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

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2023

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 25a
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 Stock Market LLC (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 4, 2023, the registrant had 47,583,959 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 our collaboration and license agreements, our cash runway, the advancement of our clinical trials, and the impact of regulatory actions on our regulatory submission and approval 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 February 27, 2023 (the "Annual Report"), 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, 2023, and in our Annual Report, 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, 2023	December 31, 2022
	(in thousands, except share and per share amounts)	
Current assets		
Cash and cash equivalents	$ 153,851	$ 228,012
Current investment securities	161,487	124,831
Accounts receivable and contract asset	104,793	102,376
Inventories	7,477	6,924
Prepaid expenses	12,567	11,817
Other current assets and receivables	2,468	2,814
Total current assets	**442,643**	**476,774**
Non-current assets		
Property, plant and equipment, net of accumulated depreciation of $46.9 million as of March 31, 2023 and $44.1 million as of December 31, 2022	50,072	50,532
Non-current investment securities	—	39,984
Operating lease right-of-use assets	32,135	32,726
Intangible assets, net, including an in-process research and development asset of $58.3 million as of March 31, 2023 and $57.3 million as of December 31, 2022	59,704	58,778
Goodwill	25,998	25,581
Deferred tax assets, net	14,331	14,528
Other non-current assets	6,121	6,061
Total non-current assets	**188,361**	**228,190**
Total assets	**$ 631,004**	**$ 704,964**
Current liabilities		
Accounts payable	$ 8,885	$ 10,984
Accrued expenses and other current liabilities	22,529	30,571
Current portion of contingent consideration	27,253	25,982
Current portion of operating lease liabilities	7,669	8,382
Total current liabilities	**66,336**	**75,919**
Non-current liabilities		
Long-term debt	103,253	102,791
Operating lease liabilities, net of current portion	31,075	31,719
Contingent consideration, net of current portion	9,641	9,334
Deferred tax liability, net	6,970	8,257
Other non-current liabilities	958	935
Total non-current liabilities	**151,897**	**153,036**
Total liabilities	**218,233**	**228,955**
Commitments and contingencies		
Shareholders' equity		
Ordinary shares, €0.05 par value: 80,000,000 shares authorized as of March 31, 2023 and December 31, 2022 and 47,546,673 and 46,968,032 ordinary shares issued and outstanding as of March 31, 2023 and December 31, 2022, respectively	2,869	2,838
Additional paid-in-capital	1,121,554	1,113,393
Accumulated other comprehensive loss	(52,494)	(58,291)
Accumulated deficit	(659,158)	(581,931)
Total shareholders' equity	**412,771**	**476,009**
Total liabilities and shareholders' equity	**$ 631,004**	**$ 704,964**

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,	
	2023	2022
	(in thousands, except share and per share amounts)	
Contract manufacturing revenues	$ 4,937	$ —
Collaboration revenues	388	1,792
Total revenues	**5,325**	**1,792**
Operating expenses:		
Cost of contract manufacturing revenues	(2,435)	—
Research and development expenses	(60,809)	(45,003)
Selling, general and administrative expenses	(17,848)	(10,987)
Total operating expenses	**(81,092)**	**(55,990)**
Other income	1,811	311
Other expense	(216)	(193)
Loss from operations	**(74,172)**	**(54,080)**
Interest income	1,669	42
Interest expense	(3,562)	(2,515)
Foreign currency (losses) / gains, net	(2,369)	8,567
Other non-operating gains, net	—	692
Loss before income tax benefit	**$ (78,434)**	**$ (47,294)**
Income tax benefit	1,207	616
Net loss	**$ (77,227)**	**$ (46,678)**
Other comprehensive loss:		
Foreign currency translation adjustments	5,797	(10,450)
Total comprehensive loss	**$ (71,430)**	**$ (57,128)**
Basic and diluted net loss per ordinary share	(1.63)	(1.00)
Weighted average shares used in computing basic and diluted net loss per ordinary share	47,436,335	46,599,114

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 MONTHS ENDED MARCH 31, 2023 AND 2022

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive (loss) / income	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
	(in thousands, except share and per share amounts)					
Balance at December 31, 2021	**46,298,635**	**$ 2,802**	**$ 1,076,972**	**$ (28,856)**	**$ (455,142)**	**$ 595,776**
Loss for the period	—	—	—	—	(46,678)	(46,678)
Other comprehensive loss	—	—	—	(10,450)	—	(10,450)
Exercises of share options	68,124	4	420	—	—	424
Restricted and performance share units distributed during the period	271,131	15	(15)	—	—	—
Share-based compensation expense	—	—	6,868	—	—	6,868
Issuance of ordinary shares relating to employee stock purchase plan	3,558	—	61	—	—	61
Balance at March 31, 2022	**46,641,448**	**$ 2,821**	**$ 1,084,306**	**$ (39,306)**	**$ (501,820)**	**$ 546,001**
Balance at December 31, 2022	**46,968,032**	**$ 2,838**	**$ 1,113,393**	**$ (58,291)**	**$ (581,931)**	**$ 476,009**
Loss for the period	—	—	—	—	(77,227)	(77,227)
Other comprehensive gain	—	—	—	5,797	—	5,797
Exercises of share options	10,055	1	86	—	—	87
Restricted and performance share units distributed during the period	566,091	30	(30)	—	—	—
Share-based compensation expense	—	—	8,061	—	—	8,061
Issuance of ordinary shares relating to employee stock purchase plan	2,495	0	44			44
Balance at March 31, 2023	**47,546,673**	**$ 2,869**	**$ 1,121,554**	**$ (52,494)**	**$ (659,158)**	**$ 412,771**

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,	
	2023	2022
	(in thousands)	
Cash flows from operating activities		
Net loss	$ (77,227)	$ (46,678)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	2,527	2,122
Share-based compensation expense	8,061	6,868
Deferred tax income	(1,207)	(616)
Changes in fair value of contingent consideration and derivative financial instrument, net	975	1,512
Unrealized foreign exchange losses / (gains), net	1,193	(7,356)
Other items, net	(469)	-
Changes in operating assets and liabilities:		
Accounts receivable and contract asset, prepaid expenses, and other current assets and receivables	(936)	17,209
Inventories	(553)	-
Accounts payable	(1,661)	7,306
Accrued expenses, other liabilities, and operating leases	(9,005)	(6,078)
Net cash used in operating activities	(78,302)	(25,711)
Cash flows from investing activities		
Purchases of property, plant, and equipment	(2,342)	(4,058)
Proceeds on maturity of investment securities	5,330	-
Acquisition of Corlieve, net of cash acquired	-	(822)
Net cash generated from / (used in) investing activities	2,988	(4,880)
Cash flows from financing activities		
Proceeds from issuance of ordinary shares related to employee stock option and purchase plans	131	485
Net cash generated from financing activities	131	485
Currency effect on cash, cash equivalents and restricted cash	1,034	(1,168)
Net decrease in cash, cash equivalents and restricted cash	(74,149)	(31,274)
Cash, cash equivalents and restricted cash at beginning of period	231,173	559,353
Cash, cash equivalents and restricted cash at the end of period	**$ 157,024**	**$ 528,079**
Cash and cash equivalents	$ 153,851	$ 524,886
Restricted cash related to leasehold and other deposits	3,173	3,193
Total cash, cash equivalents and restricted cash	**$ 157,024**	**$ 528,079**
Supplemental cash flow disclosures:		
Cash paid for interest	$ (3,057)	$ (1,906)
Non-cash (decrease) / increase in accounts payables and accrued expenses and other current liabilities related to purchases of property, plant, and equipment	$ (753)	$ (611)

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

1 General business information

uniQure N.V. (the "Company") was incorporated on January 9, 2012, initially 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 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 on the Nasdaq Global Select Market, 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 25a, 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 United States Securities and Exchange Commission (the "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, 2023, are not necessarily indicative of the results to be expected for the full year ending December 31, 2023, 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 filed by the Company with the SEC on February 27, 2023 (the "Annual Report").

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, 2022, and the notes thereto, which are included in the Annual Report. There have been no material changes in the Company's significant accounting policies during the three months ended March 31, 2023.

2.5 Recent accounting pronouncements

There have been no new accounting pronouncements or changes to accounting pronouncements during the three months ended March 31, 2023, as compared to the recent accounting pronouncements described in Note 2.3.25 of the Annual Report, which could be expected to materially impact the Company's unaudited consolidated financial statements.

3 CSL Behring collaboration

On June 24, 2020 (the "Signing Date"), uniQure biopharma B.V., a wholly owned subsidiary of the Company entered into a commercialization and license agreement (the "CSL Behring Agreement") with CSL Behring LLC ("CSL Behring"), pursuant to which CSL Behring received exclusive global rights to HEMGENIX® (the "Product").

The transaction became fully effective on May 6, 2021 ("Closing").

Accounts Receivable and Contract Asset

As of December 31, 2022, the Company recorded accounts receivable of $2.2 million from CSL Behring related to collaboration services as well as a contract asset of $100.0 million associated to a milestone due from CSL Behring following the first sale of HEMGENIX® in the U.S., which was deemed to be probable.

As of March 31, 2023, the Company had accounts receivable of $4.8 million from CSL Behring related to collaboration services and contract manufacturing revenue and as well as the contract asset of $100.0 million.

4 Investment securities

The following tables summarize the Company's investments in sovereign debt as of March 31, 2023 and December 31, 2022:

	At March 31, 2023			
	Amortized cost, as adjusted	Gross unrealized holding gains	Gross unrealized holding losses	Estimated fair value
	(in thousands)			
Current investments:				
Government debt securities (held-to-maturity)	$ 161,487	$ —	$ (277)	$ 161,210
Total	**$ 161,487**	**$ —**	**$ (277)**	**$ 161,210**

	At December 31, 2022			
	Amortized cost, as adjusted	Gross unrealized holding gains	Gross unrealized holding losses	Estimated fair value
	(in thousands)			
Current investments:				
Government debt securities (held-to-maturity)	$ 124,831	$ —	$ (283)	$ 124,548
Non-current investments:				
Government debt securities (held-to-maturity)	39,984	—	(43)	39,941
Total	**$ 164,815**	**$ —**	**$ (326)**	**$ 164,489**

Inputs to the fair value of the investments are considered Level 2 inputs.

5 Fair value measurement

The Company measures certain financial assets and liabilities at fair value, either upon initial recognition or for subsequent accounting or reporting. *ASC 820, Fair Value Measurements and Disclosures* 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 from licensing and collaboration partners, 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, 2023, and December 31, 2022:

	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, 2022					
Assets:					
Cash and cash equivalents	$ 228,012	$ —	$ —	$ 228,012	Cash and cash equivalents
Restricted cash	3,161	—	—	3,161	Other non-current assets
Total assets	$ 231,173	$ —	$ —	$ 231,173	
Liabilities:					
Contingent consideration	—	—	35,316	35,316	Contingent consideration
Consideration for post-acquisition services	—	—	297	297	Other non-current liabilities
Total liabilities	$ —	$ —	$ 35,613	$ 35,613	
At March 31, 2023					
Assets:					
Cash and cash equivalents	$ 153,851	$ —	$ —	$ 153,851	Cash and cash equivalents
Restricted cash	3,173	—	—	3,173	Other non-current assets
Total assets	$ 157,024	$ —	$ —	$ 157,024	
Liabilities:					
Contingent consideration	—	—	36,894	36,894	Contingent consideration
Consideration for post-acquisition services	—	—	328	328	Other non-current liabilities
Total liabilities	$ —	$ —	$ 37,222	$ 37,222	

Contingent consideration

The Company is required to pay up to EUR 178.8 million ($194.5 million at March 31, 2023) at March 31, 2023 to the former shareholders of Corlieve Therapeutics SAS ("Corlieve") upon the achievement of contractually defined milestones in connection with the Company's acquisition of Corlieve.

The fair value of the contingent consideration as of March 31, 2023 was $36.9 million (December 31, 2022: $35.3 million) using discount rates of approximately 14.3% to 15.0% (December 31, 2022: 14.0% to 14.4%) as well as a 66.0% (December 31, 2022: 66.0%) likelihood of Corlieve's target candidate for treatment of temporal lobe epilepsy ("AMT-260") advancing into clinical development by no later than late 2023. If as of March 31, 2023 the

Company had assumed a 100% likelihood of AMT-260 advancing into clinical development, then the fair value of the contingent consideration would have increased to $51.0 million. If as of March 31, 2023 the Company assumed that it would discontinue development of the AMT-260 program, then the contingent consideration would be released to income. Changes in fair value of the contingent consideration are recognized within research and development expenses in the consolidated statements of operations.

The following table presents the changes in fair value of contingent consideration between December 31, 2022 and March 31, 2023:

	Amount of contingent consideration
	2022
	(in thousands)
Balance at December 31, 2022	**$ 35,316**
Change in fair value (presented within research and development expenses)	975
Currency translation effects	603
Balance at March 31, 2023	**$ 36,894**

As of March 31, 2023, the Company classified $27.3 million of the total contingent consideration of $36.9 million as current liabilities. The balance sheet classification between current and non-current liabilities is based upon the Company's best estimate of the timing of settlement of the remaining relevant milestones.

Investment Securities

Refer to Note 4 "*Investment securities*" for the fair value of the investment securities as of March 31, 2023 and December 31, 2022.

6 Accrued expenses and other current liabilities

Accrued expenses and other current liabilities include the following items:

	March 31, 2023	December 31, 2022
	(in thousands)	
Accruals for goods received from and services provided by vendors-not yet billed	$ 10,929	$ 11,120
Personnel related accruals and liabilities	9,350	17,201
Accrued contract fulfillment costs and costs to obtain a contract	2,250	2,250
Total	**$ 22,529**	**$ 30,571**

7 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"). The facility was amended and restated in 2014, 2016, 2018 ("2018 Amended Facility"), January 2021 ("2021 Amended Facility") and in December 2021 ("2021 Restated Facility").

The Company drew down an additional $30.0 million at the time of the 2021 Restated Facility, resulting in total principal outstanding $100.0 million. The 2021 Restated Facility matures on December 1, 2025.

The Company is required to repay the entire principal balance on the maturity date. The interest rate is adjustable and is the greater of (i) 7.95% and (ii) 7.95% plus the prime rate less 3.25% per annum. Under the 2021 Restated Facility, the Company owes a back-end fee of $2.5 million on June 1, 2023 and a back-end fee of $4.9 million on the maturity date.

The amortized cost (including interest due presented as part of accrued expenses and other current liabilities) of the 2021 Restated Facility was $104.3 million as of March 31, 2023, compared to $103.8 million as of December 31, 2022, and is recorded net of discount and debt issuance costs. The foreign currency gain on the facility in the three ended March 31, 2023 was $0.7 million compared to a foreign currency loss of $2.1 million during the same period in 2022.

Interest expense associated with the 2021 Restated Facility during the three months ended March 31, 2023 was $3.6 million, compared to $2.4 million during the same period in 2022.

Under the 2021 Restated Facility the Company must remain current in its 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. Beginning on April 1, 2024, the Company is required to keep a minimum of unrestricted cash equal to at least 30% of the loan amount outstanding. In combination with other covenants, the 2021 Restated 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 $631.0 million, less $26.0 million of cash and cash equivalents and other current assets held by uniQure N.V. and $85.7 million of other current assets and investment held by Corlieve.

Under the 2021 Restated Facility, the occurrence of a material adverse effect, as defined therein, would entitle Hercules to declare all principal, interest and other amounts owed by the Company immediately due and payable. As of March 31, 2023, the Company was in material compliance with all covenants and provisions.

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"). The number of shares authorized for issuance under the 2014 Plan is 12,601,471. On April 28, 2023, the Company filed a definitive proxy statement with the SEC, seeking shareholder approval to, among other things, amend and restate the 2014 Plan to increase the shares available thereunder.

In June 2018, the Company's shareholders adopted and approved an employee share purchase plan ("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.

2014 Plans and ESPP

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

	Three months ended March 31,	
	2023	2022
	(in thousands)	
Cost of manufacturing services revenue	$ 24	$ —
Research and development	4,305	4,054
Selling, general and administrative	3,732	2,814
Total	**$ 8,061**	**$ 6,868**

Share-based compensation expense recognized by award type of the 2014 Plans as well as the ESPP was as follows:

	Three months ended March 31,	
	2023	2022
	(in thousands)	
Award type/ESPP		
Share options	$ 3,274	$ 3,255
Restricted share units	4,630	3,270
Performance share units	150	338
Employee share purchase plan	7	5
Total	**$ 8,061**	**$ 6,868**

As of March 31, 2023, 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	$ 32,390	2.89
Restricted share units	43,140	2.35
Performance share units	12	0.12
Total	**$ 75,542**	**2.58**

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 share options that vest must be exercised by the tenth anniversary of the initial grant date.

The following tables summarize share option activity under the 2014 Plans for the three months ended March 31, 2023:

	Options	
	Number of ordinary shares	Weighted average exercise price
Outstanding at December 31, 2022	**4,237,917**	**$ 26.13**
Granted	1,049,350	$ 20.06
Forfeited	(74,916)	$ 24.38
Expired	(51,606)	$ 54.74
Exercised	(10,055)	$ 8.64
Outstanding at March 31, 2023	**5,150,690**	**$ 24.66**
Thereof, fully vested and exercisable on March 31, 2023	2,438,321	$ 27.41
Thereof, outstanding and expected to vest after March 31, 2023	2,712,369	$ 22.20

Total weighted average grant date fair value of options issued during the period (in $ millions)	$ 12.3
Proceeds from option sales during the period (in $ millions)	$ 0.1

The fair value of each share 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	**2023**	**2022**
Expected volatility	70%	70%
Expected terms	10 years	10 years
Risk free interest rate	4.10%	2.12%
Expected dividend yield	0%	0%

RSUs

The following table summarizes the RSU activity for the three months ended March 31, 2023:

	RSUs	
	Number of ordinary shares	**Weighted average grant-date fair value**
Non-vested at December 31, 2022	**1,818,774**	**$ 20.46**
Granted	1,202,150	$ 20.06
Vested	(520,046)	$ 22.86
Forfeited	(65,982)	$ 19.50
Non-vested at March 31, 2023	**2,434,896**	**$ 19.78**
Total weighted average grant date fair value of RSUs granted during the period (in $ millions)		$ 24.1

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

PSUs

The following table summarizes the PSU activity for the three months ended March 31, 2023:

	PSUs	
	Number of ordinary shares	**Weighted average grant-date fair value**
Non-vested at December 31, 2022	**400,690**	**$ 28.82**
Vested	(46,045)	$ 28.60
Forfeited	(17,395)	$ 26.12
Non-vested at March 31, 2023	**337,250**	**$ 28.99**

The Company granted ordinary shares to certain employees in September and December 2021 and at various dates during the year ended December 31, 2022 that will be earned upon the achievement of defined milestones. Such ordinary shares will vest upon the later of a minimum service period of one year or three years, or the achievement of defined milestones, subject to the grantee's continued employment. In addition, portions of the ordinary shares granted in December 2021 to executives and other members of senior management are subject to achieving a minimum total shareholder return relative to the Nasdaq biotechnology index. The Company recognizes the compensation cost related to these grants to the extent it considers achievement of the milestones to be probable. Achievement of one of the total five defined milestones was met as of December 31, 2022 and another one of the total five defined milestones was met as of March 31, 2023.

ESPP

During the three months ended March 31, 2023, 2,495 ordinary shares were issued under the ESPP compared to 3,558 during the same period in 2022. As of March 31, 2023, a total of 113,565 ordinary shares remains available for issuance under the ESPP plan compared to a total of 123,744 as of March 31, 2022.

9 Income taxes

The Company recorded $1.2 million deferred tax benefit in relation to its operations in the United States and France during the three months ended March 31, 2023. The Company recorded $0.6 million deferred tax benefit in relation to its operations in the United States, France and Switzerland for the three months ended March 31, 2022.

The effective income tax rate of (1.5%) during the three months ended March 31, 2023 is substantially lower than the enacted rate of 25.8% in the Netherlands as the Company records a valuation allowance against its net deferred tax assets in the Netherlands. The effective income tax rate during the three months ended March 31, 2022 was (1.3%) as the Company had recorded a valuation allowance against its net deferred tax assets in the Netherlands.

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 ordinary 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, 2023 and March 31, 2022, respectively.

The potentially dilutive ordinary shares are summarized below:

	Three months ended March 31,	
	2023	2022
Anti-dilutive ordinary share equivalents		
Stock options under 2014 Plans and previous plan	5,150,690	4,139,698
Non-vested RSUs and PSUs	2,772,146	2,287,969
ESPP	801	745
Total anti-dilutive ordinary share equivalents	**7,923,637**	**6,428,412**

11 Subsequent events

None.

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. 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 with a mission to reimagine the future of medicine by delivering innovative cures that transform human lives. We are advancing a pipeline of innovative gene therapies, including our clinical candidates for the treatment of Huntington's disease and amyotrophic lateral sclerosis ("ALS"), as well as preclinical product candidates including candidates for the treatment of refractory temporal lobe epilepsy ("rTLE') and Fabry disease. In November 2022 and February 2023, our internally developed HEMGENIX®, a gene therapy for the treatment of hemophilia B, was approved for commercialization by the United States Food and Drug Administration ("FDA") and the European Medicines Agency ("EMA"), respectively. In June 2020, we agreed to license HEMGENIX® to CSL Behring LLC ("CSL Behring"), which is now responsible for commercialization of HEMGENIX®. We are manufacturing HEMGENIX® for CSL Behring and are entitled to specific milestone payments and royalties on net sales. 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:

Amyotrophic Lateral Sclerosis (AMT-162)

On January 31, 2023, we announced that we have entered into a global licensing agreement with Apic Bio for a one-time, intrathecally administered gene therapy for ALS caused by mutations in superoxide dismutase 1 ("SOD1"), a rapidly progressing, rare motor neuron disease that leads to loss of everyday functions and is uniformly fatal. With this agreement, we have added to our pipeline of gene therapies to treat neurological disorders. The FDA has cleared the investigational new drug application for APB-102 and has granted Orphan Drug and Fast Track designation. Mutations in the SOD1 gene of ALS account for approximately one-fifth of all inherited forms of this fatal disease. APB-102 is comprised of a recombinant AAVrh10 vector that expresses a miRNA designed to knock down the expression of SOD1 with the goal of slowing down or potentially reversing the progression of ALS in patients with SOD1 mutations.

We made an initial cash payment of $10.0 million to Apic Bio that was recognized as research and development expense.

Huntington's disease program (AMT-130)

AMT-130 is our novel gene therapy candidate for the treatment of Huntington's disease.

We are currently conducting a randomized, controlled and blinded Phase I/II clinical trial for AMT-130 in the U.S. The lower-dose cohort of this trial includes 10 patients, of which six patients received treatment with AMT-130 and four patients received imitation surgery. The higher-dose cohort includes 16 patients, of which 10 patients received treatment with AMT-130 and six patients received imitation surgery. Patients receiving imitation surgery have the option to cross over after 12 months if they meet the inclusion criteria for the study. We are also conducting an open-label Phase Ib/II study in the EU, which includes six patients in the lower-dose cohort and nine patients in the higher-dose cohort. All 15 patients in the EU study will receive AMT-130.

On March 21, 2022, we announced that we completed the enrollment of all 26 patients in the first two cohorts of our Phase I/II clinical trial of AMT-130 in the U.S. In July 2022, we began crossing over patients who received the imitation surgical procedure. Three of the six control patients in the higher-dose cohort have now crossed over to treatment. Two of these three patients have received the higher dose of AMT-130.

On June 23, 2022, we announced that 10 patients in our Phase Ib/II study in the EU had been treated with AMT-130. On June 23, 2022, we announced safety and biomarker data from the 10 patients enrolled in the low-dose U.S. cohort. AMT-130 was generally well-tolerated with no serious adverse events related to AMT-130 reported in the treated patients. In the four treated patients with evaluable data, mean levels of mutant Huntingtin protein in the cerebral spinal fluid ("CSF mHTT") declined at all timepoints compared to baseline, and decreased by 53.8% at 12 months of follow-up. In the six treated patients, measurements of neurofilament lights chain in the cerebral spinal fluid ("CSF NfL") initially increased as expected following the AMT-130 surgical procedure and declined thereafter, nearing baseline at 12 months of follow-up.

Select research programs

In the third quarter of 2022, we initiated a Good Laboratory Practices ("GLP") toxicology study in non-human primates for AMT-260, a gene therapy product candidate for the treatment of refractory temporal lobe epilepsy ("rTLE").

In the third quarter of 2022, we initiated a GLP toxicology study in non-human primates for AMT-191, a gene therapy product candidate for the treatment of Fabry disease.

CSL Behring commercialization and license agreement ("CSL Behring Agreement")

In November 2022, the FDA approved the marketing application for HEMGENIX® in the U.S., and in February 2023 the European Medicines Agency ("EMA") approved the marketing application for the EU.

Financial Overview

Key components of our results of operations include the following:

	Three months ended March 31,	
	2023	2022
	(in thousands)	
Total revenues	$ 5,325	$ 1,792
Cost of contract manufacturing revenues	(2,435)	—
Research and development expenses	(60,809)	(45,003)
Selling, general and administrative expenses	(17,848)	(10,987)
Net loss	(77,227)	(46,678)

As of March 31, 2023 and December 31, 2022, we had cash and cash equivalents and investment securities of $315.3 million and $392.8 million, respectively. We had a net loss of $77.2 million in the three months ended March 31, 2023, compared to net loss of $46.7 million for the same period in 2022. As of March 31, 2023 and December 31, 2022, we had accumulated deficits of $659.2 million and $581.9 million, respectively.

We anticipate that our expenses will increase for the foreseeable future and will include costs related to:

- advancing AMT-130 for our Huntington's disease gene therapy program into phase III clinical study;
- advancing our gene therapy programs for rTLE, SOD1-ALS and Fabry disease into Phase I/II clinical studies;
- potentially acquiring or in-licensing rights to new therapeutic targets, product candidates and technologies;
- advancing preclinical research and development for gene therapy product candidates targeting diseases other than those listed above;
- making potential future milestone payments related to the acquisition of Corlieve Therapeutics SAS ("Corlieve"), if any; and

- continuing to invest in expanding, developing and optimizing our manufacturing capabilities and other enabling technologies, such as next-generation viral vectors, promoters and re-dosing.

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 Securities and Exchange Commission (the "SEC") we make assumptions, judgments and estimates that can have a significant impact on our net loss and affect the reported amounts of certain assets, liabilities, revenue and expenses, and related disclosures. 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. A summary of our critical accounting policies as well as a discussion of our critical accounting estimates are presented in our Annual Report. There were no material changes to our critical accounting policies during the three months ended March 31, 2023 or reasonably possible changes of our critical accounting estimates as of March 31, 2023 that could have had a material impact on our results of operations for the three-month period ended March 31, 2023.

Cost of contract manufacturing

We entered into a development and commercial supply agreement with CSL Behring in June 2020. Since April 1, 2022, we recognize cost to manufacture HEMGENIX® under such agreement as cost of contract manufacturing.

Research and development expenses

We expense research and development ("R&D") expenses as incurred. R&D expenses include costs which relate to our primary activities of biopharmaceutical research and development. 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 research activities for enabling technology platforms, such as next-generation vectors, promoters and re-administration of gene therapies;
- costs associated with the rendering of collaboration services as well as the continued development of etranacogene dezaparvovec (the "Product");
- payments related to identifiable intangible assets without an alternative future use;
- payments to our licensors for milestones that have been achieved related to our product candidates, including approval of the marketing authorization application ("MAA");
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies; and
- changes in the fair value of liabilities recorded in relation to our acquisition of Corlieve.

Our R&D 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 the product candidates that we may develop 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 incurred 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.

Other items, net

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

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

Comparison of the three months ended March 31, 2023 and 2022

The following table presents a comparison of our results of operations for the three months ended March 31, 2023 and 2022.

	Three months ended March 31,		
	2023	2022	2023 vs 2022
	(in thousands)		
Total revenues	$ 5,325	$ 1,792	$ 3,533
Operating expenses:			
Cost of contract manufacturing revenues	(2,435)	—	(2,435)
Research and development expenses	(60,809)	(45,003)	(15,806)
Selling, general and administrative expenses	(17,848)	(10,987)	(6,861)
Total operating expenses	**(81,092)**	**(55,990)**	**(25,102)**
Other income	1,811	311	1,500
Other expense	(216)	(193)	(23)
Loss from operations	**(74,172)**	**(54,080)**	**(20,092)**
Non-operating items, net	(4,262)	6,786	(11,048)
Loss before income tax benefit	$ **(78,434)**	$ **(47,294)**	**(31,140)**
Income tax benefit	1,207	616	591
Net loss	**$ (77,227)**	**$ (46,678)**	**$ (30,549)**

Revenue

Our revenue for the three months ended March 31, 2023 and 2022 was as follows:

	Three months ended March 31,		
	2023	2022	2023 vs 2022
	(in thousands)		
Contract manufacturing revenues	$ 4,937	$ —	$ 4,937
Collaboration revenues	388	1,792	(1,404)
Total revenues	**$ 5,325**	**$ 1,792**	**$ 3,533**

Collaboration revenues

We entered into collaboration, research, and license agreements with Bristol-Myers Squibb ("BMS") in 2015 which were terminated on February 21, 2023.

For the three months ended March 31, 2023, we recognized $0.4 million and nil of collaboration revenue for CSL Behring and BMS, respectively. For the three months ended March 31, 2022, we recognized $1.4 million and $0.4 million of collaboration revenue for CSL Behring and BMS, respectively.

Contract manufacturing revenues

We recognize contract manufacturing revenue related to contract manufacturing HEMGENIX® for CSL Behring. Contract manufacturing revenue is realized when earned upon sales of HEMGENIX® to CSL Behring. We recognized $4.9 million contract manufacturing revenues in the three months ended March 31, 2023, compared to nil for the same period in 2022. We did not recognize such revenues in the three months ended March 31, 2022, as we started contract manufacturing activities to supply CSL Behring with launch supplies of HEMGENIX® following their submission of a BLA and MAA in the spring of 2022.

Cost of contract manufacturing

We incurred $2.4 million of cost of contract manufacturing related to the manufacture of the Product in the three months ended March 31, 2023, compared to nil cost of contract manufacturing in the three months ended March 31, 2022.

R&D expenses

R&D expenses for the three months ended March 31, 2023 were $60.8 million, compared to $45.0 million for the same period in 2022. Other research and development expenses are separately classified in the table below. These other expenses are not allocated as they are deployed across multiple projects under development.

	Three months ended March 31,		
	2023	2022	2023 vs 2022
		(in thousands)	
Amyotrophic Lateral Sclerosis (AMT-162)	$ 10,041	$ —	$ 10,041
Temporal lobe epilepsy (AMT-260)	4,320	2,629	1,691
Huntington's disease (AMT-130)	3,733	5,217	(1,484)
Programs in preclinical development and platform related expenses	1,885	1,293	592
Fabry disease (AMT-191)	1,088	630	458
Etranacogene dezaparvovec (AMT-060/061)	667	418	249
Total direct research and development expenses	**$ 21,734**	**$ 10,187**	**$ 11,547**
Employee and contractor-related expenses	18,703	16,164	2,539
Facility expenses	6,786	5,299	1,487
Disposables	3,906	4,533	(627)
Share-based compensation expense	4,305	4,054	251
Other expenses	4,400	2,562	1,838
Fair value changes related to contingent consideration	975	2,204	(1,229)
Total other research and development expenses	**$ 39,075**	**$ 34,816**	**$ 4,259**
Total research and development expenses	**$ 60,809**	**$ 45,003**	**$ 15,806**

Direct research and development expenses

Amyotrophic Lateral Sclerosis caused by mutations in SOD1 (AMT-162)

On January 31, 2023, we announced that we entered into a global licensing agreement with Apic Bio for AMT-162. We have incurred $10.0 million expenses recorded to research and development expense in relation to the

acquisition of assets without an alternative future use during the three-month period ended March 31, 2023. If and when we complete research and development activities for AMT-162 and AMT-162 is approved in the U.S. and Europe, we will expense up to $43.0 million in milestone payments contractually owed to Apic Bio.

Temporal lobe epilepsy (AMT-260)

In the three months ended March 31, 2023 and March 31, 2022, we incurred $4.3 million and $2.6 million respectively, for the preclinical development of temporal lobe epilepsy.

Huntington disease (AMT-130)

In the three months ended March 31, 2023 and March 31, 2022, our external costs for the development of AMT-130 were primarily related to the execution of our Phase I/II clinical trial in the United States and in Europe.

Preclinical programs & platform development

In the three months ended March 31, 2023, and March 31, 2022, we incurred $1.9 million and $1.3 million of costs, respectively, primarily related to our preclinical activities associated with product candidates for various other research programs and technology innovation projects.

Fabry disease (AMT-190)

In the three months ended March 31, 2023 and March 31, 2022, we incurred $1.1 million and $0.6 million of costs, respectively, related to our preclinical activities for the treatment of Fabry disease (AMT-190).

Hemophilia B (AMT-060/061)

We have incurred external costs for our hemophilia B program related to the execution of our Phase III clinical trial and 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. CSL Behring is responsible for the clinical and regulatory activities and commercialization of the Product. However, we managed the existing trials on behalf of CSL Behring until such responsibilities were transitioned to CSL Behring in December 2022. Direct research and development expenses related to clinical development and other regulatory activities and commercialization expenses incurred in the three months ended March 31, 2023 and March 31, 2022 are presented net of reimbursements due from CSL Behring and include settlement amounts from the transition.

Other research & development expenses

- We incurred $18.7 million in personnel and contractor-related expenses in the three months ended March 31, 2023, compared to $16.2 million for the same period in 2022. The increase was primarily a result of an increase in personnel and contractor-related expenses to support our growth;
- We incurred $6.8 million in operating expenses and depreciation expenses related to our rented facilities in the three months ended March 31, 2023, compared to $5.3 million in the same period in 2022. The increase primarily related to additional sites in Lexington which commenced in May and November 2022;
- We incurred $4.4 million of other expenses for the three months ended March 31, 2023, compared to $2.6 million for the same period in 2022. The increase primarily related to contractual payments of $3.1 million we owed to a licensor upon the Europeans Medicines Agency approval of HEMGENIX® in February 2023 partially offset by a reduction in consultant-related expenses;
- We incurred $4.3 million in share-based compensation expenses in the three months ended March 31, 2023, compared to $4.1 million for the same period in 2022;
- We incurred $3.9 million in disposable costs in the three months ended March 31, 2023, compared to $4.5 million for the same period in 2022; and
- We incurred $1.0 million of expenses in the three months ended March 31, 2023 related to an increase in the fair value of contingent consideration associated with the acquisition of Corlieve, compared to $2.2 million for the same period in 2022.

Selling, general and administrative expenses

Selling, general and administrative expenses for the three months ended March 31, 2023 were $17.8 million, compared to $11.0 million for the same period in 2022.

- We incurred $5.9 million in personnel and contractor-related expenses in the three months ended March 31, 2023, compared to $4.4 million in the same period in 2022. The increase was primarily as a result of an increase in personnel and contractor-related expenses to support our growth;
- We incurred $3.7 million in share-based compensation expenses in the three months ended March 31, 2023, compared to $2.8 million in the same period in 2022. The increase was primarily a result of an increase in awards granted, including those to newly recruited personnel as well as an increase in expense related to performance share units; and
- We incurred $3.2 million in professional fees in the three months ended March 31, 2023, compared to $1.1 million in the same period in 2022. We regularly incur accounting, audit and legal fees associated with operating as a public company. The increase from the prior period is primarily related to an increase in professional fees related to our global licensing agreement with Apic Bio.

Other items, net

We recognized $1.3 million in other income from payments received from European authorities to subsidize our research and development efforts in the Netherlands in the three months ended March 31, 2023, compared to $0.0 million for the same period in 2022.

Other items, net for the periods presented primarily related to income from the subleasing of our Amsterdam facility and expenses we incur in relation to the subleasing facility.

Other non-operating items, net

Our other non-operating items, net, for the three months ended March 31, 2023 and 2022 were as follows:

	Three months ended March 31,		
	2023	2022	2023 vs 2022
		(in thousands)	
Interest income	$ 1,669	$ 42	$ 1,627
Interest expense	(3,562)	(2,515)	(1,047)
Foreign currency (losses) / gains, net	(2,369)	8,567	(10,936)
Other non-operating gains	—	692	(692)
Total non-operating (expense) / income, net	**$ (4,262)**	**$ 6,786**	**$ (11,048)**

We recognize interest income associated with our cash and cash equivalents and investment securities. We recognized $1.7 million in interest income in the three months ended March 31, 2023, compared to $0.0 million in the same period in the prior year. Our interest income increased by $1.7 primarily due to the interest income earned on investment securities made during the three months ended December 31, 2022.

We recognized $3.6 million in interest expense for the three months ended March 31, 2023 and $2.5 million for the three months ended March 31, 2022. Our interest expense in 2023 increased due to an increase in market interest rates.

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 recognized a net foreign currency loss, related to our borrowings from Hercules and our cash and cash equivalents and investment securities as well as loans between entities within the uniQure group, of $2.4 million during the three months ended March 31, 2023, compared to a net gain of $8.6 million during the same period in 2022.

We recognized fair value changes related to the derivative financial liability related to a contingent payment due to BMS upon the consummation of a change of control transaction in the period ended March 31, 2022 (nil in the period ended March 31, 2023). As of December 31, 2022, we derecognized the derivative financial liability.

Income tax benefit

We recognized $1.2 million of deferred tax benefit in the three months ended March 31, 2023, and $0.6 million of deferred tax benefit for the same period in 2022.

Financial Position, Liquidity and Capital Resources

As of March 31, 2023, we had cash and cash equivalents, restricted cash and investment securities of $318.5 million. Until such time, if ever, as we can generate substantial cash flows from successfully commercializing our proprietary product candidates, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, royalty monetization financings, distribution, and licensing arrangements. We believe that our cash and cash equivalents will fund our operations into 2025 assuming the achievement of $100.0 million of first commercial sale milestone in the United States and into the first half of 2025 if the $75.0 million of first commercial sale milestone in any of the five contractually defined European countries as of or prior to July 2, 2023 under the CSL Behring Agreement. Our material cash requirements include the following contractual and other obligations:

Debt

As of March 31, 2023, we had an outstanding loan amount owed to Hercules Capital, Inc. ("Hercules") for an aggregate principal amount of $100.0 million. Future interest payments and financing fees associated with the loan total $42.8 million, with $15.4 million payable within 12 months. We are contractually required to repay the $100.0 million in full in December 2025.

Leases

We entered into lease arrangements for facilities, including corporate, manufacturing and office space. As of March 31, 2023, we had fixed lease payment obligations of $58.8 million, with $8.1 million payable within 12 months.

Commitments related to Corlieve acquisition (nominal amounts)

In relation to the Corlieve acquisition, we entered into commitments to make payments to the former shareholders upon the achievement of certain contractual milestones. The commitments include payments related to post-acquisition services that we agreed to as part of the transaction. As of March 31, 2023, our commitment amounts include up to $43.5 million in potential milestone payments through Phase I/II development and $174.0 million in potential milestone payments associated with Phase III development and the approvals of AMT-260 in the United States and European Union. The timing of achieving these milestones and consequently the timing of payments, as well as whether the milestone will be achieved at all, is generally uncertain. These payments are owed in Euro and have been translated at the foreign exchange rate as of March 31, 2023, of $1.09/€1.00. As of March 31, 2023, we expect these obligations will become payable between 2023 and 2031. If and when due, up to 25% of the milestone payments can be settled with our ordinary shares.

Commitments related to licensors and financial advisors

We 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) or as a result of collecting payments related to our sale of the exclusive global rights to the Product to CSL Behring. We also owe payments to a financial advisor related to any payments we will collect under the CSL Behring Agreement.

The table below summarizes our consolidated cash flow data for the three months ended:

	Three months ended March 31,	
	2023	2022
	(in thousands)	
Cash, cash equivalents and restricted cash at the beginning of the period	$ 231,173	$ 559,353
Net cash used in operating activities	(78,302)	(25,711)
Net cash generated from / (used in) investing activities	2,988	(4,880)
Net cash generated from financing activities	131	485
Foreign exchange impact	1,034	(1,168)
Cash, cash equivalents and restricted cash at the end of period	**$ 157,024**	**$ 528,079**

We had previously 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, with the exception of generating income in 2021 after receiving the upfront payment upon Closing of the CSL Behring Agreement. We continue to incur losses in the current period. We recorded a net loss of $77.2 million in the three months ended March 31, 2023, compared to a net loss of $46.7 million during the same period in 2022. As of March 31, 2023, we had an accumulated deficit of $659.2 million.

Sources of liquidity

From our first institutional venture capital financing in 2006 through the current period, 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. In May 2021, we received a $462.4 million cash payment due from CSL Behring upon Closing. We have collected $55.0 million related to CSL Behring's global regulatory submissions for etranacogene dezaparvovec in March and April 2022, and are eligible to receive additional milestone payments, as well as royalties on net sales from CSL Behring.

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. We did not issue ordinary shares under the Sales Agreement for the three months ended March 31, 2023 and March 31, 2022.

We are subject to certain covenants under our December 2021 amendment with Hercules Capital, Inc ("2021 Restated 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 2021 Restated Facility may limit our ability to obtain debt financing. The 2021 Restated Facility permits us to issue up to $500.0 million of convertible debt as well as to enter into a transaction to sell the royalties under the CSL Behring agreement subject to certain conditions.

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, royalty monetization financings, 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 $78.3 million for the three months ended March 31, 2023 and consisted of net loss of $77.2 million adjusted for non-cash items, including depreciation and amortization expense of $2.5 million, share-based compensation expense of $8.1 million, changes in the fair value of contingent consideration of $1.0 million, unrealized foreign exchange losses of $1.2 million and a change in deferred taxes of $1.2 million. Net cash generated from operating activities also included unfavorable changes in operating assets and liabilities of $12.2 million. There was a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $0.9 million. These changes also relate to a net decrease in accounts payable, accrued expenses, other liabilities, and operating leases of $10.7 million, primarily related to a decrease of $7.9 million from personnel related accruals.

Net cash used in operating activities was $25.7 million for the three months ended March 31, 2022 and consisted of a net loss of $46.7 million adjusted for non-cash items, including depreciation and amortization expense of $2.1 million, share-based compensation expense of $6.9 million, changes in the fair value of contingent

consideration and the derivative financial liability of $1.5 million, unrealized foreign exchange gains of $7.4 million and a change in deferred taxes of $0.6 million. Net cash generated from operating activities also included favorable changes in operating assets and liabilities of $18.4 million. There was a net decrease in accounts receivable and contract asset, prepaid expenses, and other current assets and receivables of $17.2 million, primarily related to the collection of $20.0 million of the contract asset related to CSL milestones of $55.0 million in March 2022. These changes also relate to a net increase in accounts payable, accrued expenses, other liabilities, and operating leases of $1.2 million.

Net cash generated from / (used in) investing activities

In the three months ended March 31, 2023, we generated $3.0 million in our investing activities compared to using $4.9 million for the same period in 2022.

	Three months ended March 31,	
	2023	2022
	(in thousands)	
Proceeds from maturity of investment securities	$ 5,330	$ —
Build out of Amsterdam site	(686)	(3,740)
Build out of Lexington site	(1,656)	(318)
Acquisition of Corlieve, net of cash acquired	—	(822)
Total investments	**$ 2,988**	**$ (4,880)**

During the three months ended March 31, 2023, we received $5.3 million from the repayment of investment securities (nil for three months ended March 31, 2022).

The build out of the Amsterdam site and Lexington site consumed $0.7 million and $1.7 million cash respectively during the three months ended March 31, 2023, compared to $3.7 million and $0.3 million for the same period in 2022.

We paid EUR 0.9 million ($0.9 million) to acquire remaining outstanding shares of Corlieve in February 2022 (nil in current period).

Net cash generated from financing activities

In the three months ended March 31, 2023, we generated $0.1 million from financing activities compared to $0.5 million for the same period in 2022.

	Three months ended March 31,	
	2023	2022
	(in thousands)	
Cash flows from financing activities		
Proceeds from issuance of shares related to employee stock option and purchase plans	$ 131	$ 485
Net cash generated from financing activities	**$ 131**	**$ 485**

During the three months ended March 31, 2023, we received $0.1 million from the exercise of options to purchase ordinary shares in relation to our share incentive plans compared to $0.5 million for the same period in 2022.

Funding requirements

Our future capital requirements will depend on many factors, including but not limited to:

- contractual milestone payments and royalties we might be owed in accordance with the CSL Behring Agreement;
- earnout payments we might owe the former shareholders of Corlieve, which are subject to the achievement of specific development and regulatory milestones;
- the scope, timing, results, and costs of our current and planned clinical trials, including those for AMT-130 in Huntington's disease;
- the scope of any equity, debt or royalty monetization financings;

- 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 manufacturing products for CSL Behring;
- 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 costs associated with maintaining quality compliance and optimizing our manufacturing processes, including the operating costs associated with our Lexington, Massachusetts manufacturing facility; and
- the costs associated with increasing the scale and capacity of our manufacturing capabilities.

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 the 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, 2023, have not materially changed from our market risks and our exposure to market risk discussed in Part II, Item 7A of our Annual Report.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer ("CEO") and chief financial officer ("CFO"), evaluated the effectiveness of our disclosure controls and procedures (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, 2023. Based on such evaluation, our CEO and CFO concluded that as of March 31, 2023, 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 2023, 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.

Part II – OTHER INFORMATION

Item 1. Legal Proceedings

None.

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, 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 have encountered, and may continue to encounter, delays in, and impediments to the progress of our clinical trials or failure to demonstrate the safety and efficacy of our product candidates.
- We may not be successful in our efforts to use our gene therapy technology platform to build a pipeline of additional product candidates, and we may not be successful in our efforts to create innovative programs, platform technologies or other technologies to be competitive with others.
- We may not be successful in our efforts to in-license or acquire product candidates that align with our research and development strategy, and any such transactions may not achieve the expected cash flows or could result in additional costs and challenges.
- 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.
- 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 also have experienced and could continue to experience increased competition for, and compensation expenses associated with employee recruiting and employee retention, which could adversely affect our business.
- 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 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 and other proprietary technology, which could increase the possibility that a competitor will discover them or that our trade secrets and other proprietary technology 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. The amount of capital required will depend in part on the future payments we receive from CSL Behring related to HEMGENIX® royalties, commercial supply, and

contractual milestones, including a $75.0 million payment that CSL Behring would owe on the occurrence of a first sale of HEMGENIX® in the European Union prior to July 2, 2023.

- Our relationships with employees, customers, and third parties are subject to applicable laws and regulations, the non-compliance of any of which could 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.
- Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches or other errors or disruptions, which could result in a material disruption of our product development programs, such as potential issues with data integrity or loss of data.
- 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.
- Our business, operations and supply chain have been, and may continue to be, materially and adversely affected by the ongoing Covid pandemic.

Risks Related to the Development of Our Product Candidates

Our product candidates in development have not yet 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.

Our pipeline consists of product candidates in research or development that have not been approved for commercial sale. We have not generated any revenues from the sale of products or manufacturing of a product for a third party related to our product candidates in development and do not expect to generate any such revenue this year. 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 have encountered and may encounter future 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.

For example, we experienced an immaterial but unexpected delay when our clinical trials of HEMGENIX® were placed on clinical hold by the FDA from December 2020 to April 2021, following a preliminary diagnosis of hepatocellular carcinoma in one patient. Similarly, we experienced an unexpected delay in the enrollment of our Phase Ib/II clinical trial for Huntington's disease between July and October 2022 as a result of our voluntary postponement and comprehensive safety investigation into suspected unexpected serious adverse reactions in three patients.

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;
- changes in standards of care which may necessitate the modification of our clinical trials or the conduct of new 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;
- recommendations from DSMBs to discontinue, pause, or modify the trial;
- 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;
- 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 paying 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 emergence 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 (such as the EU Clinical Trials Regulation), 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 in 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 U.S. 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 or 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.

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.

Fast track product, breakthrough therapy, priority review, or 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. An 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. Moreover, in the U.S., FDA expects that sponsors with products under these programs will be prepared for a more rapid pace of development, including with respect to manufacturing or any combination medical devices, such as companion diagnostics. If we are unable to meet these expectations, we may not be able to fully avail ourselves of certain advantages of these programs.

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), etranacogene dezaparvovec, and AMT-130. 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 or otherwise being dependent upon additional regulatory approvals. 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.

It is possible that our product candidates would be 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 could be materially harmed.

Our manufacturing facility in Lexington is subject to ongoing regulation and periodic inspection by the FDA, EU member state, and other regulatory bodies to ensure compliance with current cGMP requirements. 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, EU member state, 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, EMA, EU and other regulatory authority 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, which may result in delays in regulatory approvals, inability to produce sufficient amounts of commercial product, 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, war or cases of force majeure and acts of god (including the effects of the Covid 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 U.S. 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 and methods, or develop new processes and methods to meet our product supply needs and obligations.

The manufacture of our AAV gene therapies 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 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 gene therapy product candidates we will need to complete the validation of our manufacturing processes and methods, and we may need to develop and validate new or larger scale manufacturing processes and methods. If we are unable to consistently manufacture our gene therapy product candidates or any approved products in accordance with our pre-specified quality parameters and applicable regulatory standards, it could adversely impact our ability to validate our manufacturing processes and methods, to meet our production needs, to file a 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.

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 U.S., 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 U.S., 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 may also be delayed in completing their review of any marketing applications submitted by us or our partners. 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.

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 U.S., 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 U.S. or EU, 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 U.S., there have been a number of recent changes relating to gene therapy development. By example, FDA issued a number of new guidance documents, and continues to issue guidance documents, on human gene therapy development, one of which was specific to human gene therapy for hemophilia, one that was specific to neurodegenerative diseases, 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 U.S. 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 U.S. 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 U.S., 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 U.S. 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. Moreover, in the U.S. the exact scope of orphan exclusivity is currently uncertain and evolving due to a recent court decision.

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 U.S., whether two gene therapies are considered to be the same for the purpose of determining clinical superiority was recently updated via a final guidance document specific to gene therapies, and depends on a number of factors, including the expressed transgene, the vector, and other product or product candidate features. Depending on the products, whether two products are ultimately considered to be the same may be determined by FDA on a case-by-case basis, making it difficult to make predictions regarding when the FDA might be able to make an approval of a product effective and whether periods of exclusivity will effectively block competitors seeking to market products that are the same or similar to ours for the same intended use. 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 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 U.S., this could mean that a competing biosimilar product may be able to apply to the FDA and obtain approval either as a biosimilar to one of our products or even as an interchangeable product. 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 judgment. 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 U.S. period of exclusivity to a shorter timeframe. Future proposed budgets, international trade agreements and other arrangements or proposals may affect periods of exclusivity.

If any of our product candidates receive regulatory approval, we and/or our partners will be subject to extensive regulatory requirements. Failure to fulfill and comply with the applicable regulatory requirements could result in regulatory enforcement actions that would be detrimental to our business.

Following any regulatory approval, the FDA and the EMA may impose certain post-approval requirements related to a product. Specifically, any approved products will be subject to continuing and comprehensive regulation concerning the product's design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution. Regulatory authorities may also require post-marketing testing, known as Phase 4 testing, a risk evaluation and mitigation strategy, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Failure to comply with any of these requirements could result in regulatory, administrative, or other enforcement action, that would be detrimental to our business.

For instance, the FDA and other government agencies closely regulate the post-approval marketing and promotion of approved products, including off-label promotion, industry-sponsored scientific and educational activities, and the Internet and social media. Approved products may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Failure to comply with regulatory promotional standards could result in actions being brought against us by these agencies.

Moreover, if a company obtains FDA approval for a product via the accelerated approval pathway, the company would be required to conduct a post-marketing confirmatory trial to verify and describe the clinical benefit in support of full approval. FDA can require that this confirmatory trial be commenced prior to FDA granting a product accelerated approval. An unsuccessful post-marketing study or failure to complete such a study could result in the expedited withdrawal of the FDA's marketing approval for a product using a statutorily defined streamlined process.

Changes to some of the conditions established in an approved application, including changes in labeling, indications, manufacturing processes or facilities, may require a submission to and approval by the FDA or the EMA, as applicable, before the change can be implemented. A New Drug Application ("NDA")/BLA or MAA supplement for a new indication typically requires clinical data similar to that in the original application. The applicable regulatory authorities would review such supplement using similar procedures and actions as in reviewing NDAs/BLAs and MAAs.

Adverse event reporting and submission of periodic reports is required following marketing approval. Regulatory authorities may withdraw product approvals or request product recalls, as well as impose other enforcement actions, if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

In addition, the manufacture, testing, packaging, labeling, and distribution of products after approval will need to continue to conform to cGMPs. Drug and biological product manufacturers and certain of their subcontractors are subject to periodic unannounced inspections by the FDA or the EMA for compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. In addition, prescription drug manufacturers in the U.S. must comply with applicable provisions of the Drug Supply Chain Security Act and provide and receive product tracing information, maintain appropriate licenses, ensure they only work with other properly licensed entities and have procedures in place to identify and properly handle suspect and illegitimate products.

Where we partner with third parties for the development, approval, and marketing of a product, such third parties will be subject to the same regulatory obligations as we will. However, as we will not control the actions of the applicable third parties, we will be reliant on them to meet their contractual and regulatory obligations. Accordingly, actions taken by any of our partners could materially and adversely impact our business.

Risks Related to Commercialization

If we, or our commercial partner, 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 revenues from HEMGENIX® or any other product will depend on the successful development and eventual commercialization of our product candidates. The success of HEMGENIX® or other product candidates will depend on many factors, including:

- successful execution of our contractual relationship with CSL Behring for the commercialization of HEMGENIX®;
- 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 HEMGENIX® and other products according to required quality specifications;
- obtaining and maintaining patent and trade secret protection and non-patent, exclusivities for our product candidates;
- 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 of HEMGENIX® and other products;
- any price concessions, rebates, or discounts we may need to provide;
- complying with any applicable post-approval commitments and 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.

CSL Behring may not facilitate a first commercial sale in the European Union prior to July 2, 2023, and we may not receive the $75.0 million first commercial sale milestone in any of the five contractually defined European countries prior to July 2, 2023 under the CSL Behring Agreement unless the CSL Behring Agreement is amended.

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.

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 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 U.S., 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. Public and medical community adoption of any of our gene therapies will also depend on factors including the ease of administration in comparison to other therapeutics. By example, the need for complex surgeries for the administration of a product candidate may impact the acceptance of a product.

In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product and product candidates, prescribing treatments that involve the use of our product and product candidates, 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, or our commercial partner, obtain approval to commercialize any of our product candidates outside of the U.S., 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 U.S., 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 U.S.;
- 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 U.S.;
- 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.

In February 2022, armed conflict escalated between Russia and Ukraine. The sanctions announced by the U.S. and other countries following Russia's invasion of Ukraine against Russia to date include restrictions on selling or importing goods, services or technology in or from affected regions and travel bans and asset freezes impacting connected individuals and political, military, business and financial organizations in Russia. The U.S. and other countries could impose wider sanctions and take other actions should the conflict further escalate. It is not possible to predict the broader consequences of this conflict, which could include further sanctions, embargoes, regional instability, geopolitical shifts and adverse effects on macroeconomic conditions, currency exchange rates and financial markets, all of which could impact our business, financial condition and results of operations.

We may be adversely affected by the effects of inflation.

Inflation has the potential to adversely affect our liquidity, business, financial condition and results of operations by increasing our overall cost structure. The existence of inflation in the economy has resulted in, and may continue to result in, higher interest rates and capital costs, shipping costs, supply shortages, increased costs of labor, weakening exchange rates and other similar effects. As a result of inflation, we have experienced and may continue to experience, cost increases. Although we may take measures to mitigate the impact of this inflation, if these measures are not effective our business, financial condition, results of operations and liquidity could be materially adversely affected. Even if such measures are effective, there could be a difference between the timing of when these beneficial actions impact our results of operations and when the cost inflation is incurred.

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 face worldwide competition from larger pharmaceutical companies, specialty pharmaceutical companies and biotechnology firms, universities and other research institutions and government agencies that are developing and commercializing pharmaceutical products. Our key competitors focused on developing therapies in various indications, include among others, Pfizer, Freeline Therapeutics, Intellia Therapeutics, Sangamo Biosciences, Voyager

Therapeutics, Passage Bio, Roche, PTC Therapeutics, Prilenia Therapeutics, CombiGene, Caritas Therapeutics, Alnylam, Wave Life Sciences, Bayer AG, Amicus Therapeutics and 4D Molecular Therapeutics.

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 the 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 large part on our ability to obtain and maintain this protection in the U.S., 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. Patents we own currently are and may become subject to future patent opposition or similar proceedings. For example, we are currently defending a patent case in each of Canada, the United Kingdom, and the US and have filed Notices of Appeal at the CAFC contesting three FWDs. These oppositions and future patent oppositions 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 U.S.. 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 U.S. 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 U.S. 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 U.S. 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.

In addition, legal proceedings relating to intellectual property claims, with or without merit, are unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

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 U.S. 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 U.S. 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 Business Development

Our business development strategy may not produce the cash flows expected or could result in additional costs and challenges.

Any business development transaction could expose us to unknown liabilities and risks, and we may incur additional costs and expenses necessary to address an acquired company's failure to comply with laws and governmental rules and regulations. We could incur additional costs related to resources to align our business practices and operations. Moreover, we cannot assure that the anticipated benefits of any acquisition would be realized in a timely manner, if at all.

Risks Related to Pricing and Reimbursement

We, and our commercial partner, face uncertainty related to insurance coverage of, and pricing and reimbursement for HEMGENIX® and other 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 U.S. 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 ("MFN") 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. While this rule has now been rescinded, government negotiation of certain Medicare drug pricing continues to be the focus of recent proposed legislation.

The pricing review period and pricing negotiations for new medicines take considerable time and have uncertain results. Pricing review and negotiation usually begin 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 HEMGENIX® and other 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 had a loss in the year ended December 31, 2022, incurred significant losses in previous years and expect to incur losses during the current and over the next several years and may never achieve or maintain profitability.

We had a net loss of $77.2 million in the three months ended March 31, 2023, and a net loss of $126.8 million in the full year 2022. As of March 31, 2023, we had an accumulated deficit of $659.2 million. In the past, 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 expect to finance our operations in 2023 and 2024 primarily from our existing cash resources including payments we collected and expect to collect in relation to the CSL Behring Agreement. 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.

We anticipate that our expenses will increase for the foreseeable future and will include costs related to:

- advancing AMT-130 for our Huntington's disease gene therapy program into phase III clinical study;
- advancing our gene therapy programs for rTLE, SOD1-ALS and Fabry disease into Phase I/II clinical studies;
- potentially acquiring or in-licensing rights to new therapeutic targets, product candidates and technologies;
- making potential future milestone payments related to the acquisition of Corlieve, if any
- advancing preclinical research and development for gene therapy product candidates targeting other diseases; and
- continuing to invest in expanding, developing and optimizing our manufacturing capabilities and other enabling technologies, such as next-generation viral vectors, promoters and re-dosing.

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 ongoing activities and 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 under our 2021 Restated Facility with Hercules Capital Inc. ("Hercules") that we entered into on December 15, 2021 when the Company and Hercules amended and restated the 2021 Amended Facility (the "2021 Restated Facility") 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, 2023, we had $100.0 million of outstanding principal of borrowings under the 2021 Restated Facility, which we are required to repay in full in December 2025. 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 2021 Restated 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 employees, customers and third parties are subject to applicable laws and regulations, the non-compliance of any of which could have a material adverse effect on our business, financial condition, and results of operations.

Healthcare providers, physicians, other practitioners, 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 U.S. and international 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 from participation in government funded healthcare programs and the curtailment or restructuring of our operations.

Additionally, we are subject to various labor and employment laws and regulations. These laws and regulations relate to matters such as employment discrimination, wage and hour laws, requirements to provide meal and rest periods or other benefits, family leave mandates, employee and independent contractor classification rules, requirements regarding working conditions and accommodations to certain employees, citizenship or work authorization and related requirements, insurance and workers' compensation rules, healthcare laws, scheduling notification requirements and anti-discrimination and anti-harassment laws. Complying with these laws and regulations, including ongoing changes thereto, subjects us to substantial expense and non-compliance could expose us to significant liabilities. In particular, we are subject to allegations of Sarbanes-Oxley whistleblower retaliation and employment discrimination and retaliation, and we may in the future be subject to additional claims of non-compliance with similar or other Laws and regulations.

The costs associated with a violation of any of the foregoing 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, imposes 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 10,000,000 per occurrence. 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 U.S., 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, Congress subsequently has extended the period over which these reductions are in effect. While President Biden previously signed legislation temporarily to eliminate this reduction through the end of 2021, recent legislation will restart the reductions, which will thereafter remain in effect through 2031 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 pricing and the reimbursement our customers may receive for our products, and increased manufacturer rebates. 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 future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize current or future drug candidates in foreign markets for which we may rely on collaborations with third parties. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials, manufacturing, commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions.

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 might increase our vulnerability to the above risk.

While we have experienced and addressed system failures, cyber-attacks, and security breaches in the past, 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. 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.

Climate change, environmental, social and governance and sustainability initiatives may result in regulatory or structural industry changes that could require significant operational changes and expenditures, reduce demand for the Company's products and adversely affect our business, financial condition, and results of operations.

Greenhouse gases may have an adverse effect on global temperatures, weather patterns, and the frequency and severity of extreme weather and natural disasters. Such events could have a negative effect on our business. Concern over climate change may result in new or additional legislative and regulatory requirements to reduce or mitigate the effects of climate change on the environment, which could result in future tax, transportation cost, and utility increases. Moreover, natural disasters and extreme weather conditions may impact the productivity of our facilities, the operation of our supply chain, or consumer buying patterns. Any of these risks could have a material adverse effect on our business.

Climate change, environmental, social and governance and sustainability initiatives may result in regulatory or structural industry changes that could require significant operational changes and expenditures, reduce demand for the Company's products and adversely affect our business, financial condition, and results of operations.

Climate change, environmental, social and governance and sustainability are a growing global movement. Continuing political and social attention to these issues has resulted in both existing and pending international agreements and national, regional and local legislation, regulatory measures, reporting obligations and policy changes. Also, there is increasing societal pressure in some of the areas where we operate, to limit greenhouse gas emissions as

well as other global initiatives. These agreements and measures, including the Paris Climate Accord, may require, or could result in future legislation, regulatory measures or policy changes that would require operational changes, taxes, or purchases of emission credits to reduce emission of greenhouse gases from our operations, which may result in substantial capital expenditures.

Furthermore, increasing attention to climate change, ESG and sustainability has resulted in governmental investigations, and public and private litigation, which could increase our costs or otherwise adversely affect our business or results of operations. In addition, organizations that provide information to investors on corporate governance and related matters have developed ratings processes for evaluating companies on their approach to ESG matters. Such ratings are used by some investors to inform their investment and voting decisions. Unfavorable ESG ratings may lead to increased negative investor sentiment toward us, which could have a negative impact on the price of our securities and our access to and costs of capital.

Any or all of these ESG and sustainability initiatives may result in significant operational changes and expenditures, reduced demand for our products, cause us reputational harm, and could materially adversely affect our business, financial condition, and results of operations.

Risks Related to Employee Matters and Managing Growth

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

Our future growth and success will depend in large part on our continued ability to attract, retain, manage and motivate our employees. The loss of the services of any member of our senior management or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results. 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.

The competition for qualified personnel in the pharmaceutical field is intense, and there is a limited pool of qualified potential employees to recruit. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our business may be harmed and our growth strategy may be limited.

Additionally, we are reliant on our employees, contractors, consultants, vendors and other parties with whom we have relationships to behave ethically and within the requirements of the law. The failure of any employee or other such third parties to act within the bounds of the applicable laws, regulations, agreements, codes and other requirements, or any misconduct or illegal actions or omissions by such persons, could materially damage our business.

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 4, 2023, 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 4, 2023, was $21.15 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 EU, the U.S., 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 38.8% of our issued shares (including such shares to be issued in relation to exercisable options to purchase ordinary shares) as of March 31, 2023. 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 those 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 consequences 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 and 2022 but not for 2017 through 2021. A corporation organized outside the U.S. 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 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 U.S. As a result, it may not be possible for shareholders to effect service of process within the U.S. 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 U.S. 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 U.S. 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 U.S, 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 U.S. 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 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 actions that would be different than those that would be taken by a company organized under the law of some U.S. jurisdictions.

Risks Related to the Current Covid Pandemic

Our business, operations, human resources and supply chain have been, and may continue to be, materially and adversely affected by the ongoing Covid pandemic.

On March 11, 2020, the World Health Organization ("WHO") declared the ongoing outbreak of coronavirus disease ("Covid") a pandemic. The Covid pandemic is affecting the U.S. and global economies and has affected and may continue to affect our operations and those of third parties on which we rely. The Covid 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 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.

Global supply chains have been disrupted, causing shortages, which could further impact our clinical trials. This disruption of our employees, distributors and suppliers has historically impacted and may continue to impact our future operating results. Additionally, to the extent that inspections of facilities by governmental authorities are required, the review of our marketing applications or supplements may further be delayed as regulatory authorities, such as FDA, have significantly limited facility inspections during the pandemic.

Any such requirements or guidelines that we adopt could have a material impact on our business operations.

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

10.1*t	† Consulting Agreement, effective March 31, 2023, by and between uniQure, Inc., and Alex Kuta
31.1*	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer
31.2*	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer
32.1±	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101*	The following financial information from our Quarterly Report on Form 10-Q for the period ended March 31, 2023, filed with the Securities and Exchange Commission on May 9, 2023, 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, 2023, filed with the Securities and Exchange Commission on May 9, 2023, is formatted in Inline Extensible Business Reporting Language ("iXBRL")

† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission

* Filed herewith.

± Furnished herewith.

t Indicates a management contract or compensatory plan or arrangement

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 Officer)

By: /s/ Christian Klemt

Christian Klemt
Chief Financial Officer
(Principal Financial Officer)

Dated May 9, 2023

Exhibit 10.1

CONSULTING AGREEMENT

THIS CONSULTING AGREEMENT (the "Agreement"), made this March 31, 2023 (the "Effective Date"), is entered into by uniQure, Inc., a Delaware corporation with its principal place of business at 113 Hartwell Ave., Lexington, Massachusetts, 02421 (the "Company"), and Alex Kuta, an individual residing at [REDACTED] (the "Consultant" or the "Regulatory Consultant").

INTRODUCTION

WHEREAS, Consultant has served as the Company's Chief Regulatory officer until his retirement as of the Effective Date of this Agreement; and

WHEREAS, the Company and the Consultant desire to establish the terms and conditions under which the Consultant will provide transition services to the Company to assist with the transition of the Company following Consultant's retirement;

NOW THEREFORE, in consideration of the mutual covenants and promises contained herein and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by the parties hereto, the parties agree as follows:

1. Services. The Consultant shall have the title "Regulatory Consultant" and agrees to perform such advisory and related services related to the Company's regulatory affairs and to the transition of the organization of the Company following the retirement of Consultant, as may reasonably be requested from time to time by the Company (the "Services").

2. Term.

2.1 This Agreement shall commence effective as of the close of business on the date hereof (the "Effective Date") and shall expire at the close of business on March 31, 2024, unless sooner terminated in accordance with the provisions of Section 3 (the "Term").

2.2 As of the close of business on the Effective Date, Consultant has resigned his employment with Company, including any and all roles as an employee, officer and director of Company and each of Company's affiliates, and his employment agreement dated on or about August 20, 2019 is terminated, subject to any provisions that survive termination.

3. Termination. Either party may, without prejudice to any right or remedy it may have due to any failure of the other party to perform its obligations under this Agreement, terminate this Agreement upon written notice to the other party. In the event of such termination, the Consultant shall be entitled to payment hereunder and for expenses paid or incurred prior to the effective date of termination. Such payments shall constitute full settlement of all claims of the Consultant of every description against the Company.

4. Compensation.

4.1 Consideration.

(a) Consulting Fees. The Company shall pay to the Consultant consulting fees of fifteen thousand dollars ($15,000) per month (one hundred eighty thousand dollars ($180,000) total), which Company may pay in weekly installments of $3,461.54 or pursuant to another equivalent payment schedule. Payment shall be made by means reasonably determined by Company in its sole discretion and are subject to the termination provisions of Section 3. The parties represent and warrant that, to the best of their knowledge, the compensation constitutes fair market value for the Services.

(b) Treatment of Existing Equity Awards. This Agreement is intended to be effective immediately upon termination of the Consultant's Employment Agreement dated on or about August 20, 2019 such that the Consultant's contractual relationship with the Company is continuous and Consultant remains eligible to participate in the 2014 Share Incentive Plan of uniQure N.V., including continued vesting of any equity awards or grants in effect as of the Effective Date.

(c) Health Insurance. Provided Consultant is eligible and elects to continue receiving group medical and/or dental insurance pursuant to the federal "COBRA" law following the Effective Date, Company shall pay the cost of such coverage for Consultant and his spouse for the period from April 1, 2023 through March 31, 2024.

4.2 Reimbursement of Expenses. The Company shall reimburse the Consultant for all reasonable and necessary expenses incurred or paid by the Consultant and approved by the Company in connection with, or related to, the performance of his or her services pursuant to this Agreement, subject to the receipt of copies of invoices or receipts therefor for reasonable meals, accommodations, and travel expenses, including economy class airfare, and first-class train ticket. The Consultant shall submit to the Company an itemized statement, in a form satisfactory to the Company, of such expenses incurred in relation to the performance of the Services. The Company shall pay the Consultant the amount shown on such statement within 30 days after receipt thereof. All expenses shall be submitted and paid in accordance with the Company's travel and expense policies, which may be amended from time to time in the Company's sole discretion.

4.3 Benefits and Taxes. The Consultant shall not be entitled to any benefits, coverages, or privileges, including, without limitation, social security, unemployment, medical or pension payments, made available to employees of the Company.

5. Cooperation. The Consultant shall use his or her best efforts in the performance of his or her obligations under this Agreement. The Company shall provide such access to its information and property as may be reasonably required to permit the Consultant to perform his or her obligations hereunder. The Consultant agrees to declare in an appropriate way that he or she is a consultant to the Company whenever he or she writes or speaks in public about the Company or on any issue relating to the Company.

6. Proprietary Information and Personal Data.

6.1 Proprietary Information.

(a) The Consultant acknowledges that his or her relationship with the Company is one of high trust and confidence and that during his or her service to the Company he will have access to and contact with Proprietary Information. The Consultant agrees that he or she will not, during the Term or at any time, thereafter, disclose to others, or use for his or her benefit or the benefit of others, any Proprietary Information.

(b) For purposes of this Agreement, Proprietary Information shall mean, confidential, non-public and or proprietary business, clinical, technical and other information owned by or in the possession, custody or control of Company, including, without limitation, formula, vendor information, customer information, apparatus, equipment, trade secret, process, research, report, clinical data, technical data, assays, know-how, computer program, software, software documentation, hardware design, technology, marketing or business plan, forecast, unpublished financial statement, budget, license, price, cost and employee list that is communicated to, learned of, developed or otherwise acquired by the Consultant in the course of his or her service as a consultant to the Company. Company shall own any intellectual property generated using the Proprietary Information of Company.

(c) The Consultant's obligations under this Section 6.1 shall not apply to any information that (i) is or becomes known to the general public under circumstances involving no breach by the Consultant or others of the terms of this Section 6.1, (ii) is generally disclosed to third parties by the Company without restriction on such third parties, (iii) is approved for release by written authorization of the Board of Directors of the Company, (iv) was known to Consultant before the consulting services were performed, or (v) Consultant is required to disclose by law, government regulation, or court order.

(d) The Consultant represents that his or her retention as a consultant with the Company and his or her performance under this Agreement does not, and shall not, breach any agreement that obligates him or her to keep in confidence any trade secrets or confidential or proprietary information of his or her or of any other party or to refrain from competing, directly or indirectly, with the business of any other party. The Consultant shall not disclose to the Company any trade secrets or confidential or proprietary information of any other party.

(e) Despite any obligation to protect Company's Proprietary Information, this Agreement places no restrictions on the Consultant's freedom to disclose to anyone (including but not limited to patients and employers) the existence or terms of this Agreement, of the type of services Consultant performs for Company, or the amount of compensation that Consultant receives under this Agreement. This provision, Section 6, shall survive termination or expiration of this Agreement for a period of seven (7) years.

6.2 Personal Data

(a) Company processes the following personal data of its contractual partners: name, field of expertise, BIG registration number, place of work, total compensation

paid under this Agreement, hourly rate, past experience of the Company with Consultant. These personal data will be processed for administrative, statistical, information and marketing purposes in accordance with the applicable legal provisions on data protection. Personal data of its contractual partners are used exclusively for these purposes by the Company, its members of the uniQure group and their employees. The use includes the transfer of data to other entities of the Company thereby including those companies which are located outside of the EEA where the legal protection of personal data may not be the same as in the Netherlands. Consultant consents to the onward transfer and use of the Consultant's personal data to other entities of the uniQure group of companies located in the United States of America. Consultant is free to withdraw his consent at any time. With respect to his personal data, Consultant always has the right to access his personal data, and, in the event the data are incorrect or irrelevant considering the purposes of processing, the right to request correction, removal or blocking thereof as well as the right to raise objections against a processing of those data. Requests may be submitted to uniQure biopharma B.V., attn. Legal Counsel, Paasheuvelweg 25A, 1105 BP, Amsterdam.

(b) In case the Services allow the Consultant access to data as defined in the applicable data protection legislation ("personal data"), the Consultant shall at all times:

- collect and process personal data in accordance with the provisions of this Agreement or as otherwise instructed by Company from time to time;
- ensure that any personal data relating to individuals other than the categories of data specified in the specifications of the Services will not be collected;
- collect and process personal data solely for the purposes of the Services and in the manner specified in the specifications of the Services and not further to process such data in any other manner;
- collect and process personal data fairly and lawfully;
- not disclose personal data to any third party without the prior permission in writing of the Company, or where such disclosure is required by any local law, regulation or supervisory authority in which case Consultant will, wherever possible, notify the Company prior to complying with any such request for disclosure and shall comply with all reasonable directions of the Company with respect to such disclosure;
- ensure that all personal data are accurate and, where necessary, kept up to date and use best efforts to ensure that trial data which are inaccurate or incomplete are erased or rectified;
- comply with all written instructions issued by the Company to de-identify the personal data from time to time;
- ensure that the Company is notified promptly (and in any event within five days of receipt) of any communication received from a subject relating to subject access rights; and
- ensure that the technical and organizational measures specified in the specifications of the Services are taken to protect personal data against accidental or unlawful destruction or accidental loss or damage, alteration,

unauthorized disclosure, or access and against all other unauthorized disclosure or access and against all other unauthorized or unlawful forms of processing.

- Assist Company in complying with any applicable security breach notification duties and shall report any breach of security leading to the accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to, personal data transmitted, stored, or otherwise processed to the applicable authority without Company's prior written approval.

7. Representations.

7.1 The Company and Consultant declare that this Agreement is in no way associated with any business or sales activities between the parties hereto and, in particular, Consultant is by no means obligated to prescribe, recommend, or purchase any goods from the Company.

7.2 The Consultant represents and warrants that the performance of Services pursuant to this Agreement does not represent an infringement of his or her employment obligations and that it is in accordance with the statutory and internal regulations of his or her employer and all other statutory or other regulations. In the event of a conflict or potential conflict, the Consultant must disclose any actual or potential conflict to Company, and the parties will reasonably cooperate to resolve any such conflict. If either party reasonably believes that the conflict cannot be resolved, that party may terminate this Agreement, and no further services shall be performed.

7.3 The Consultant will perform the Services in accordance with generally accepted professional standards as well as standards designated by the Company. The Consultant shall perform all work performed as part of the contractual relationship with the Company in a manner consistent with all applicable laws, regulations and standards including all applicable anti-bribery and antitrust laws. The Consultant has not made or provided, and will not make or provide, any payment or benefit, directly or indirectly, to government officials, customers, business partners, healthcare professionals or any other person to secure an improper benefit or unfair business advantage, affect private or official decision-making, affect prescription behavior, or induce someone to breach professional duties or standards.

7.4 The Consultant will immediately report to the Company in writing any suspected or detected violation of the above principles in connection with the Company's business and, in such cases, will cooperate fully with the Company in reviewing the matter. If the Company believes, in good faith, that the Consultant has violated any of the above principles, the Company shall have the unilateral right to terminate the contractual relationship with immediate effect.

7.5 The Consultant hereby represents that, except as the Consultant has disclosed in writing to the Company, the Consultant is not bound by the terms of any agreement with any third party to refrain from using or disclosing any trade secret or confidential or proprietary information in the course of his or her consultancy with the Company, to refrain from

competing, directly or indirectly, with the business of such third party or to refrain from soliciting employees, customers or suppliers of such third party. The Consultant further represents that his or her performance of all the terms of this Agreement and the performance of the services as a consultant of the Company do not and will not breach any agreement with any third party to which the Consultant is a party (including, without limitation, any nondisclosure or non-competition agreement), and that the Consultant will not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any current or previous employer or any other party.

7.6 Consultant hereby acknowledges that it, and any of its representatives, if applicable, will have access to material non-public information concerning the Company. Consultant acknowledges that he, and any of his or her representatives, if applicable, are aware, that the United States or other applicable securities laws prohibit any person, who has received from an issuer material non-public information relating to an issuer of securities, from purchasing or selling securities of such issuer or from communicating such information to any other person under circumstances in which it is reasonably foreseeable that such person is likely to purchase or sell such securities.

8. Intellectual Property Rights. Consultant's rights, title and interest in inventions, discoveries and developments conceived or reduced to practice in the performance of Company funded consulting services made by Consultant (including any of its employees, agents, or representatives) whether solely or jointly with Company employees, agents or representatives ("Inventions") shall be immediately assigned to Company, and, to the extent not immediately assigned, shall be assigned in writing promptly upon the request of Company.

9. Notices. All notices required or permitted under this Agreement shall be in writing and shall be deemed effective upon personal delivery or upon deposit in the United States Post Office, by registered or certified mail, postage prepaid, addressed to the other party at the address shown above, or at such other address or addresses, including electronic mail addresses, as either party shall designate to the other in accordance with this Section 9. Additionally, a copy of all notices shall be sent to the Company at [REDACTED].

10. Use of Name. Neither party shall use the name of the other party, nor any variation thereon, nor adaptation thereof may be used in any advertising, promotional sales literature, or other publicity without the prior written approval of the party whose name is to be used.

11. Pronouns. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular forms of nouns and pronouns shall include the plural, and vice versa.

12. Entire Agreement. This Agreement constitutes the entire agreement between the parties and supersedes all prior agreements and understandings, whether written or oral, relating to the subject matter of this Agreement, provided, however, that this Agreement does not alter the surviving obligations of Consultants' Employment Agreement or his Confidentiality,

Developments, and Restrictive Covenants Agreement each dated on or about August 20, 2019 and further provided that this Agreement does not alter the terms of any equity award or grant to Consultant from Company or any affiliate of Company on or before the Effective Date.

13. Amendment. This Agreement may be amended or modified only by a written instrument executed by both the Company and the Consultant.

14. Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the laws of the Netherlands, without giving effect to the conflict or choice of law provisions thereof.

15. Successors and Assigns. This Agreement shall be binding upon, and inure to the benefit of, both parties and their respective successors and assigns, including any corporation with which, or into which, the Company may be merged, or which may succeed to its assets or business, provided, however, that the obligations of the Consultant are personal and shall not be assigned by him or her.

16. Delegation and Assignment. The Consultant acknowledges that it is prohibited from subcontracting, delegating, or assigning any of its rights or obligations under this Agreement without the Company's prior written consent. In case of subcontracting, the Consultant shall enter into a written agreement with the subcontractor containing terms that are similar to and at least as stringent as the terms of this Agreement. The Company may assign its rights or obligations under this Agreement to a third party provided it will cause such party to be bound to the terms of this Agreement.

17. Remedies. The Consultant acknowledges that any breach of the provisions of Section 6 of this Agreement may result in serious and irreparable injury to the Company for which the Company may not be adequately compensated by monetary damages alone. The Consultant agrees, therefore, that, in addition to any other remedy it may have, the Company may be entitled to enforce the specific performance of this Agreement by the Consultant and to seek both temporary and permanent injunctive relief (to the extent permitted by law).

18. Miscellaneous.

18.1 No delay or omission by the Company in exercising any right under this Agreement shall operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion shall be effective only in that instance and shall not be construed as a bar or waiver of any right on any other occasion.

18.2 The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit, or affect the scope or substance of any section of this Agreement.

18.3 In the event that any provision of this Agreement shall be invalid, illegal, or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby. Parties shall negotiate on a provision that comes closest to the desired purpose of the illegal, invalid, or unenforceable provision.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year set forth above.

uniQure, Inc.

By: /s/ Matt Kapusta
Matt Kapusta
Chief Executive Officer

Consultant

By: /s/ Alex Kuta
Alex Kuta
Consultant

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
(Principal Executive Officer)
May 9, 2023

Exhibit 31.2

Certification of Chief Financial Officer

I, Christian Klemt, 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/ CHRISTIAN KLEMT

Christian Klemt
Chief Financial Officer
(Principal Financial Officer)
May 9, 2023

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, 2023, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Matthew Kapusta, Chief Executive Officer, and Christian Klemt, Chief Financial Officer of the Company, hereby certify, 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
(Principal Executive Officer)

May 9, 2023

By: /s/ CHRISTIAN KLEMT

Christian Klemt
Chief Financial Officer
(Principal Financial Officer)

May 9, 2023

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.