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 September 30, 2022

OR

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

For the transition period from _____ to _____

Commission file number: 001-36294

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

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

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

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

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

Title of each class:	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, par value €0.05	QURE	The Nasdaq Global Select Market

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐.

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

Large accelerated filer ☒	Accelerated filer ☐
Non-accelerated filer ☐	Smaller reporting company ☐
	Emerging growth company ☐

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

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

As of October 28, 2022, the registrant had 46,815,109 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 25, 2022 (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 September 30, 2022, 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

	September 30, 2022	December 31, 2021
	(in thousands, except share and per share amounts)	
Current assets		
Cash and cash equivalents	$ 440,313	$ 556,256
Accounts receivable and contract asset	3,603	58,768
Inventories	4,075	-
Prepaid expenses	13,692	10,540
Other current assets and receivables	2,894	2,675
Total current assets	**464,577**	**628,239**
Non-current assets		
Property, plant and equipment, net of accumulated depreciation of $40.5 million as of September 30, 2022 and $36.9 million as of December 31, 2021	47,886	43,505
Operating lease right-of-use assets	27,804	25,573
Intangible assets, net, including an in-process research and development asset of $52.5 million as of September 30, 2022 and $60.8 million as of December 31, 2021	53,837	62,686
Goodwill	23,418	27,633
Deferred tax assets, net	14,627	15,647
Other non-current assets	6,085	5,897
Total non-current assets	**173,657**	**180,941**
Total assets	**$ 638,234**	**$ 809,180**
Current liabilities		
Accounts payable	$ 7,566	$ 2,502
Accrued expenses and other current liabilities	26,437	28,487
Current portion of contingent consideration	23,537	—
Current portion of operating lease liabilities	6,434	5,774
Total current liabilities	**63,974**	**36,763**
Non-current liabilities		
Long-term debt	102,394	100,963
Operating lease liabilities, net of current portion	29,893	28,987
Contingent consideration, net of current portion	9,158	29,542
Deferred tax liability, net	8,592	12,913
Other non-current liabilities	3,053	4,236
Total non-current liabilities	**153,090**	**176,641**
Total liabilities	**217,064**	**213,404**
Commitments and contingencies		
Shareholders' equity		
Ordinary shares, €0.05 par value: 80,000,000 shares authorized as of September 30, 2022 and December 31, 2021 and 46,815,109 and 46,298,635 ordinary shares issued and outstanding as of September 30, 2022 and December 31, 2021, respectively	2,830	2,802
Additional paid-in-capital	1,100,078	1,076,972
Accumulated other comprehensive loss	(93,000)	(28,856)
Accumulated deficit	(588,738)	(455,142)
Total shareholders' equity	**421,170**	**595,776**
Total liabilities and shareholders' equity	**$ 638,234**	**$ 809,180**

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE (LOSS) INCOME

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
	(in thousands, except share and per share amounts)		(in thousands, except share and per share amounts)	
License revenues	$ —	$ —	$ —	$ 462,400
Collaboration revenues	1,449	1,989	3,738	3,911
Total revenues	**1,449**	**1,989**	**3,738**	**466,311**
Operating expenses:				
Cost of contract revenues	—	—	—	(23,178)
Cost of contract manufacturing	(861)	—	(1,693)	—
Research and development expenses	(48,068)	(36,432)	(139,263)	(101,209)
Selling, general and administrative expenses	(13,324)	(12,023)	(36,802)	(42,323)
Total operating expenses	**(62,253)**	**(48,455)**	**(177,758)**	**(166,710)**
Other income	1,485	1,680	4,981	9,622
Other expense	(199)	(214)	(621)	(673)
(Loss) / income from operations	**(59,518)**	**(45,000)**	**(169,660)**	**308,550**
Interest income	39	46	117	123
Interest expense	(3,069)	(1,924)	(8,279)	(5,377)
Foreign currency gains, net	14,362	10,436	42,328	21,645
Other non-operating (losses) / gains, net	—	—	635	—
(Loss) / income before income tax benefit / (expense)	**$ (48,186)**	**$ (36,442)**	**$ (134,859)**	**$ 324,941**
Income tax benefit / (expense)	329	(89)	1,263	(3,560)
Net (loss) / income	**$ (47,857)**	**$ (36,531)**	**$ (133,596)**	**$ 321,381**
Other comprehensive loss:				
Foreign currency translation adjustments	(25,370)	(13,288)	(64,144)	(27,790)
Total comprehensive (loss) / gain	**$ (73,227)**	**$ (49,819)**	**$ (197,740)**	**$ 293,591**
Earnings per ordinary share - basic				
Basic net (loss) / income per ordinary share	$ (1.02)	$ (0.79)	$ (2.86)	$ 7.00
Earnings per ordinary share - diluted				
Diluted net (loss) / income per ordinary share	$ (1.02)	$ (0.79)	$ (2.86)	$ 6.87
Weighted average shares - basic	46,772,430	46,152,404	46,680,667	45,888,769
Weighted average shares - diluted	46,772,430	46,152,404	46,680,667	46,780,963

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE THREE-MONTH PERIOD ENDED SEPTEMBER 30, 2022 AND 2021

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive (loss)	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
	(in thousands, except share and per share amounts)					
Balance at June 30, 2021	**46,050,250**	**$ 2,788**	**$ 1,062,234**	**$ (4,595)**	**$ (426,819)**	**$ 633,608**
Loss for the period	—	—	—	—	(36,531)	(36,531)
Other comprehensive loss	—	—	—	(13,288)	—	(13,288)
Exercise of share options	84,811	5	909	—	—	914
Restricted share units distributed during the period	69,165	4	(4)	—	—	—
Share-based compensation expense	—	—	5,955	—	—	5,955
Issuance of ordinary shares relating to employee stock purchase plan	3,550	—	97	—	—	97
Balance at September 30, 2021	**46,207,776**	**$ 2,797**	**$ 1,069,191**	**$ (17,883)**	**$ (463,350)**	**$ 590,755**
Balance at June 30, 2022	**46,684,583**	**$ 2,823**	**$ 1,092,176**	**$ (67,630)**	**$ (540,881)**	**$ 486,488**
Loss for the period	—	—	—	—	(47,857)	(47,857)
Other comprehensive loss	—	—	—	(25,370)	—	(25,370)
Exercise of share options	47,290	2	258	—	—	260
Restricted and performance share units distributed during the period	79,821	4	(4)	—	—	—
Share-based compensation expense	—	—	7,608	—	—	7,608
Issuance of ordinary shares relating to employee stock purchase plan	3,415	1	40	—	—	41
Balance at September 30, 2022	**46,815,109**	**$ 2,830**	**$ 1,100,078**	**$ (93,000)**	**$ (588,738)**	**$ 421,170**

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE NINE-MONTH PERIOD ENDED SEPTEMBER 30, 2022 AND 2021

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive income / (loss)	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
	(in thousands, except share and per share amounts)					
Balance at December 31, 2020	**44,777,799**	**$ 2,711**	**$ 1,016,018**	**$ 9,907**	**$ (784,731)**	**$ 243,905**
Income for the period	—	—	—	—	321,381	321,381
Other comprehensive loss	—	—	—	(27,790)	—	(27,790)
Issuance of ordinary shares	921,730	55	29,510	—	—	29,565
Income tax benefit of past share issuance cost	—	—	2,977	—	—	2,977
Exercises of share options	156,787	10	1,814	—	—	1,824
Restricted and performance share units distributed during the period	346,736	21	(21)	—	—	—
Share-based compensation expense	—	—	18,747	—	—	18,747
Issuance of ordinary shares relating to employee stock purchase plan	4,724	—	146	—	—	146
Balance at September 30, 2021	**46,207,776**	**$ 2,797**	**$ 1,069,191**	**$ (17,883)**	**$ (463,350)**	**$ 590,755**
Balance at December 31, 2021	**46,298,635**	**$ 2,802**	**$ 1,076,972**	**$ (28,856)**	**$ (455,142)**	**$ 595,776**
Loss for the period	—	—	—	—	(133,596)	(133,596)
Other comprehensive loss	—	—	—	(64,144)	—	(64,144)
Exercise of share options	119,884	6	707	—	—	713
Restricted and performance share units distributed during the period	387,285	21	(21)	—	—	—
Share-based compensation expense	—	—	22,290	—	—	22,290
Issuance of ordinary shares relating to employee stock purchase plan	9,305	1	130	—	—	131
Balance at September 30, 2022	**46,815,109**	**$ 2,830**	**$ 1,100,078**	**$ (93,000)**	**$ (588,738)**	**$ 421,170**

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF CASH FLOWS

	Nine months ended September 30,	
	2022	2021
	(in thousands)	
Cash flows from operating activities		
Net (loss) / income	$ (133,596)	$ 321,381
Adjustments to reconcile net (loss) / income to net cash (used in) / generated from operating activities:		
Depreciation and amortization expense	6,206	5,447
Share-based compensation expense	22,290	18,747
Deferred tax (income) / expense	(1,263)	3,560
Changes in fair value of contingent consideration and derivative financial instrument, net	6,875	416
Unrealized foreign exchange gains, net	(36,390)	(23,242)
Other non-current assets, net	(581)	(2,862)
Changes in operating assets and liabilities:		
Accounts receivable and contract asset, prepaid expenses, and other current assets and receivables	41,992	(1,993)
Inventories	(4,075)	-
Accounts payable	4,529	2,003
Accrued expenses, other liabilities, and operating leases	3,633	11,592
Net cash (used in) / generated from operating activities	(90,380)	335,049
Cash flows from investing activities		
Purchases of property, plant, and equipment	(12,622)	(13,885)
Acquisition of Corlieve, net of cash acquired	(1,900)	(49,949)
Net cash used in investing activities	(14,522)	(63,834)
Cash flows from financing activities		
Proceeds from issuance of ordinary shares related to employee stock option and purchase plans	844	1,971
Proceeds from loan increment, net of debt issuance costs	-	34,603
Proceeds from issuance of ordinary shares	-	30,899
Share issuance costs from issuance of ordinary shares	-	(1,334)
Repayment of debt acquired through acquisition of Corlieve	-	(1,175)
Net cash generated from financing activities	844	64,964
Currency effect on cash, cash equivalents and restricted cash	(11,876)	(2,589)
Net (decrease) / increase in cash, cash equivalents and restricted cash	(115,934)	333,590
Cash, cash equivalents and restricted cash at beginning of period	559,353	247,680
Cash, cash equivalents and restricted cash at the end of period	**$ 443,419**	**$ 581,270**
Cash and cash equivalents	$ 440,313	$ 578,464
Restricted cash related to leasehold and other deposits	3,106	2,806
Total cash, cash equivalents and restricted cash	**$ 443,419**	**$ 581,270**
Supplemental cash flow disclosures:		
Cash paid for interest	$ (6,410)	$ (4,503)
Non-cash (decrease) / increase in accounts payables and accrued expenses and other current liabilities related to purchases of property, plant, and equipment	$ 1,766	$ 415

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

1 General business information

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

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

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

2 Summary of significant accounting policies

2.1 Basis of preparation

The Company prepared these unaudited consolidated financial statements in compliance with generally accepted accounting principles in the United States of America ("U.S. GAAP") and applicable rules and regulations of the 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 and nine months ended September 30, 2022, are not necessarily indicative of the results to be expected for the full year ending December 31, 2022, 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.

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, 2021, and the notes thereto, which are included in the Company's Annual Report. There have been no material changes in the Company's significant accounting policies during the nine months ended September 30, 2022, except as noted below.

Inventories

The Company started producing commercial materials in April 2022 to supply CSL Behring LLC ("CSL Behring") with etranacogene dezaparvovec (the "Product") in accordance with the June 2020 Development and Commercial Supply Agreement between the Company and CSL Behring. From this date onwards, the Company presents the costs associated with the aforementioned activities as cost of contract manufacturing. The Company capitalizes inventory to be sold to CSL Behring to the extent it expects to generate probable future benefits from such sales. Refer to Note 3, *"CSL Behring collaboration"* for further detail.

Per ASC 330, Inventory, inventory is stated at the lower of cost or estimated net realizable value, on a first-in, first-out basis. The Company capitalizes raw materials to the extent these can be used in the manufacturing of the Product. The Company uses standard costs, approximating average costs to determine its cost basis for work in progress and finished goods. The Company's assessment of recoverability value requires the use of estimates regarding the net realizable value of its inventory balances, including an assessment of excess or obsolete inventory. As applicable, write-downs resulting from adjustments to net realizable value will be recorded to cost of contract manufacturing.

2.5 Recent accounting pronouncements

There have been no new accounting pronouncements or changes to accounting pronouncements during the nine months ended September 30, 2022, as compared to the recent accounting pronouncements described in Note 2.3.23 of the Company's 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 uniQure N.V., entered into a commercialization and license agreement (the "CSL Behring Agreement") with CSL Behring, pursuant to which CSL Behring received exclusive global rights to etranacogene dezaparvovec, the Company's investigational gene therapy for patients with hemophilia B.

The transaction became fully effective on May 6, 2021, one day after the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (the "HSR Act") expired on May 5, 2021 ("Closing").

The Company, as of the effective date, identified two material performance obligations related to the CSL Behring Agreement:

(i) Sale of the exclusive global rights to the Product ("License Sale"); and

(ii) Generate information to support the regulatory approval of the current and next generation manufacturing process of the Product and to provide any such information generated to CSL Behring ("Manufacturing Development").

License Sale

The Company continued to develop the Product between the Signing Date and Closing and performed certain reimbursable activities to fulfill the transfer of the global rights ("Additional Covenants" that are included as part of the "License Sale"). The Additional Covenants are not considered distinct from the performance obligation to sell the license to CSL Behring as CSL Behring could not benefit from the Additional Covenants on their own, or have these activities be performed with readily available resources.

The Company determined that the fixed upfront payment of $450.0 million and the $12.4 million that the Company received in relation to the Additional Covenants should be allocated to the License Sale. The Company determined that the License Sale was completed on May 6, 2021, when it transferred the license and CSL Behring assumed full responsibility for the development and commercialization of the Product. At Closing, the Company evaluated the amounts of potential payments and the likelihood that the payments will be received. The Company utilized the most likely amount method to estimate the variable consideration to be included in the transaction price. Since the Company cannot control the achievement of regulatory and first commercial sales milestones, the Company concluded that the potential payments are constrained as of Closing. The Company determined that it would recognize revenue related to these payments only to the extent that it becomes probable that no significant reversal of recognized cumulative revenue will occur thereafter. Similarly, the Company records expenses related to its existing license and other agreements as well as its financial advisor for a mid-single digit percentage of any such revenue recognized associated to meeting a milestone. The Company includes payments related to sales milestones in the transaction price when their achievement becomes probable, and it will include royalties on the sale of the Product once these have been earned. The Company recognized nil and $462.4 million of license revenue in the three and nine months ended September 30, 2021 related to the License Sale. During the three and nine months ended September 30, 2022, the Company did not recognize any license revenue.

Collaboration Services

The Company recognized $0.7 million and $2.1 million of collaboration revenue in the three and nine months ended September 30, 2022, compared to $0.5 and $0.9 million in the three and nine months ended September 30, 2021. The Company generates such collaboration revenue from services rendered in relation to completing the HOPE-B clinical trial on behalf of CSL Behring as well as additional development services that CSL Behring requested. These collaboration services are reimbursed at the pre-agreed full-time-employee rate ("FTE-rate").

Contract Manufacturing

The Company commenced capitalizing inventory in April 2022 for the Product to be sold to CSL Behring.

On September 6, 2022, CSL Behring notified the Company of its intent to transfer manufacturing technology related to the Product to a third-party contract manufacturer designated by CSL Behring. CSL Behring also requested that the Company continue to serve as a manufacturer of the Product after the Company completes the technology transfer to a third party. The Company and CSL Behring are in the process of negotiating the terms of the transfer of manufacturing responsibility pursuant to the CSL Behring Agreement.

Accounts Receivable and Contract Asset

As of December 31, 2021, the Company recorded accounts receivable of $2.9 million from CSL Behring related to collaboration services as well as a contract asset of $55.0 million associated with milestone payments due upon CSL Behring's global regulatory submissions for etranacogene dezaparvovec, which were deemed to be probable. In March and April 2022, CSL Behring submitted marketing applications in the United States and European Union, and as of March and April 2022, the Company had collected the $55.0 million owed. As of September 30, 2022, the Company had accounts receivable of $3.0 million from CSL Behring.

4 Inventories

The Company commenced capitalizing inventory in April 2022 when the Company started producing commercial materials to supply the Product to CSL Behring. The following table summarizes the inventory balances for the nine months ended September 30, 2022:

	September 30, 2022	December 31, 2021
	(in thousands)	
Raw materials	$ 1,447	$ —
Work in progress	2,178	—
Finished goods	450	—
Inventories	**$ 4,075**	**$ —**

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. U.S. GAAP requires disclosure of methodologies used in determining the reported fair values and establishes a hierarchy of inputs used when available. The three levels of the fair value hierarchy are described below:

Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company can access at the measurement date.

Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active or models for which the inputs are observable, either directly or indirectly.

Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and are unobservable.

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

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

The following table sets forth the Company's assets and liabilities that are required to be measured at fair value on a recurring basis as of September 30, 2022, and December 31, 2021:

	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, 2021					
Assets:					
Cash and cash equivalents	$ 556,256	$ —	$ —	$ 556,256	Cash and cash equivalents
Restricted cash	3,097	—	—	3,097	Other non-current assets
Total assets	$ 559,353	$ —	$ —	$ 559,353	
Liabilities:					
Contingent consideration	—	—	29,542	29,542	Contingent consideration
Derivative financial instrument	—	—	2,805	2,805	Other non-current liabilities
Consideration for post-acquisition services	—	—	846	846	Other non-current liabilities
Total liabilities	$ —	$ —	$ 33,193	$ 33,193	
At September 30, 2022					
Assets:					
Cash and cash equivalents	$ 440,313	$ —	$ —	$ 440,313	Cash and cash equivalents
Restricted cash	3,106	—	—	3,106	Other non-current assets
Total assets	$ 443,419	$ —	$ —	$ 443,419	
Liabilities:					
Contingent consideration	—	—	32,695	32,695	Current portion of contingent consideration; contingent consideration, net of current portion
Derivative financial instrument	—	—	2,171	2,171	Other non-current liabilities
Consideration for post-acquisition services	—	—	312	312	Other non-current liabilities
Total liabilities	$ —	$ —	$ 35,178	$ 35,178	

Contingent consideration

The Company is required to pay up to EUR 178.8 million ($175.2 million) at September 30, 2022 to the former shareholders of Corlieve upon the achievement of contractually defined milestones in connection with the Company's acquisition of Corlieve. The fair market value of the contingent consideration was determined using unobservable initial inputs with respect to (i) the probability of achieving the relevant milestones, or POS, (ii) the estimated timing of achieving such milestones, and (iii) the interest rate used to discount the payments. The Company determined the fair market value of the contingent consideration by calculating the probability-adjusted payments based on each milestone's probability of achievement. The probability-adjusted payments were then discounted to present value using a discount rate representing the Company's credit risk. The discount rate was determined using the effective interest rate of the Company's existing debt facility adjusted for difference in maturity dates based on market data on effective yields for US bonds with a CCC credit rating.

The fair value of the contingent consideration as of September 30, 2022 was $32.7 million (December 31, 2021: $29.5 million) using discount rates of approximately 11.9% to 13.3% (December 31, 2021: 10.9% to 11.9%) as well as a 66.0% (December 31, 2021: 55.0%) 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 September 30, 2022 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 $45.4 million. If as of September 30, 2022 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, 2021 and September 30, 2022:

	Amount of contingent consideration
	2022
	(in thousands)
Balance at December 31, 2021	**$ 29,542**
Change in fair value (presented within research and development expenses)	7,510
Currency translation effects	(4,357)
Balance at September 30, 2022	**$ 32,695**

As of September 30, 2022, the Company classified $23.5 million of the total contingent consideration of $32.7 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.

Derivative financial instrument

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

On December 1, 2020, the Company and BMS agreed that upon the consummation of a change of control transaction of uniQure that occurs prior to December 1, 2026 or BMS' delivery of a target cessation notice for all four collaboration targets, the Company (or its third party acquirer) shall pay to BMS a one-time, non-refundable, non-creditable cash payment of $70.0 million, provided that (x) if $70.0 million is greater than five percent (5.0%) of the net proceeds (as contractually defined) from such change of control transaction, the payment shall be an amount equal to five percent of such net proceeds, and (y) if $70.0 million is less than one percent of such net proceeds, the change of control payment shall be an amount equal to one percent of such net proceeds ("CoC-payment"). The Company has not consummated any change of control transaction as of September 30, 2022 that would obligate it to make a CoC-payment.

The Company determined that the CoC-payment should be recorded as a derivative financial liability as of December 1, 2020 and that subsequent changes in the fair market value of this derivative financial liability should be recorded in profit and loss. The fair market value of the derivative financial liability is materially impacted by probability that market participants assign to the likelihood of the occurrence of a change of control transaction that would give rise to a CoC-payment. This probability represents an unobservable input. The Company determines the fair market value of the derivative financial liability by using a present value model based on expected cash flow. The expected cash flows are materially impacted by the probability that market participants assign to the likelihood of the occurrence of a change of control transaction within the biotechnology industry. The Company estimated this unobservable input using the best information available as of September 30, 2022 and December 31, 2021. The Company obtained reasonably available market information that it believed market participants would use in determining the likelihood of the occurrence of a change-of control transaction within the biotechnology industry. Selecting and evaluating market information involves considerable judgement and uncertainty. Based on all such information and its judgment, the Company estimated that the fair market value of the derivative financial liability (presented within "Other non-current liabilities") as of September 30, 2022 was $2.2 million and as of December 31, 2021 was $2.8 million. The change in the fair market value of the derivative financial liability was nil for the three months ended September 30, 2022 and was $0.6 million for the nine months ended September 30, 2022 related to a decrease in the fair market value (nil in the same periods in 2021). The decrease in fair market value for the nine months ended September 30, 2022 was recorded as a gain within Other non-operating (losses) / gains.

6 Accrued expenses and other current liabilities

Accrued expenses and other current liabilities include the following items:

	September 30, 2022	December 31, 2021
	(in thousands)	
Accruals for goods received from and services provided by vendors-not yet billed	$ 13,497	$ 13,012
Personnel related accruals and liabilities	12,940	12,603
Accrued contract fulfillment costs and costs to obtain a contract	—	2,872
Total	**$ 26,437**	**$ 28,487**

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"). On January 29, 2021, the Company drew down $35.0 million as part of the amendment of the facility at that time.

Pursuant to the 2021 Restated Facility, Tranche A and Tranche B of the 2021 Amended Facility with a total outstanding balance of $70.0 million were consolidated into one tranche with a total commitment of $100.0 million. The Company drew down an additional $30.0 million at the time of the December 2021 amendment, resulting in total principal outstanding as of September 30, 2022 of $100.0 million. The 2021 Restated Facility extended the loan's maturity date from June 1, 2023 until December 1, 2025. The interest-only period was extended from January 1, 2023 to December 1, 2024, or December 1, 2025 if, prior to June 30, 2024, either (a) the Biologics License Application ("BLA") for AMT-061 is approved by the U.S. Food and Drug Administration ("FDA") or (b) AMT-130 is advanced into a pivotal trial. 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 4.85% of the outstanding debt. The Company is required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. The Company continues to owe a $2.5 million back-end fee related to the 2021 Amended Facility which is due on June 1, 2023.

The amortized cost (including interest due presented as part of accrued expenses and other current liabilities) of the 2021 Restated Facility was $103.3 million as of September 30, 2022, compared to $101.6 million as of December 31, 2021, and is recorded net of discount and debt issuance costs. The foreign currency loss on the facility in the three and nine months ended September 30, 2022 was $6.6 million and $15.0 million, respectively compared to a foreign currency loss of $1.8 million and $4.0 million during the same periods in 2021 for the 2018 Amended Facility and the 2021 Amended Facility.

Interest expense associated with the 2021 Restated Facility during the three and nine months ended September 30, 2022 was $3.0 million and $8.1 million, respectively compared to $1.9 million and $5.2 million, respectively, during the same periods in 2021 for the 2018 Amended Facility and the 2021 Amended Facility.

As a covenant in the 2021 Restated Facility the Company has periodic reporting requirements and is required to keep a minimum cash balance deposited in bank accounts in the United States equivalent to the lesser of (i) 65% of the outstanding balance of principal due or (ii) 100% of worldwide cash and cash equivalents. This restriction on cash and cash equivalents only relates to the location of the cash and cash equivalents, and such cash and cash equivalents can be used at the discretion of the Company. The Company, beginning on April 1, 2023, is also required to keep a minimum of unrestricted cash of at least 50% of the loan amount outstanding. If, prior to June 30, 2024, either (a) the BLA for AMT-061 is approved by the FDA or (b) AMT-130 is advanced into a pivotal trial, the minimum cash covenant will be lowered to at least 30% of the loan amount outstanding and its effectiveness will be deferred to April 1, 2024. 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 $638.2 million, less $75.3 million of cash and cash equivalents and other current assets held by uniQure N.V. and $80.2 million of other current assets and investment held by Corlieve Therapeutics SAS.

The 2021 Restated Facility contains provisions that include the occurrence of a material adverse effect, as defined therein, which would entitle Hercules to declare all principal, interest and other amounts owed by the Company immediately due and payable. As of September 30, 2022, 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"). At the annual general meeting of shareholders in June 2021, the Company's shareholders approved an increase in the number of ordinary shares authorized for issuance under the 2014 Plan from 8,601,471 to 12,601,471.

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 September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
	(in thousands)		(in thousands)	
Research and development	$ 3,730	$ 3,249	$ 12,090	$ 9,222
Selling, general and administrative	3,758	2,707	9,932	9,525
Cost of contract manufacturing	120	—	268	—
Total	**$ 7,608**	**$ 5,956**	**$ 22,290**	**$ 18,747**

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

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
	(in thousands)		(in thousands)	
Award type/ESPP				
Share options	$ 3,448	$ 2,965	$ 10,141	$ 9,155
Restricted share units	3,957	2,582	11,354	8,364
Performance share units	197	403	777	1,206
ESPP	6	6	18	22
Total	**$ 7,608**	**$ 5,956**	**$ 22,290**	**$ 18,747**

As of September 30, 2022, 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	$ 27,720	2.64
Restricted share units	28,629	2.04
Total	**$ 56,349**	**2.34**

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

Share options

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

The following tables summarize option activity under the Company's 2014 Plans for the nine months ended September 30, 2022:

	Options	
	Number of ordinary shares	Weighted average exercise price
Outstanding at December 31, 2021	**3,308,325**	**$ 31.02**
Granted	1,399,466	$ 15.75
Forfeited	(183,870)	$ 38.74
Expired	(133,381)	$ 35.79
Exercised	(115,884)	$ 6.03
Outstanding at September 30, 2022	**4,274,656**	**$ 26.22**
Thereof, fully vested and exercisable on September 30, 2022	2,068,810	$ 28.33
Thereof, outstanding and expected to vest after September 30, 2022	2,205,846	$ 24.24

Total weighted average grant date fair value of options issued during the period (in $ millions)	$ 12.5
Proceeds from option sales during the period (in $ millions)	$ 0.7

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

	Three months ended September 30,		Nine months ended September 30,	
Assumptions	**2022**	**2021**	**2022**	**2021**
Expected volatility	70%	75%	70%	75%
Expected terms	10 years	10 years	10 years	10 years
Risk free interest rate	4.16%	1.47%	2.12% - 4.16%	1.21 - 1.85%
Expected dividend yield	0%	0%	0%	0%

Restricted share units ("RSUs")

The following table summarizes the RSUs activity for the nine months ended September 30, 2022:

	RSU	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2021	**710,617**	**$ 38.89**
Granted	1,562,133	$ 15.91
Vested	(283,349)	$ 39.47
Forfeited	(176,110)	$ 23.76
Non-vested at September 30, 2022	**1,813,291**	**$ 20.47**

Total weighted average grant date fair value of RSUs granted during the period (in $ millions)	$ 24.8

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

Performance share units ("PSUs")

The following table summarizes the PSUs activity for the nine months ended September 30, 2022:

	PSU	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2021	**632,930**	**$ 33.54**
Granted	34,700	**$** 15.11
Vested	(103,970)	$ 52.14
Forfeited	(48,800)	$ 29.35
Non-vested at September 30, 2022	**514,860**	**$ 28.94**

PSUs granted in 2019 vested on the third anniversary of the grant, subject to the grantee's continued employment.

The Company granted shares to certain employees in September and December 2021 and at various dates during the nine months ended September 30, 2022 that will be earned upon achievement of defined milestones. Earned 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 December 2021 shares granted 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.

ESPP

During the nine months ended September 30, 2022, 9,305 ordinary shares were issued under the ESPP compared to 4,724 during the same period in 2021. As of September 30, 2022, a total of 117,997 ordinary shares remain available for issuance under the ESPP plan compared to a total of 127,302 as of September 30, 2021.

9 Income taxes

The Company recorded $0.3 and $1.3 million deferred tax benefit in relation to its operations in the United States and France during the three and nine months ended September 30, 2022, respectively. The Company recorded $0.1 million and $3.6 million in deferred income tax expense in the prior year in the United States and the Netherlands for the three and nine months ended September 30, 2021, respectively, of which nil and $3.0 million in the three and nine months periods related to the Netherlands, respectively.

The effective income tax rate of -0.7% and -0.9% during the three and nine months ended September 30, 2022 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 and nine months ended September 30, 2021 was 0.2% and -1.1%, respectively, as the Company had recorded a valuation allowance against all its net deferred tax assets in the Netherlands.

10 Basic and diluted earnings per share

Basic net (loss) / income per ordinary share is computed by dividing net (loss) / income for the period by the weighted average number of ordinary shares outstanding during the period. Diluted earnings per ordinary share are calculated by adjusting the weighted average number of ordinary shares outstanding, assuming conversion of all potentially dilutive ordinary shares. For the three and nine months ended September 30, 2021, dilutive net income per ordinary share is computed using the treasury method. As the Company has incurred a loss in the three and nine months ended September 30, 2022, all potentially dilutive ordinary shares for these periods would have an antidilutive effect, if converted, and thus have been excluded from the computation of loss per share for the three and nine months ended September 30, 2022.

The potentially dilutive ordinary shares are summarized below:

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
	(in thousands, except share amounts)		(in thousands, except share amounts)	
Numerator:				
Net (loss) / income attributable to ordinary shares	$ (47,857)	$ (36,531)	$ (133,596)	$ 321,381
	(47,857)	**(36,531)**	**(133,596)**	**321,381**
Denominator:				
Weighted-average number of ordinary shares outstanding - basic	46,772,430	46,152,404	46,680,667	45,888,769
Stock options under 2014 Plans and previous plan	—	—	—	784,942
Non-vested RSUs and PSUs	—	—	—	105,870
Employee share purchase plan	—	—	—	1,382
Weighted-average number of ordinary shares outstanding - diluted	**46,772,430**	**46,152,404**	**46,680,667**	**46,780,963**

The following table presents ordinary share equivalents that were excluded from the calculation of diluted net (loss) / income per ordinary share for the three and nine months ended September 30, 2022 and 2021 as the effect of their inclusion would have been anti-dilutive:

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Anti-dilutive ordinary share equivalents				
Stock options under 2014 Plans and previous plan	4,284,656	3,357,412	4,284,656	2,572,470
Non-vested RSUs and PSUs	2,328,151	841,480	2,328,151	735,610
Employee share purchase plan	721	1,219	721	1,219
Total anti-dilutive ordinary share equivalents	**6,613,528**	**4,200,111**	**6,613,528**	**3,309,299**

The anti-dilutive ordinary shares are presented without giving effect to the application of the treasury method or exercise prices that exceeded the price of the Company's ordinary shares as of the three and nine months ended September 30, 2022.

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

Business Developments

Below is a summary of our recent significant business developments:

Huntington's disease program (AMT-130)

AMT-130 is our novel gene therapy candidate for the treatment of Huntington's disease. AMT-130 utilizes our proprietary, gene-silencing miQURE platform and incorporates an AAV vector carrying a micro ribonucleic acid ("miRNA") specifically designed to silence the huntingtin gene and the potentially highly toxic exon 1 protein fragment. We are currently conducting a Phase I/II clinical trial for AMT-130 in the United States ("U.S.") and a Phase Ib/II study in the European Union ("EU"). Together, these studies are intended to establish safety, proof of concept, and the optimal dose of AMT-130 to take forward into Phase III development or into a confirmatory study should an accelerated registration pathway be feasible. AMT-130 has received Orphan Drug and Fast Track designations from the U.S. Food and Drug Administration ("FDA") and Orphan Medicinal Product Designation from the European Medicines Agency ("EMA").

On March 21, 2022, we announced that we have completed the enrollment of all 26 patients in the first two cohorts of our randomized, double-blinded, Phase I/II clinical trial of AMT-130 taking place in the U.S. In the study, patients are randomized to either treatment with AMT-130 or to an imitation surgical procedure. The treated patients have received a single administration of AMT-130 using MRI-guided, convection-enhanced stereotactic neurosurgical delivery directly into the striatum (caudate and putamen). The trial consists of a blinded 12-month period followed by unblinded long-term follow-up for five years. The low-dose cohort 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. In July 2022 we crossed over one of these six patients and treated the patient with the lower dose of AMT-130. A third cohort, which will include up to 18 additional randomized patients receiving the higher dose, will explore the use of alternative stereotactic navigation systems to simplify placement of catheters for infusions of AMT-130.

On June 23, 2022, we announced safety and biomarker data from the 10 patients enrolled in the low-dose cohort. At 12 months of follow-up on the patients in the low-dose cohort:

- AMT-130 was generally well-tolerated with no serious adverse events related to AMT-130 reported in the treated patients. There were two serious adverse events unrelated to AMT-130, including a deep-vein thrombosis in the elbow of one patient that was resolved with anticoagulants and transient post-operative delirium in a second patient that was resolved through supportive care.

- 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 (range 44% decrease to 71% decrease). In the three control patients with evaluable data, mean levels of CSF mHTT showed an increase compared to baseline at one, three, six and nine months of follow-up, and decreased by 16.8% compared at 12 months of follow-up (range 35% increase to 47% decrease).

- In the six treated patients, measurements of neurofilament light chain in the cerebral spinal fluid ("CSF NfL"), a biomarker of neuronal damage, initially increased as expected following the AMT-130 surgical procedure and declined thereafter, nearing baseline at 12 months of follow-up. At 12 months, mean CSF NfL showed an 8% increase compared to baseline (range 46% increase to 14% decrease). Two of the six treated patients were at or below baseline at 12 months of follow-up, with an additional patient below baseline at 15 and 18 months of follow-up. In the four control patients, mean CSF NfL remained stable or slightly declined over 12 months (range 1% increase to 35% decrease).

Also on June 23, 2022, we announced that 10 patients in our European Phase Ib/II study had been treated with AMT-130. The open-label study will enroll a total of 15 patients in two dose cohorts.

In July 2022, we learned that three patients of the 14 patients that were treated with the higher dose of AMT-130 in our Phase Ib/II clinical trial had experienced certain serious adverse reactions that were potentially attributable to AMT-130. Two patients experienced localized inflammatory responses and related symptoms shortly after the procedure, while the third patient experienced severe headaches and other related symptoms. All three patients were treated and released from the hospital. The reactions in these three patients each have been classified as suspected unexpected serious adverse reactions ("SUSARs") and reported to the appropriate regulatory agencies in the U.S. and Europe.

Following a review of these SUSARs by the independent Data Safety Monitoring Board for the clinical trial (the "DSMB") in July 2022, the DSMB recommended postponement of further enrollment and dosing of high-dose patients and postponement of further site activation until the DSMB had conducted a comprehensive safety investigation.

We completed a comprehensive safety investigation in October 2022. The DSMB recommended resuming treatment at the higher dose of AMT-130 for the remaining five European patients and any patients in the U.S. trial who are eligible to cross over from the control arm to the treatment. All three patients have experienced full resolution of the reported SUSARSs.

We have added additional risk mitigation procedures including closer patient monitoring during the first two weeks after the administration of AMT-130 and a seven-day, post-surgical in-person visit. The DSMB recommended that the use of immunosuppression remain at the discretion of the treating physician. We plan to resume patient dosing in the open-label European study in the fourth quarter of 2022 and complete enrollment of the remaining five of the nine patient higher-dose cohort in the first half of 2023.

CSL Behring collaboration

On June 24, 2020, (the "Signing Date"), uniQure biopharma B.V., a wholly owned subsidiary of uniQure N.V., entered into a commercialization and license agreement (the "CSL Behring Agreement") with CSL Behring pursuant to which CSL Behring received exclusive global rights to etranacogene dezaparvovec, the investigational gene therapy for patients with hemophilia B (the "Product"). The transaction became fully effective on May 6, 2021, one day after the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 expired ("Closing").

In accordance with the CSL Behring agreement, CSL Behring is solely responsible for all regulatory activities, including any filings and agency interactions associated with etranacogene dezaparvovec and the companion diagnostic test for neutralizing antibodies to AAV5.

In March and April 2022, CSL Behring submitted marketing applications for etranacogene dezaparvovec in the U.S. and European Union. On March 28, 2022, CSL Behring announced that EMA had accepted the Marketing Authorization Application ("MAA"). On May 24, 2022, we announced that the FDA had accepted for review the Biologics License Application ("BLA"). In March and April 2022, we received the $55.0 million owed to us by CSL Behring related to the global regulatory submissions.

In July 2022, CSL Behring was notified by the Committee for Advanced Therapies ("CAT") in Europe that they will be unable to complete their review in accordance with the accelerated assessment timetable and will now switch to a standard review procedures. In the United States, the BLA remains under Priority Review at this time having Breakthrough Designation Status.

In July 2022, following a comprehensive multi-day facility inspection, the EMA notified us that Good Manufacturing Practice ("GMP") certification can be issued for our Lexington manufacturing site to produce commercial supply of etranacogene dezaparvovec. In August 2022, we completed the FDA pre-license inspection of the Lexington facility.

In August 2022, the GMP certification for the Amsterdam facility was amended to include release testing of the Product in the European Union following inspection by the Inspectie Gezondheidszorg en Jeugd ("IGJ").

On September 6, 2022 as discussed above, CSL Behring notified us of its intent to transfer manufacturing technology related to the Product to a third-party contract manufacturer designated by CSL Behring and to retain the Company as a source for manufacturing.

Preclinical programs

In May 2022, we presented certain preclinical findings on our gene therapy candidates for refractory temporal lobe epilepsy, Fabry disease, Parkinson's disease, Amyotrophic lateral sclerosis, and Alzheimer's disease at the American Society of Gene and Cell Therapy Hybrid Congress.

In July and August 2022, respectively, we initiated Investigational New Drug-enabling ("IND-enabling"), Good Laboratory Practice ("GLP") toxicology studies in non-human primates for our gene therapy candidates in refractory temporal lobe epilepsy and Fabry disease.

Covid pandemic

The coronavirus disease ("Covid") caused by the severe acute respiratory syndrome coronavirus 2 ("Sars-CoV 2 virus") was characterized as a pandemic by the World Health Organization ("WHO") on March 11, 2020. Since then, various variants of the Sars-CoV 2 virus causing Covid have been identified.

The broader implications of Covid, including the implications from the various variants, on our results of operations and overall financial performance remain uncertain. We have experienced and continue to experience increased lead times in the delivery of equipment and disposables that we use to manufacture materials for our various programs. Currently, these have not materially impacted our development timelines and we continue to adapt to the current environment to minimize the effect to our business. However, we may experience more pronounced disruptions in our operations in the future.

Russian-Ukrainian war

Our business is not directly impacted by the war as we do not operate in either Russia or the Ukraine. However, the war might potentially amplify the disruptive impact of the Covid pandemic.

Intellectual Property

On May 11, 2021, Pfizer, Inc. filed three petitions at the United States Patent & Trademark Office ("USPTO") seeking Inter Partes Review of U.S. Patent Nos. 9,982,248 (the "'248 Patent") and 10,465,180 (the "'180 Patent" and together with the '248 Patent, the "Patents"). The petitions collectively seek to invalidate all claims of the Patents. In August 2021, we filed our responses asking the USPTO to deny institution of the IPR proceedings. On November 17, 2021, the Patent Trials and Appeals Board ("PTAB") issued decisions granting institution on all three IPR proceedings. The parties completed briefing of the substantive issues in July 2022 and a hearing was held before the PTAB in August 2022. We expect a decision from the PTAB on or about November 2022.

Financial Overview

Key components of our results of operations include the following:

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
	(in thousands)		(in thousands)	
Total revenues	$ 1,449	$ 1,989	$ 3,738	$ 466,311
Cost of contract revenues	—	—	—	(23,178)
Cost of contract manufacturing	(861)	—	(1,693)	—
Research and development expenses	(48,068)	(36,432)	(139,263)	(101,209)
Selling, general and administrative expenses	(13,324)	(12,023)	(36,802)	(42,323)
Net (loss) / income	(47,857)	(36,531)	(133,596)	321,381

As of September 30, 2022 and December 31, 2021, we had cash and cash equivalents of $440.3 million and $556.3 million, respectively. We had a net loss of $47.9 million and $133.6 in the three and nine months ended September 30, 2022, respectively, compared to net loss of $36.5 million and net income of $321.4 million for the same periods in 2021. As of September 30, 2022 and December 31, 2021, we had accumulated deficits of $588.7 million and $455.1 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 temporal lobe epilepsy and Fabry into Phase I/II clinical studies;
- advancing preclinical research and development for gene therapy product candidates targeting other diseases;
- 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;
- potentially acquiring or in-licensing rights to new therapeutic targets, product candidates and technologies; and
- making potential future milestone payments related to the acquisition of Corlieve, if any.

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

Critical Accounting Policies and Estimates

In preparing our consolidated financial statements in accordance with U.S. GAAP and pursuant to the rules and regulations promulgated by the SEC we make assumptions, judgments and estimates that can have a significant impact on our net 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 nine months ended September 30, 2022 or reasonably possible changes of our critical accounting estimates as of September 30, 2022 that could have had a material impact on our results of operations for the three and nine-month period ended September 30, 2022.

Cost of contract revenues

We expense contract fulfillment costs associated with the sale of the exclusive global rights to the Product recognized under the CSL Behring Agreement as cost of contract revenues.

Cost of contract manufacturing

Since April 1, 2022, we expense cost to manufacture the Product under the CSL Behring June 2020 Development and Commercial Supply Agreement as cost of contract manufacturing. We capitalize the cost to manufacture the Product as inventory to the extent we expect to realize probable future benefits.

Research and development expenses

We expense research and development ("R&D") expenses as incurred. Research and development 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 characterization, consistency and comparability studies;
- costs incurred for the development and improvement of our manufacturing processes and methods;
- costs incurred for the supply of materials for our target candidates;
- 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 the Product between the Signing Date and Closing;
- 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 research and development expenses may vary substantially from period to period based on the timing of our research and development activities, including manufacturing campaigns, regulatory submissions and enrollment of patients in clinical trials. The successful development of our product candidates is highly uncertain. Estimating the nature, timing or cost of the development of any of our product candidates involves considerable judgement due to numerous risks and uncertainties associated with developing gene therapies, including the uncertainty of:

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

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

Selling, general and administrative expenses

Our general and administrative expenses consist principally of employee, office, consulting, legal and other professional and administrative expenses. We 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. Our selling costs in the prior year included employee expenses as well as professional fees related to the preparation of a commercial launch of etranacogene dezaparvovec and advisory fees related to obtaining the CSL Behring Agreement.

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. For the three and nine months ended September 30, 2021, other income consisted of an employee retention credit under the U.S. Coronavirus Aid, Relief, and Economic Security Act ("CARES Act"), and for the nine months ended September 30, 2021, it also included the recognition of the equity stake received in VectorY B.V.

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

Results of Operations

Comparison of the three months ended September 30, 2022 and 2021

The following table presents a comparison of our results of operations for the three months ended September 30, 2022 and 2021.

	Three months ended September 30,		
	2022	2021	2022 vs 2021
		(in thousands)	
Total revenues	$ 1,449	$ 1,989	$ (540)
Operating expenses:			
Cost of contract manufacturing	(861)	—	(861)
Research and development expenses	(48,068)	(36,432)	(11,636)
Selling, general and administrative expenses	(13,324)	(12,023)	(1,301)
Total operating expenses	**(62,253)**	**(48,455)**	**(13,798)**
Other income	1,485	1,680	(195)
Other expense	(199)	(214)	15
Loss from operations	**(59,518)**	**(45,000)**	**(14,518)**
Other non-operating items, net	11,332	8,558	2,774
Net loss before income tax expense	**$ (48,186)**	**$ (36,442)**	**$ (11,744)**
Income tax benefit / (expense)	329	(89)	418
Net loss	**$ (47,857)**	**$ (36,531)**	**$ (11,326)**

Revenue

Our revenue for the three months ended September 30, 2022 and 2021 was as follows:

	Three months ended September 30,		
	2022	2021	2022 vs 2021
		(in thousands)	
Collaboration revenue	1,449	1,989	(540)
Total revenues	**$ 1,449**	**$ 1,989**	**$ (540)**

CSL Behring

We recognized $0.7 million collaboration revenue in the three months ended September 30, 2022, compared to $0.5 million for the same period in 2021 from the CSL Behring Agreement. Since May 6, 2021, we recognize collaboration revenue related to services we provide in accordance with the CSL Behring Agreement.

BMS

We recognized $0.8 million collaboration revenue in the three months ended September 30, 2022 compared to $1.5 million for the three months ended September 30, 2021.

Cost of contract manufacturing

We incurred $0.9 million of cost of contract manufacturing related to the manufacture of the Product in the three months ended September 30, 2022, which we did not capitalize as inventory in accordance with our accounting policies, compared to nil cost of contract manufacturing in the three months ended September 30, 2021.

Research and development expenses

Research and development expenses for the three months ended September 30, 2022 were $48.1 million, compared to $36.4 million for the same period in 2021. 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 September 30,		
	2022	2021	2022 vs 2021
	(in thousands)		
Huntington's disease (AMT-130)	4,330	2,720	1,610
Temporal lobe epilepsy (AMT-260)	2,499	92	2,407
Fabry disease (AMT-190)	549	114	435
Etranacogene dezaparvovec (AMT-060/061)	277	2,086	(1,809)
Other programs in preclinical development and platform related expenses	886	2,244	(1,358)
Total direct research and development expenses	**$ 8,541**	**$ 7,256**	**$ 1,285**
Employee and contractor-related expenses	15,553	14,623	930
Facility expenses	6,482	4,813	1,669
Disposables	6,012	4,795	1,217
Fair value changes related to contingent consideration	5,503	416	5,087
Share-based compensation expense	3,730	3,248	482
Other expenses	2,247	1,281	966
Total other research and development expenses	**$ 39,527**	**$ 29,176**	**$ 10,351**
Total research and development expenses	**$ 48,068**	**$ 36,432**	**$ 11,636**

Direct research and development expenses

Huntington disease (AMT-130)

In the three months ended September 30, 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. In the three months ended September 30, 2021, 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.

Temporal lobe epilepsy (AMT-260)

In the three months ended September 30, 2022 and September 30, 2021, we incurred $2.5 million and $0.1 million, respectively, for the preclinical development of temporal lobe epilepsy, which we acquired from Corlieve Therapeutics SAS (“Corlieve”) on July 30, 2021.

Fabry disease (AMT-190)

In the three months ended September 30, 2022 and September 30, 2021, we incurred $0.5 million and $0.1 million of costs, respectively, primarily related to our preclinical activities for the treatment of Fabry disease (AMT-190).

Hemophilia B (AMT-060/061)

In the three months ended September 30, 2022 and September 30, 2021, the external costs for our hemophilia B program were primarily related to the execution of our Phase III clinical trial and Manufacturing Development. Up to the Closing of the CSL Behring Agreement in May 2021, we also incurred costs related to the preparation of the global regulatory submissions and to prepare for the commercialization of the Product. After the Closing, CSL Behring is responsible for the clinical and regulatory activities and commercialization of the Product, with the Company managing the existing trials on behalf of CSL Behring. Direct research and development expenses related to clinical development incurred in the three months ended September 30, 2022 and September 30, 2021 are presented net of reimbursements due from CSL Behring.

In the same periods in 2022 and 2021, we also incurred costs related to 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. Our Phase IIb dose-confirmation study was initiated in January 2018 and dosing occurred in July and August 2018. Patients were dosed as part of our Phase I/II clinical trial of AMT-060 in 2015 and 2016. These costs are presented net of reimbursements due from CSL Behring.

Preclinical programs & platform development

In the three months ended September 30, 2022, we incurred $0.9 million of costs primarily related to our preclinical activities associated with product candidates for the treatment of various other research programs and technology innovation projects.

In the three months ended September 30, 2021, we incurred $2.2 million of costs primarily related to our preclinical activities associated with product candidates for the treatment of SCA3 (AMT-150), as well as various other research programs and technology innovation projects.

Other research & development expenses

- We incurred $15.6 million in personnel and contractor related expenses in the three months ended September 30, 2022, compared to $14.6 million for the same period in 2021. The increase was primarily a result of the recruitment of personnel to support the development of our product candidates;
- We incurred $6.5 million in operating expenses and depreciation expenses related to our rented facilities in the three months ended September 30, 2022, compared to $4.8 million in the same period in 2021 as a result of investments we made to expand our facilities;
- We incurred $6.0 million in disposable costs compared to $4.8 million for the same period in 2021 as we continue to expand our activities to support the development of our product candidates;
- We incurred $5.5 million of expenses in the three months ended September 30, 2022 related to an increase in the fair value of contingent consideration associated with the acquisition of Corlieve Therapeutics SAS (“Corlieve”), compared to $0.4 million in the same period in 2021;
- We incurred $3.7 million in share-based compensation expenses in the three months ended September 30, 2022, compared to $3.2 million for the same period in 2021. The increase was primarily a result of an increase in awards granted, including those to newly recruited personnel; and
- We incurred $2.2 million of other expenses for the three months ended September 30, 2022, compared to $1.3 million for the same period in 2021.

Selling, general and administrative expenses

Selling, general and administrative expenses for the three months ended September 30, 2022 were $13.3 million, compared to $12.0 million for the same period in 2021.

- We incurred $5.2 million in personnel and contractor related expenses in the three months ended September 30, 2022, compared to $3.8 million in the same period in 2021;
- We incurred $3.8 million in share-based compensation expenses in the three months ended September 30, 2022, compared to $2.7 million in the same period in 2021; and

- We incurred $1.6 million in professional fees in the three months ended September 30, 2022, compared to $1.5 million in the same period in 2021. We regularly incur accounting, audit and legal fees associated with operating as a public company.

Other items, net

We recognized nil in other income related to the employee retention credit under the U.S. CARES Act in the three months ended September 30, 2022, compared to $1.3 million for the same period in 2021.

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 September 30, 2022, compared to $0.0 million for the same period in 2021.

Other income also includes income from subleasing of a portion of our Amsterdam facility. We present expenses related to such income as other expense.

Other non-operating items, net

Our other non-operating items, net, for the three months ended September 30, 2022 and 2021 were as follows:

	Three months ended September 30,		
	2022	2021	2022 vs 2021
		(in thousands)	
Interest income	$ 39	$ 46	$ (7)
Interest expense - Hercules long-term debt	(3,069)	(1,924)	(1,145)
Foreign currency gains, net	14,362	10,436	3,926
Total other non-operating income, net	**$ 11,332**	$ **8,558**	$ **2,774**

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

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

We recognized a net foreign currency gain, related to our borrowings from Hercules and our cash and cash equivalents as well as loans between entities within the uniQure group, of $14.4 million during the three months ended September 30, 2022, compared to a net gain of $10.4 million during the same period in 2021.

Income tax benefit / (expense)

We recognized $0.3 million of deferred tax benefit in the three months ended September 30, 2022, and $0.1 million of deferred tax expense for the same period in 2021.

Comparison of the nine months ended September 30, 2022 and 2021

The following table presents a comparison of our results of operations for the nine months ended September 30, 2022 and 2021.

	Nine months ended September 30,		
	2022	2021	2022 vs 2021
	(in thousands)		
Total revenues	$ 3,738	$ 466,311	$ (462,573)
Operating expenses:			
Cost of contract revenues	—	(23,178)	23,178
Cost of contract manufacturing	(1,693)	—	(1,693)
Research and development expenses	(139,263)	(101,209)	(38,054)
Selling, general and administrative expenses	(36,802)	(42,323)	5,521
Total operating expenses	**(177,758)**	**(166,710)**	**(11,048)**
Other income	4,981	9,622	(4,641)
Other expense	(621)	(673)	52
(Loss) / income from operations	**(169,660)**	**308,550**	**(478,210)**
Non-operating items, net	34,801	16,391	18,410
(Loss) / income before income tax benefit / (expense)	$ **(134,859)**	$ **324,941**	**(459,800)**
Income tax benefit / (expense)	1,263	(3,560)	4,823
Net (loss) / income	**$ (133,596)**	**$ 321,381**	**$ (454,977)**

Revenue

Our revenue for the nine months ended September 30, 2022 and 2021 was as follows:

	Nine months ended September 30,		
	2022	2021	2022 vs 2021
	(in thousands)		
License revenue	$ —	$ 462,400	$ (462,400)
Collaboration revenue	3,738	3,911	(173)
Total revenues	**$ 3,738**	**$ 466,311**	**$ (462,573)**

CSL Behring

We did not recognize any license revenue related to the CSL Behring Agreement in the nine months ended September 30, 2022. In the nine months ended September 30, 2021, we recognized $462.4 million in license revenue related to the sale of the exclusive global rights to the Product (“License Sale”) on Closing of the CSL Behring Agreement in May 2021.

We recognized $2.1 million collaboration revenue in the nine months ended September 30, 2022, compared to $0.9 million for the same period in 2021. Since May 6, 2021, we recognize collaboration revenue related to services we provide in accordance with the CSL Behring Agreement.

BMS

We recognized $1.6 million collaboration revenue in the nine months ended September 30, 2022 compared to $3.0 million for the nine months ended September 30, 2021.

Cost of contract revenues

We did not recognize any cost of contract revenues for the nine months ended September 30, 2022 compared to $23.2 million for the nine months ended September 30, 2021. The cost recorded in 2021 included $16.7 million of expenses related to payments owed to our licensors on Closing as well as $6.5 million of other external expenses incurred to fulfill the License Sale to CSL Behring.

Cost of contract manufacturing

We incurred $1.7 million of cost of contract manufacturing related to the manufacture of the Product in the nine months ended September 30, 2022, which we did not capitalize as inventory in accordance with our accounting policies, compared to nil cost of contract manufacturing in the nine months ended September 30, 2021.

Research and development expenses

Research and development expenses for the nine months ended September 30, 2022 were $139.3 million, compared to $101.2 million for the same period in 2021. 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.

	Nine months ended September 30,		
	2022	2021	2022 vs 2021
		(in thousands)	
Huntington's disease (AMT-130)	$ 15,721	$ 7,161	$ 8,560
Temporal lobe epilepsy (AMT-260)	11,394	92	11,302
Fabry disease (AMT-190)	1,664	252	1,412
Etranacogene dezaparvovec (AMT-060/061)	1,008	8,350	(7,342)
Other programs in preclinical development and platform related expenses	3,919	6,175	(2,256)
Total direct research and development expenses	**$ 33,706**	**$ 22,030**	**$ 11,676**
Employee and contractor-related expenses	46,786	39,294	7,492
Facility expenses	17,150	13,836	3,314
Disposables	15,077	11,884	3,193
Share-based compensation expense	12,090	9,210	2,880
Fair value changes related to contingent consideration	7,510	416	7,094
Other expenses	6,944	4,539	2,405
Total other research and development expenses	**$ 105,557**	**$ 79,179**	**$ 26,378**
Total research and development expenses	**$ 139,263**	**$ 101,209**	**$ 38,054**

Direct research and development expenses

Huntington disease (AMT-130)

In the nine months ended September 30, 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. In the nine months ended September 30, 2021, 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.

Temporal lobe epilepsy (AMT-260)

In the nine months ended September 30, 2022 and September 30, 2021, we incurred $11.4 million and $0.1 million, respectively, for the preclinical development of temporal lobe epilepsy, which we acquired from Corlieve on July 30, 2021.

Fabry disease (AMT-190)

In the nine months ended September 30, 2022 and September 30, 2021, we incurred $1.7 million and $0.3 million of costs, respectively, primarily related to our preclinical activities for the treatment of Fabry disease (AMT-190).

Hemophilia B (AMT-060/061)

In the nine months ended September 30, 2022 and September 30, 2021, the external costs for our hemophilia B program were primarily related to the execution of our Phase III clinical trial and Manufacturing Development. Up to the Closing of the CSL Behring Agreement in May 2021, we also incurred costs related to the preparation of the global regulatory submissions and to prepare for the commercialization of the Product. After the Closing, CSL Behring is responsible for the clinical and regulatory activities and commercialization of the Product, with the Company managing the existing trials on behalf of CSL Behring. Direct research and development expenses related to clinical development incurred in the nine months ended September 30, 2022 and September 30, 2021 are presented net of reimbursements due from CSL Behring.

In the same periods in 2022 and 2021, we also incurred costs related to 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. Our Phase IIb dose-confirmation study was initiated in January 2018 and dosing occurred in July and August 2018. Patients were dosed as part of our Phase I/II clinical trial of AMT-060 in 2015 and 2016. These costs are presented net of reimbursements due from CSL Behring.

Preclinical programs & platform development

In the nine months ended September 30, 2022, we incurred $3.9 million of costs primarily related to our preclinical activities associated with product candidates for various other research programs and technology innovation projects.

In the nine months ended September 30, 2021, we incurred $6.2 million of costs primarily related to our preclinical activities associated with product candidates for the treatment of SCA3 (AMT-150), as well as various other research programs and technology innovation projects.

Other research & development expenses

- We incurred $46.8 million in personnel and contractor related expenses in the nine months ended September 30, 2022, compared to $39.3 million for the same period in 2021. The increase was primarily a result of the recruitment of personnel to support the development of our product candidates;
- We incurred $17.2 million in operating expenses and depreciation expenses related to our rented facilities in the nine months ended September 30, 2022, compared to $13.8 million in the same period in 2021 as a result of investments we made to expand our facilities;
- We incurred $15.1 million in disposable costs compared to $11.9 million for the same period in 2021 as we continue to expand our activities to support the development of our product candidates;
- We incurred $12.1 million in share-based compensation expenses in the nine months ended September 30, 2022, compared to $9.2 million for the same period in 2021. The increase was primarily a result of an increase in awards granted, including those to newly recruited personnel;
- We incurred $7.5 million of expenses in the nine months ended September 30, 2022 related to an increase in the fair value of contingent consideration associated with the acquisition of Corlieve Therapeutics SAS (“Corlieve”), compared to $0.4 million for the same period in 2021; and
- We incurred $6.9 million of other expenses for the nine months ended September 30, 2022, compared to $4.5 million for the same period in 2021.

Selling, general and administrative expenses

Selling, general and administrative expenses for the nine months ended September 30, 2022 were $36.8 million, compared to $42.3 million for the same period in 2021.

- We incurred $14.8 million in personnel and contractor related expenses in the nine months ended September 30, 2022, compared to $11.8 million in the same period in 2021. The increase in the nine months ended September 30, 2022, relates to the recruitment of personnel;
- We incurred $9.9 million in share-based compensation expenses in the nine months ended September 30, 2022, compared to $9.5 million in the same period in 2021;
- We incurred $4.3 million in professional fees in the nine months ended September 30, 2022, compared to $6.5 million in the same period in 2021. We regularly incur accounting, audit and legal fees associated with operating as a public company. The decrease from the prior period is primarily related to a decrease in professional fees related to the licensing transaction with CSL Behring; and
- We incurred nil financial advisory fees in relation to our licensing transaction with CSL Behring in the nine months ended September 30, 2022, compared to $4.5 million in the same period in 2021.

Other items, net

In the nine months ended September 30, 2022, we recognized $0.3 million in other income in relation to the equity stake received in VectorY B.V. in conjunction with a settlement agreement entered into in April 2021 compared to $3.0 million such income for the same period in 2021.

We recognized nil in other income related to the employee retention credit under the U.S. CARES Act in the nine months ended September 30, 2022, compared to $2.6 million in other income for the same period in 2021.

We recognized $3.9 million in other income from payments received from European authorities to subsidize our research and development efforts in the Netherlands in the nine months ended September 30, 2022, compared to $3.0 million for the same period in 2021.

Other income also includes income from subleasing of a portion of our Amsterdam facility. We present expenses related to such income as other expense.

Other non-operating items, net

Our other non-operating items, net, for the nine months ended September 30, 2022 and 2021 were as follows:

	Nine months ended September 30,		
	2022	2021	2022 vs 2021
	(in thousands)		
Interest income	$ 117	$ 123	$ (6)
Interest expense	(8,279)	(5,377)	(2,902)
Foreign currency gains, net	42,328	21,645	20,683
Other non-operating gains	635	—	635
Total non-operating income, net	**$ 34,801**	**$ 16,391**	**$ 18,410**

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

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

We recognized a net foreign currency gain, related to our borrowings from Hercules and our cash and cash equivalents as well as loans between entities within the uniQure group, of $42.3 million during the nine months ended September 30, 2022, compared to a net gain of $21.6 million during the same period in 2021.

We recognize 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 ("CoC-payment") as described elsewhere in this Quarterly Report on Form 10-Q.

Income tax benefit / (expense)

We recognized $1.3 million of deferred tax benefit in the nine months ended September 30, 2022, and $3.6 million of deferred tax expense for the same period in 2021.

Financial Position, Liquidity and Capital Resources

As of September 30, 2022, we had cash, cash equivalents and restricted cash of $443.4 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, distribution, and licensing arrangements. We believe that our cash and cash equivalents will fund our operations into the first half of 2025 assuming the achievement of $100.0 million of first commercial sale milestone in the United States and $75.0 million of first commercial sale milestone in any of the five contractually defined European countries as of or prior to July 1, 2023 under the CSL Behring Agreement. Our material cash requirements include the following contractual and other obligations:

Debt

As of September 30, 2022, we had an outstanding loan amount owed to Hercules Capital, Inc. ("Hercules") for an aggregate principal amount of $100.0 million. We are contractually required to repay the $100.0 million in equal installments between December 2024 and December 2025, or in full in December 2025 if, prior to June 30, 2024, either (a) the Biologics License Application ("BLA") for AMT-061 is approved by the FDA, or (b) AMT-130 is advanced into a pivotal trial. Future interest payments and financing fees associated with the loan total $38.0 million, with $13.6 million payable within 12 months.

Leases

We entered into lease arrangements for facilities, including corporate, manufacturing and office space. As of September 30, 2022, we had fixed lease payment obligations of $58.6 million, with $8.0 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 Stock Purchase Agreement between the Company and Corlieve ("SPA"). As of September 30, 2022, our commitment amounts include up to $40.4 million in potential milestone payments through Phase I/II development and $156.8 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 September 30, 2022, of $0.98/€1.00. As of September 30, 2022, 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 License Sale 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 nine months ended:

	Nine months ended September 30,	
	2022	2021
	(in thousands)	
Cash, cash equivalents and restricted cash at the beginning of the period	$ 559,353	$ 247,680
Net cash (used in) / generated from operating activities	(90,380)	335,049
Net cash used in investing activities	(14,522)	(63,834)
Net cash generated from financing activities	844	64,964
Foreign exchange impact	(11,876)	(2,589)
Cash, cash equivalents and restricted cash at the end of period	**$ 443,419**	**$ 581,270**

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 $47.9 million and $133.6 million in the three and nine months ended September 30, 2022, compared to a net loss of $36.5 million and net income of $321.4 million during the same periods in 2021. As of September 30, 2022, we had an accumulated deficit of $588.7 million.

Sources of liquidity

From our first institutional venture capital financing in 2006 through May 2021, we funded our operations primarily through private and public placements of equity securities and convertible and other debt securities as well as payments from our collaboration partners. 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. In the year ended December 30, 2021, we received net proceeds of $29.6 million from the issuance of 921,730 ordinary shares that took place during March and April 2021.

On January 29, 2021, we drew down $35 million under our 2021 amendment ("2021 Amended Facility") with Hercules. We drew down a further $30 million under our December 2021 amendment ("2021 Restated Facility") with Hercules in December 2021.

We are subject to certain covenants under our 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, 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 $90.4 million for the nine months ended September 30, 2022 and consisted of net loss of $133.6 million adjusted for non-cash items, including depreciation and amortization expense of $6.2 million, share-based compensation expense of $22.3 million, changes in the fair value of contingent consideration and the derivative financial liability of $6.9 million, unrealized foreign exchange gains of $36.4 million and a change in deferred taxes of $1.3 million. Net cash generated from operating activities also included favorable changes in operating assets and liabilities of $46.1 million. There was a net decrease in accounts receivable and contract asset, prepaid expenses, and other current assets and receivables of $42.0 million, primarily related to the collection of $55.0 million of the contract asset related to CSL milestones of $55.0 million in March 2022 and April 2022. There was an increase in inventories of $4.1 million related to the production of etranacogene dezaparvovec under the CSL Behring Agreement. These changes also relate to a net increase in accounts payable, accrued expenses, other liabilities, and operating leases of $8.2 million, primarily related to an increase in accounts payable.

Net cash generated from operating activities was $335.0 million for the nine months ended September 30, 2021 and consisted of a net income of $321.4 million adjusted for non-cash items, including depreciation and amortization expense of $5.4 million, share-based compensation expense of $18.7 million, a change in fair value of contingent consideration of $0.4 million, unrealized foreign exchange gains, net of $23.2 million, deferred tax expense of $3.6 million and other non-cash items of $2.9 million. Net cash generated from operating activities also included favorable changes in operating assets and liabilities of $11.6 million. These changes primarily related to a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $2.0 million primarily related to various prepayments and a net increase in accounts payable, accrued expenses, other liabilities, and operating leases of $13.6 million primarily related to an increase in amounts to be paid to licensors upon the CSL Behring Closing and an increase in various other accruals for services provided by vendors and personnel accruals. Net income primarily consisted of $462.4 million license revenue recognized on Closing.

Net cash used in investing activities

In the nine months ended September 30, 2022, we used $14.5 million in our investing activities compared to $63.8 million for the same period in 2021.

	Nine months ended September 30,	
	2022	2021
	(in thousands)	
Build out of Amsterdam site	$ (8,265)	(9,853)
Build out of Lexington site	(4,357)	(4,032)
Acquisition of Corlieve, net of cash acquired	(1,900)	(49,949)
Total investments	**$ (14,522)**	**$ (63,834)**

The build out of the Amsterdam site and Lexington site consumed $8.3 million and $4.4 million cash respectively during the nine months ended September 30, 2022, compared to $9.9 million and $4.0 million for the same period in 2021.

We paid EUR 42.1 million ($49.9 million), net of EUR 2.8 million ($3.4 million) of cash acquired, during the nine months ended September 30, 2021 to acquire 97.7% of the outstanding shares of Corlieve on July 30, 2021.

We paid EUR 1.8 million ($1.9 million) to acquire the remaining outstanding shares of Corlieve in February, July and September 2022.

Net cash generated from financing activities

In the nine months ended September 30, 2022, we generated $0.8 million in our financing activities compared to $65.0 million for the same period in 2021.

	Nine months ended September 30,	
	2022	2021
	(in thousands)	
Cash flows from financing activities		
Proceeds from issuance of shares related to employee stock option and purchase plans	$ 844	$ 1,971
Proceeds from loan increment, net of debt issuance costs	-	34,603
Proceeds from issuance of ordinary shares, net of issuance costs	-	29,565
Repayment of debt assumed through Corlieve Transaction	-	(1,175)
Net cash generated from financing activities	**$ 844**	**$ 64,964**

During the nine months ended September 30, 2022, we received $0.8 million from the exercise of options to purchase ordinary shares in relation to our share incentive plans compared to $2.0 million for the same period in 2021.

In January 2021, we received $34.6 million net proceeds from the Hercules 2021 Amended Facility (nil for same period in 2022).

We received net proceeds of $29.6 million associated with our ATM offering in March and April 2021 (nil for 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, which are subject to CSL Behring obtaining required regulatory approvals, including MAA approval from the EMA, BLA approval from the FDA, and approval of a diagnostic test for neutralizing antibodies from the FDA;
- earnout payments we might owe the former shareholders of Corlieve, which are subject to the achievement of specific development and regulatory milestones;
- repayments of the principal amount of our venture debt loan with Hercules, which following the December 15, 2021 amendment will be due in equal installments between December 2024 and December 2025 or in full in December 2025 if, prior to June 30, 2024, either (a) the BLA for AMT-061 is approved by the FDA or (b) AMT-130 is advanced into a pivotal trial;
- the scope, timing, results, and costs of our current and planned clinical trials, including those for AMT-130 in Huntington's disease;
- the extent to which we acquire or in-license other businesses, products, product candidates or technologies;
- the amount and timing of revenue, if any, we receive from commercial sales of any product candidates for which we, or our collaboration partner, receives marketing approval in the future;
- the amount and timing of revenue, if any, we receive from manufacturing products 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 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 nine months ended September 30, 2022, 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 September 30, 2022. Based on such evaluation, our CEO and CFO concluded that as of September 30, 2022, 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 third quarter of 2022, 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

Please refer to "Item 3. Legal Proceedings" in our Annual Report, for information regarding terminated material legal proceedings. Except as set forth therein, there have been no new material legal proceedings.

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:

- Our business, operations and supply chain have been, and may continue to be, materially and adversely affected by the ongoing Covid pandemic.
- We have encountered, and may continue to encounter, delays in, and impediments to the progress of our clinical trials or fail 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 cannot predict when our partner, CSL Behring, will obtain marketing approval to commercialize the product candidate for Hemophilia B, when or if a first sale of etranacogene dezaparvovec occurs, or whether etranacogene dezaparvovec will be commercially successful once approved. If our partner is unable to achieve marketing approval and successfully commercializes etranacogene dezaparvovec or experiences significant delays in doing so, 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, which could increase the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

- We will likely need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations which could have a material adverse effect on our business, financial condition, results of operations, and cash flows.
- Our relationships with customers and third-party payers will be subject to applicable anti-kickback, anti-bribery, fraud and abuse and other laws and regulations, which, if we are found in violation thereof, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.
- We are subject to laws governing data protection in the different jurisdictions in which we operate. The implementation of such data protection regimes is complex, and should we fail to fully comply, we may be subject to penalties that may have an adverse effect on our business, financial condition, and results of operations.
- Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches 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.

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 WHO declared the ongoing outbreak of Covid a pandemic. The Covid pandemic is affecting the United States and global economies and has affected and may continue to affect our operations and those of third parties on which we rely. The Covid 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.

We may also be subject to further laws, regulations, guidelines, executive orders and other requirements at the federal, state and local levels related to the pandemic, which we may be required to undertake or that we choose to undertake. Any such requirements or guidelines that we adopt could have a material impact on our business operations.

Risks Related to the Development of Our Product Candidates

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

All of our product candidates are in research or development. We have not generated any revenues from the sale of products or manufacturing of a product for a third party and do not expect to generate any such revenue until this year, at the earliest. 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 etranacogene dezaparvovec 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 as a result of comprehensive safety investigation into suspected unexpected serious adverse reactions in three patients between July and October 2022.

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 to pay substantial application user fees;
- occurrence of serious adverse events or other undesirable side effects associated with a product candidate that are viewed to outweigh its potential benefits;
- disagreements with regulatory authorities regarding the interpretation of our clinical trial data and results, or the 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 forthcoming 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 with the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

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

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

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

Any inability to successfully initiate or complete preclinical and clinical development could result in additional costs to us or impair our ability to receive marketing approval, to generate revenues from product sales or obtain regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, including changes in the vector or manufacturing process used, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. It is also possible that any such manufacturing 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. A RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to speed the FDA marketing application review timeframe for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. PRIME is a scheme provided by the EMA, similar to the FDA's breakthrough therapy designation, to enhance support for the development of medicines that target an unmet medical need.

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

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

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

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

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

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

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

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

A small number of patients have experienced serious adverse events during our clinical trials of either AMT-060 (our first-generation hemophilia B gene therapy) or etranacogene dezaparvovec. 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. We currently expect that a diagnostic test will be required to determine the levels of neutralizing antibodies present in a patient seeking treatment with etranacogene dezaparvovec, and that regulatory approval of such a diagnostic test will be required. The approval could adversely affect the timing of a first commercial sale of etranacogene dezaparvovec if it does not occur, or if it occurs after or delays regulatory approval of etranacogene dezaparvovec. Currently, CSL Behring is working directly with a third-party provider to gain regulatory health approval of such a diagnostic test, which is based on the clinical diagnostic test used during the development of etranacogene dezaparvovec.

It is also 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. Moreover, before approving a BLA for any product candidate, the FDA will inspect our manufacturing facility and processes. Any failure to follow and document our adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical study, may result in the termination of or a hold on a clinical study, or may delay or prevent filing or approval of marketing applications for our products.

Failure to comply with applicable regulations could also result in the FDA, 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, that may result in delays in regulatory approvals or otherwise adversely affect our ability to manufacture sufficient amounts of our products.

Many factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, 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 United States and the Netherlands governing the use, manufacture, distribution, storage, handling, treatment, and disposal of these materials. In addition to ensuring the safe handling of these materials, applicable requirements require increased safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for damages that result, and any such liability could exceed our assets and resources, and could result in material harm to our business, financial condition, and results of operations.

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

The manufacture of our AAV gene therapies, including etranacogene dezaparvovec, is complex and requires significant expertise. Even with the relevant experience and expertise, manufacturers of gene therapy products often encounter difficulties in production, particularly in scaling out and validating initial production, and ensuring that the product meets required specifications. These problems include difficulties with production costs and yields, quality control, including stability and potency of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. In the past, we have manufactured certain batches of 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 United States, the EMA, and other regulatory agencies of the member states of the European Union, and similar regulatory authorities in other jurisdictions. Failure to obtain marketing approval for a product candidate in a specific jurisdiction will prevent us from commercializing the product candidate in that jurisdiction.

The process of obtaining marketing approval for our product candidates in the United States, the European Union, and other countries is expensive and may take many years, if approval is obtained at all. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities 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.

Our partner, CSL Behring, is currently pursuing the approval of etranacogene dezaparvovec for which marketing authorization applications are currently under review in the United States and European Union. If CSL Behring experiences delays in obtaining marketing approval in the United States, the European Union, or other countries, the commercial prospects of etranacogene dezaparvovec and our ability to achieve contractual milestone payments and royalties on net sales may be harmed and our ability to generate revenues might be materially impaired.

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

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

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

Regulatory requirements affecting gene therapy have changed frequently and continue to evolve, and agencies at both the U.S. federal and state level, as well as congressional committees and foreign governments, have sometimes expressed interest in further regulating biotechnology. In the United States, there have been a number of recent changes relating to gene therapy development. By example, FDA issued a number of new guidance documents, 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 United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. While certain of our product candidates have received orphan drug designation, there is no guarantee that we will be able to receive such designations in the future. The FDA may grant orphan designation to multiple sponsors for the same compound or active molecule and for the same indication. If another sponsor receives FDA approval for such product before we do, we would be prevented from launching our product in the United States for the orphan indication for a period of at least seven years unless we can demonstrate clinical superiority.

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

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

Additionally, regulatory criteria with respect to orphan products is evolving, especially in the area of gene therapy. By example, in the United States, whether two gene therapies are considered to be the same for the purpose of determining clinical superiority 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 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 all available periods of regulatory exclusivity for our product candidates. However, there is no guarantee that we will be granted these periods of regulatory exclusivity or that we will be able to maintain these periods of exclusivity.

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

If we do not obtain or maintain periods of market exclusivity, we may face competition sooner than otherwise anticipated. For instance, in the United States, this could mean that a competing biosimilar product may be able to submit an application to the FDA and obtain approval 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 United States period of exclusivity to a shorter timeframe. Future proposed budgets, international trade agreements and other arrangements or proposals may affect periods of exclusivity.

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. 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.

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. By example, the decisions associated with regulatory filings and approvals for AMT-061 have been, and will continue to be, largely controlled by CSL Behring, and we will not have final decision-making authority in that regard. 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 product revenues will depend on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on many factors, including:

- successful execution of our contractual relationship with CSL Behring for the commercialization of etranacogene dezaparvovec;
- successful completion of preclinical studies and clinical trials, and other work required by regulators;

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

CSL Behring may not receive a conditional marketing authorization based on an accelerated assessment by the EMA for AMT-061 product candidate to facilitate a first commercial sale in the European Union on or before July 1, 2023, and we, thus, may not receive the $75.0 million first commercial sale milestone in any of the five contractually defined European countries as of or prior to July 1, 2023 under the CSL Behring Agreement.

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

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

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

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

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

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

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

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

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

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

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

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

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

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. 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 United States, a variety of risks associated with international operations could materially adversely affect our business.

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

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

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 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, Triplet Therapeutics, CombiGene, AvroBio, Caritas 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 good laboratory practices, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with good clinical practices ("GCPs") for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical and preclinical investigators, and trial sites. If we or any of our third-party service providers fail to comply with applicable GCPs or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the data generated in our trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional studies.

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

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

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

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

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

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

Any collaboration may pose several risks, including the following:

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

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

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

Risks Related to Our Intellectual Property

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

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

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

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

The agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business and financial condition.

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

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

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

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

Successful challenges to our patents may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to 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.

Additionally, the product candidate and intellectual property rights that we acquired in the acquisition of Corlieve were developed and owned by Corlieve and its licensors and we cannot ensure that we will be able to continue to successfully advance this product candidate going forward.

Risks Related to Pricing and Reimbursement

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

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

Government authorities and other third-party payers, such as private health insurers and health maintenance organizations, decide for which medications they will pay and, subsequently, establish reimbursement levels. Reimbursement systems vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. Government authorities and third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and procedures and negotiating or requiring payment of manufacturer rebates. Increasingly, third party payers require drug companies to provide them with predetermined discounts from list prices, are exerting influence on decisions regarding the use of particular treatments and are limiting covered indications. Additionally, in the United States and some foreign jurisdictions, pending or potential legislative and regulatory changes regarding the healthcare system and insurance coverage could result in more rigorous coverage criteria and downward pressure on drug prices, and may affect our ability to profitably sell any products for which we obtain marketing approval. For example, on November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation ("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 now has 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 begins only after the receipt of regulatory marketing approval, and some authorities require approval of the sale price of a product before it can be marketed. In some markets, particularly the countries of the European Union, prescription pharmaceutical pricing remains subject to continuing direct governmental control and to drug reimbursement programs even after initial approval is granted and price reductions may be imposed. Prices of medical products may also be subject to varying price control mechanisms or limitations as part of national health systems if products are considered not cost-effective or where a drug company's profits are deemed excessive. In addition, pricing and reimbursement decisions in certain countries can lead to mandatory price reductions or additional reimbursement restrictions in other countries. Because of these restrictions, any product candidates for which we may obtain marketing approval may be subject to price regulations that delay or prohibit our or our partners' commercial launch of the product in a particular jurisdiction. In addition, we or any collaborator may elect to reduce the price of our products to increase the likelihood of obtaining reimbursement approvals. If countries impose prices, which are not sufficient to allow us or any collaborator to generate a profit, we or any collaborator may refuse to launch the product in such countries or withdraw the product from the market. If pricing is set at unsatisfactory levels, or if the price decreases, our business could be harmed, possibly materially. If we fail to obtain and sustain an adequate level of coverage and reimbursement for our products by third party payers, our ability to market and sell our products could be adversely affected and our business could be harmed.

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

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

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

Risks Related to Our Financial Position and Need for Additional Capital

We had a gain in the year ended December 31, 2021, but 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 $133.6 million in the nine months ended September 30, 2022, and a net gain of $329.6 million in the full year 2021. As of September 30, 2022, we had an accumulated deficit of $588.7 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 2022 and 2023 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 temporal lobe epilepsy and Fabry into Phase I/II clinical studies;
- advancing preclinical research and development for gene therapy product candidates targeting other diseases;
- 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;
- potentially acquiring or in-licensing rights to new therapeutic targets, product candidates and technologies; and
- making potential future milestone payments related to the acquisition of Corlieve, if any.

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

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

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

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

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

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

As of September 30, 2022, we had $100.0 million of outstanding principal of borrowings under the 2021 Restated Facility, which we are required to repay in equal installments between December 2024 and December 2025 or in full in December 2025 if, prior to June 30, 2024, either (a) the BLA for AMT-061 is approved by the FDA or (b) AMT-130 is advanced into a pivotal trial. 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 customers and third-party payers will be subject to applicable anti-kickback, anti-bribery, fraud and abuse and other laws and regulations, which, if we are found in violation thereof, could expose us to criminal sanctions, civil and administrative penalties, contractual damages, reputational harm and diminished profits and future earnings.

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 US 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. The costs associated with any of these actions could be substantial and could cause irreparable harm to our reputation or otherwise have a material adverse effect on our business, financial condition, and results of operations.

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

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

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

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

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

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

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

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

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, 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 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.

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 October 28, 2022, the sale price of our ordinary shares ranged from a high of $82.49 to a low of $4.72. The closing price on October 28, 2022, was $19.04 per ordinary share. The stock market in general and the market for smaller biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our ordinary shares may be influenced by many factors, including:

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

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

Our directors, executive officers and major shareholders holding more than 5% of our outstanding ordinary shares, in the aggregate, beneficially own approximately 55.4% of our issued shares (including such shares to be issued in relation to exercisable options to purchase ordinary shares) as of September 30, 2022. As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to control many matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could control the election of the board directors and the approval of any merger, consolidation, or sale of all or substantially all our assets. These shareholders may have interests that differ from those of other of our shareholders and conflicts of interest may arise.

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

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

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

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

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

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

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

Risks for U.S. Holders

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

Based on our average value of our gross assets, our cash and cash equivalents as well as the price of our shares we qualified as a passive foreign investment company ("PFIC") for U.S. federal income tax for 2016 but not for 2017 through 2021. A corporation organized outside the United States generally will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which at least 75% of its gross income is passive income or on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held to produce passive income. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions. Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will continue to qualify as a PFIC in future taxable years. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate, and may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were considered a PFIC for the current taxable year or any future taxable year, a U.S. holder would be required to file annual information returns for such year, whether the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year. In certain circumstances a U.S. holder may be able to make certain tax elections that would lessen the adverse impact of PFIC status; however, to make such elections the U.S. holder will usually have to have been provided information about the company by us, and we do not intend to provide such information.

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

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

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

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

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

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

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

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

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

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

EXHIBIT INDEX

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 September 30, 2022, filed with the Securities and Exchange Commission on November 2, 2022, 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 September 30, 2022, filed with the Securities and Exchange Commission on November 2, 2022, is formatted in Inline Extensible Business Reporting Language ("iXBRL")

* Filed herewith.

± Furnished herewith.

SIGNATURE

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

UNIQURE, N.V.

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

By: /s/ Christian Klemt
Christian Klemt
Chief Financial Officer
(Principal Financial Officer)

Dated November 2, 2022

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)
November 2, 2022

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)
November 2, 2022

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 September 30, 2022, 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)

November 2, 2022

By: /s/ CHRISTIAN KLEMT

Christian Klemt
Chief Financial Officer
(Principal Financial Officer)

November 2, 2022

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.