communicated to the other Party in accordance with this Clause), by registered mail with return receipt or by courier.

If to Investor
Legal Counsel & Compliance Officer
Gooimeer 2 – 35, 1411 DC
Naarden, The Netherlands

With a copy to: [*]

[*]

If to uniQure:

uniQure N.V.
Chief Legal Officer
Paasheuvelweg 25A,1105 BA
Amsterdam The Netherlands

With a copy to: [*]

8.2 Notices, announcements, summons and/or communications pursuant to or in connection with this Agreement shall be deemed to have been received at the following moments:

(a) if sent by registered letter: at the date of delivery evidenced by the return receipt; and

(a) if sent by courier: at the date of delivery by the courier to the addressee.

9. JURISDICTION AND GOVERNING LAW

9.1 The District Court of Amsterdam, the Netherlands has exclusive jurisdiction in first instance to settle any dispute arising out of or in connection with this Agreement (including a dispute relating to the existence, validity or termination of this Agreement or any non-contractual obligation arising out of or in connection with this Agreement.

9.2 Clause 9.1 shall also apply to disputes arising out of or in connection with agreements which are connected with this Agreement, unless the relevant agreement (including in particular the Parties Agreements) expressly provides otherwise.

9.3 This Agreement and all contractual and non-contractual obligations arising out of or in connection to it are governed by Dutch law.

The rest of this page is intentionally left blank, signature page follows.

uniQure N.V.

/s/ Matthew Kapusta
Name: Matthew Kapusta
Title: CEO & Executive Director

ForUniQure B.V.

/s/ Sander Slootweg
Name: Sander Slootweg
Title: Director

/s/ Vincent van Houten
Name: Vincent van Houten
Title: Director

Forbion 1 Management B.V., in its capacity as director of ForUniqure B.V.

/s/ Sander Slootweg
Name: Sander Slootweg
Title: Director

/s/ Vincent van Houten
Name: Vincent van Houten
Title: Director

Forbion International Management B.V., in its capacity as director of VectorY B.V.

/s/ Sander Slootweg
Name: Sander Slootweg
Title: Director

/s/ Marco Boorsma
Name: Marco Boorsma
Title: Director

Forbion Capital Partners Management Holding B.V., in its capacity as shareholder of Forbion 1 Management B.V. and Forbion International Management B.V.

/s/ Sander Slootweg
Name: Sander Slootweg
Title: Director

/s/ Vincent van Houten
Name: Vincent van Houten
Title: Director

Exhibit 31.1

Certification of Chief Executive Officer

I, Matthew Kapusta, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of uniQure N.V.;

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 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;

(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;

5. The registrant's other certifying officer 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.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Chief Executive Officer
May 10, 2021

Exhibit 31.2

Certification of Chief Financial Officer

I, Matthew Kapusta, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of uniQure N.V.;

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 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;

(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;

5. The registrant's other certifying officer 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.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Principal Financial Officer
May 10, 2021

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Quarterly Report of uniQure N.V. (the "Company") on Form 10-Q for the period ended March 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Matthew Kapusta, Chief Executive Officer and Principal Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1 the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2 the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Chief Executive Officer and
Principal Financial Officer
May 10, 2021

A signed original of this written statement required by Section 906 has been provided to uniQure N.V. and will be retained by uniQure N.V. and furnished to the SEC or its staff upon request.