Table of Contents

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, 2024

OR

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

For the transition period from _____ to _____

Commission file number: 001-36294

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

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

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

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

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

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

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

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

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

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

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

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

As of October 31, 2024, the registrant had 48,743,140 ordinary shares, par value €0.05, outstanding.

TABLE OF CONTENTS

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 concerning: our ability to fund our future operations; our financial position, revenues, costs, expenses, uses of cash and capital requirements; our need for additional financing or the time period for which our existing cash resources will be sufficient to meet our operating requirements; the success, progress, number, scope, cost, duration, timing or results of our research and development activities, preclinical and clinical trials, including the timing for initiation or completion of or availability of results from any preclinical studies and clinical trials or for the submission, review or approval of any regulatory filing; the timing of, and our ability to, obtain and maintain regulatory approvals for any of our product candidates; the potential benefits that may be derived from any of our product candidates; our strategies, prospects, plans, goals, expectations, forecasts or objectives; our collaboration, royalty financing and license agreements; our ability to identify and develop new product candidates and technologies; our intellectual property position; our commercialization, marketing and manufacturing capabilities and strategy; our estimates regarding future expenses and needs for additional financing; our restructuring efforts and the results of our strategic review, including the divestment of our Lexington facility; our ability to identify, recruit and retain key personnel; our financial performance; and our liquidity and working capital requirements.

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 (the "SEC"), including our most recent Annual Report on Form 10-K filed with the SEC on February 28, 2024 (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 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 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, 2024	December 31, 2023
	(in thousands, except share and per share amounts)	
Current assets		
Cash and cash equivalents	$ 251,626	$ 241,360
Current investment securities	183,615	376,532
Accounts receivable	5,322	4,193
Inventories, net	—	12,024
Prepaid expenses	19,286	15,089
Other current assets and receivables	4,289	2,655
Total current assets	**464,138**	**651,853**
Non-current assets		
Property, plant and equipment, net of accumulated depreciation of $ 30.8 million as of September 30, 2024 and $55.7 million as of December 31, 2023	25,566	46,548
Other investments	28,260	2,179
Operating lease right-of-use assets	14,833	28,789
Intangible assets, net, including in-process research and development asset of $59.8 million as of September 30, 2024 and $ 59.1 million as of December 31, 2023	76,609	60,481
Goodwill	24,084	26,379
Deferred tax assets, net	10,863	12,276
Other non-current assets	1,453	3,184
Total non-current assets	**181,668**	**179,836**
Total assets	**$ 645,806**	**$ 831,689**
Current liabilities		
Accounts payable	$ 5,441	$ 6,586
Accrued expenses and other current liabilities	32,301	30,534
Current portion of contingent consideration	29,233	28,211
Current portion of operating lease liabilities	4,298	8,344
Total current liabilities	**71,273**	**73,675**
Non-current liabilities		
Long-term debt	51,113	101,749
Liability from royalty financing agreement	426,687	394,241
Operating lease liabilities, net of current portion	12,185	28,316
Contingent consideration, net of current portion	12,181	14,795
Deferred tax liability, net	7,627	7,543
Other non-current liabilities, net of current portion	8,919	3,700
Total non-current liabilities	**518,712**	**550,344**
Total liabilities	**589,985**	**624,019**
Commitments and contingencies		
Shareholders' equity		
Ordinary shares, €0.05 par value: 80,000,000 shares authorized as of September 30, 2024 and December 31, 2023 and 48,738,874 and 47,833,830 ordinary shares issued and outstanding as of September 30, 2024 and December 31, 2023, respectively	2,932	2,883
Additional paid-in-capital	1,166,291	1,148,749
Accumulated other comprehensive loss	(56,698)	(53,553)
Accumulated deficit	(1,056,704)	(890,409)
Total shareholders' equity	**55,821**	**207,670**
Total liabilities and shareholders' equity	**$ 645,806**	**$ 831,689**

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
	(in thousands, except share and per share amounts)		(in thousands, except share and per share amounts)	
License revenues	$ 2,111	$ 497	$ 5,182	$ 1,290
Contract manufacturing revenues	—	349	6,114	6,596
Collaboration revenues	176	561	10,602	1,268
Total revenues	**2,287**	**1,407**	**21,898**	**9,154**
Operating expenses:				
Cost of license revenues	(264)	—	(648)	—
Cost of contract manufacturing revenues	(757)	(1,006)	(17,060)	(4,793)
Research and development expenses	(30,595)	(65,400)	(104,942)	(172,245)
Selling, general and administrative expenses	(11,575)	(18,074)	(41,279)	(57,103)
Total operating expenses	**(43,191)**	**(84,480)**	**(163,929)**	**(234,141)**
Other income	2,591	1,424	5,950	4,537
Other expense	(1,915)	(228)	(2,385)	(673)
Loss from operations	**(40,228)**	**(81,877)**	**(138,466)**	**(221,123)**
Interest income	4,866	7,495	17,179	12,393
Interest expense	(16,611)	(15,444)	(48,865)	(25,846)
Foreign currency gains / (losses), net	7,564	186	5,430	(1,809)
Loss before income tax (expense) / benefit	**$ (44,409)**	**$ (89,640)**	**$ (164,722)**	**$ (236,385)**
Income tax benefit / (expense)	31	69	(1,573)	1,113
Net loss	**$ (44,378)**	**$ (89,571)**	**$ (166,295)**	**$ (235,272)**
Other comprehensive loss:				
Foreign currency translation loss, net	(415)	(6,118)	(3,252)	(267)
Defined benefit pension gain, net of taxes	37	—	107	—
Total comprehensive loss	**$ (44,756)**	**$ (95,689)**	**$ (169,440)**	**$ (235,539)**
Basic and diluted net loss per ordinary share	(0.91)	(1.88)	(3.42)	(4.94)
Weighted average shares used in computing basic and diluted net loss per ordinary share	48,718,533	47,770,101	48,576,339	47,619,875

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

uniQure N.V.

UNAUDITED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE THREE MONTHS ENDED SEPTEMBER 30, 2024 AND 2023

	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, 2023	**47,702,331**	**$ 2,877**	**$ 1,130,515**	**$ (52,440)**	**$ (727,632)**	**$ 353,320**
Loss for the period	—	—	—	—	(89,571)	(89,571)
Other comprehensive loss, net	—	—	—	(6,118)	—	(6,118)
Exercises of share options	400	—	2	—	—	2
Restricted share units distributed during the period	100,296	5	(5)	—	—	—
Share-based compensation expense	—	—	11,097	—	—	11,097
Issuance of ordinary shares relating to employee stock purchase plan	7,264	1	53	—	—	54
Balance at September 30, 2023	**47,810,291**	**$ 2,883**	**$ 1,141,662**	**$ (58,558)**	**$ (817,203)**	**$ 268,784**
Balance at June 30, 2024	**48,694,569**	**$ 2,930**	**$ 1,162,823**	**$ (56,320)**	**$ (1,012,326)**	**$ 97,107**
Loss for the period	—	—	—	—	(44,378)	(44,378)
Other comprehensive loss, net	—	—	—	(378)	—	(378)
Exercises of share options	3,900	—	32	—	—	32
Restricted share units distributed during the period	40,405	2	(2)	—	—	—
Share-based compensation expense	—	—	3,438	—	—	3,438
Balance at September 30, 2024	**48,738,874**	**$ 2,932**	**$ 1,166,291**	**$ (56,698)**	**$ (1,056,704)**	**$ 55,821**

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 MONTHS ENDED SEPTEMBER 30, 2024 AND 2023

	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 December 31, 2022	**46,968,032**	**$ 2,838**	**$ 1,113,393**	**$ (58,291)**	**$ (581,931)**	**$ 476,009**
Loss for the period	—	—	—	—	(235,272)	(235,272)
Other comprehensive loss, net	—	—	—	(267)	—	(267)
Exercises of share options	12,882	1	122	—	—	123
Restricted and performance share units distributed during the period	817,107	43	(43)	—	—	—
Share-based compensation expense	—	—	28,052	—	—	28,052
Issuance of ordinary shares relating to employee stock purchase plan	12,270	1	138	—	—	139
Balance at September 30, 2023	**47,810,291**	**$ 2,883**	**$ 1,141,662**	**$ (58,558)**	**$ (817,203)**	**$ 268,784**
Balance at December 31, 2023	**47,833,830**	**$ 2,883**	**$ 1,148,749**	**$ (53,553)**	**$ (890,409)**	**$ 207,670**
Loss for the period	—	—	—	—	(166,295)	(166,295)
Other comprehensive loss, net	—	—	—	(3,145)	—	(3,145)
Exercises of share options	3,900	—	32	—	—	32
Restricted share units distributed during the period	890,994	48	(48)	—	—	—
Share-based compensation expense	—	—	17,509	—	—	17,509
Issuance of ordinary shares relating to employee stock purchase plan	10,150	1	49	—	—	50
Balance at September 30, 2024	**48,738,874**	**$ 2,932**	**$ 1,166,291**	**$ (56,698)**	**$ (1,056,704)**	**$ 55,821**

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,	
	2024	2023
	(in thousands)	
Cash flows from operating activities		
Net loss	$ (166,295)	$ (235,272)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	8,285	7,712
Amortization of discount on investment securities	(8,472)	(6,529)
Share-based compensation expense	17,509	28,052
Royalty financing agreement interest expense	37,671	14,940
Deferred tax expense / (income)	1,573	(1,113)
Changes in fair value of contingent consideration	(2,032)	15,441
Provision for inventory write-downs	6,297	—
Unrealized foreign exchange (gains) / losses, net	(5,726)	3,119
Other items, net	(2,460)	2,146
Changes in operating assets and liabilities:		
Accounts receivable, prepaid expenses, and other current assets and receivables	(5,764)	96,551
Inventories	(3,876)	(8,730)
Accounts payable	(512)	(4,784)
Accrued expenses, other liabilities, and operating leases	(6,082)	(6,007)
Contingent consideration milestone payment	—	(1,914)
Net cash used in operating activities	(129,884)	(96,388)
Cash flows from investing activities		
Proceeds on maturity of debt securities	480,806	106,307
Investment in debt securities	(279,586)	(366,439)
Divestment of commercial manufacturing facility	(8,300)	—
Purchases of property, plant, and equipment	(3,328)	(5,116)
Net cash generated from / (used in) investing activities	189,592	(265,248)
Cash flows from financing activities		
Proceeds from royalty financing agreement	—	374,350
Payment of debt issuance costs	—	(4,288)
Proceeds from issuance of ordinary shares related to employee stock option and purchase plans	81	262
Repayment of long-term debt	(53,050)	—
Contingent consideration milestone payment	—	(7,649)
Net cash generated (used in) / generated from financing activities	(52,969)	362,675
Currency effect on cash, cash equivalents and restricted cash	1,796	424
Net increase in cash, cash equivalents and restricted cash	8,535	1,463
Cash, cash equivalents and restricted cash at beginning of period	244,544	231,173
Cash, cash equivalents and restricted cash at the end of period	**$ 253,079**	**$ 232,636**
Cash and cash equivalents	$ 251,626	$ 229,484
Restricted cash related to leasehold and other deposits	1,453	3,152
Total cash, cash equivalents and restricted cash	**$ 253,079**	**$ 232,636**
Supplemental cash flow disclosures:		
Cash paid for interest	$ (16,892)	$ (12,996)
Non-cash decrease in accounts payables and accrued expenses and other current liabilities related to purchases of property, plant, and equipment	$ (673)	$ (995)

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

uniQure N.V.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(Unaudited)

1 General business information

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

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

2 Summary of significant accounting policies

2.1 Basis of preparation

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

The unaudited consolidated financial statements are presented in United States ("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. There has been a reclassification of $2.2 million from Other non-current assets to Other investments within the comparative consolidated balance sheets at December 31, 2023 to improve the consistency and comparability of the consolidated financial statements.

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, 2024, are not necessarily indicative of the results to be expected for the full year ending December 31, 2024, or for any other future year or interim period. The accompanying financial statements should be read in conjunction with the audited financial statements and the related notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2023 filed by the Company with the SEC on February 28, 2024 (the "Annual Report").

2.3 Use of estimates

The preparation of the financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of revenues and expenses during the reporting period. 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, 2023, and the notes thereto, which are included in the Annual Report. There have been no material changes in the Company's significant accounting policies during the nine months ended September 30, 2024 except as described within Note 3 "*Divestiture of commercial manufacturing activities*" and Note 5 "*CSL Behring collaboration*."

2.5 Recent accounting pronouncements

There have been no new accounting pronouncements or changes to accounting pronouncements during the nine months ended September 30, 2024, as compared to the recent accounting pronouncements described in Note 2.3.27 of the Annual Report, which could be expected to materially impact the Company's unaudited consolidated financial statements.

3 Divestiture of commercial manufacturing activities

Description of transaction

On June 29, 2024, affiliates of the Company agreed with Genezen Holdings Inc. and its affiliate Genezen MA, Inc. (together "Genezen") to sell the Company's commercial manufacturing activities located in Lexington, MA (the "Lexington Transaction"). The Lexington Transaction closed on July 22, 2024 (the "Closing").

Genezen extended offers of employment to a significant majority of the Company's employees located at the Lexington facility (the "Lexington Facility"), with the remaining employees terminated effective August 30, 2024.

uniQure Inc. and uniQure biopharma B.V., both wholly owned subsidiaries of the Company, entered into an Asset Purchase Agreement ("APA") with Genezen on June 29, 2024. Pursuant to the APA, Genezen agreed to acquire the manufacturing equipment with a carrying value of $5.7 million and related manufacturing operations, inventory with a carrying value of $8.8 million and certain other assets with a carrying value of $ 12.3 million associated with the Lexington Facility on Closing.

As consideration, the Company received (i) shares of newly issued Series C preferred stock of Genezen Holdings Inc. which are convertible into Genezen common stock and will accrue an 8.0% per annum cumulative dividend, (ii) a convertible promissory note with a nominal amount of $12.5 million, bearing interest at 8.0% per annum and maturing 63 months following the date of issuance and (iii) a right to purchase HEMGENIX® at terms considered favorable to market terms.

The Company recorded the Series C preferred stock in Genezen Holdings Inc. issued to the Company at Closing at its fair market value of $12.5 million. The Company subsequently measures these non-marketable equity securities at cost less any impairment, adjusted to fair value if there are observable price changes in orderly transactions for an identical or similar investment of the Genezen Holdings Inc., in accordance with topic ASC 321, *Investments – Equity Securities.* The value of the Series C preferred stock was $ 12.5 million as of September 30, 2024.

The convertible promissory note was recognized at its fair value of $ 13.3 million at Closing. The convertible promissory note is classified as not held for sale and subsequently measured at amortized cost, net of allowance for credit losses in accordance with topic ASC 310, *Receivables* as it did not meet the definition of a debt security under topic *ASC 320, Investments – Debt Securities.* The Company accrues interest income on its convertible promissory note using the effective interest method over the convertible promissory note's contractual term. The convertible promissory note had a balance of $13.4 million and nil as of September 30, 2024 and December 31, 2023, respectively. During the three and nine months ended September 30, 2024, the Company recognized $0.1 million and $0.1 million, respectively, of interest income. As of September 30, 2024, the Company has not recorded an allowance for credit losses related to the convertible promissory note.

uniQure Inc., Genezen and the landlord of the Lexington Facility entered into an agreement for uniQure to assign and Genezen to assume the existing lease agreement between uniQure and the landlord at Closing. The Company also amended its original July 2013 guarantee to continue guaranteeing rental payments owed by Genezen until the end of the current term on May 31, 2029. In the event of Genezen's default related to rental payments owed to the landlord, uniQure is entitled to terminate the assignment agreement and step into the original lease agreement. On Closing, the Company de-recognized its right of use asset with a carrying amount of $11.8 million and related lease liability for the facility, of $17.9 million, which were classified as held-for-sale as at June 30, 2024. Following the Closing, $1.7 million of deposits were released and reclassified from restricted cash into cash.

At Closing, uniQure Inc. entered into a Commercial Supply Agreement ("CSA") with Genezen. Pursuant to the terms of the CSA, the parties agreed to subcontract the manufacturing of HEMGENIX® to Genezen. The CSA includes a minimum term of three years and minimum purchase commitments of HEMGENIX® commercial supplies of $ 43.3 million over the first three years, unless certain contractual provisions are triggered. The CSA provides the Company with rights to purchase HEMGENIX® at terms considered favorable to arms-length market terms. In accordance with ASC 805 *Business Combinations,* the Company recorded an intangible asset valued at $ 16.7 million with respect to these favorable terms. The intangible asset will be amortized on a straight-line basis over a three-year term, commencing at Closing. Amortization expense of $1.2 million (presented within Other expense in the Consolidated Statement of Operations and Comprehensive Loss) was recorded during the three and nine-month periods ended September 30, 2024.

The Company's obligations with respect to the supply of HEMGENIX® to CSL Behring pursuant to the Development and Commercial Supply Agreement between uniQure biopharma B.V. and CSL Behring Inc (the "DCSA") remain in effect notwithstanding the subcontracting to Genezen. The Company expects to resell HEMGENIX® material purchased from Genezen via its minimum commitments to CSL Behring at a loss. In accordance with ASC 330 *Inventory,* the Company, at Closing, recognized a liability of $ 8.8 million related to the net losses expected from the purchase of these minimum commitments. The liability is accounted for as a reduction of the consideration received. The Company will subsequently adjust the liability for any changes to the losses expected to be incurred. Changes to the liability are recorded as Other expense within the Company's Consolidated Statements of Operations and Comprehensive Loss. As of September 30, 2024, the Company classified $2.4 million of the liability as accrued expenses and other current liabilities and $5.5 million within Other non-current liabilities in the Consolidated Balance Sheets.

The Lexington Transaction was accounted for as a divestment of the Company's commercial manufacturing activities. The net fair value of consideration received of $25.4 million, less costs associated with the sale of $ 3.3 million, exceeded the $20.9 million fair market value of the net assets transferred (including allocated goodwill) by $ 1.2 million. The excess over the fair market value was recognized as a net gain in Other income on the Company's Consolidated Statement of Operations and Comprehensive Loss.

At Closing, the Company paid a total of $ 8.3 million to Genezen and a third party related to adjustments of working capital and to obtain consent to proceed with the divestment.

Additionally, uniQure biopharma B.V. entered into a development and other manufacturing services agreement ("DMSA") with Genezen at Closing. Pursuant to the DMSA, the Company is entitled to receive, as a preferred customer, manufacturing and development services to support the Company's investigational gene therapy programs and other services related to HEMGENIX® (other than its manufacturing and supply obligations under the CSA). The DMSA has a minimum term of three years and requires the Company to purchase services for a total minimum of $ 14.0 million.

4 Restructuring

As part of the Lexington Transaction, the Company terminated certain employees that did not transfer to Genezen. The Company incurred $1.4 million of expenses related to termination benefits offered to these employees, which were recorded as Research and Development Expense and Selling, General and Administrative Expense during the nine-month period ended September 30, 2024.

On August 1, 2024, the Company announced an organizational restructuring (the "Restructuring"). As a result, the Company recorded $4.1 million of severance and other personnel-related expenses during the three-month period ended September 30, 2024.

A summary of the charges for the three and nine months ended September 30, 2024 by major activity type is as follows (nil in prior periods):

	Three months ended September 30, 2024	Nine months ended September 30, 2024
Severance and other personnel costs	(in thousands)	
Research and development	$ 3,378	$ 4,475
General and administrative	706	1,040
Total	**$ 4,084**	**$ 5,515**

In October 2023, the Company announced a reorganization and recorded a $ 1.0 million liability as of December 31, 2023 related to the termination of certain employees. A summary of the changes in the severance and other personnel liabilities related to the workforce reduction, which are included within Accrued Expenses and Other Current Liabilities on the Consolidated Balance Sheets, are as follows:

	Amount of liability
	(in thousands)
Balance as of December 31, 2023	$ **1,027**
Severance and other personnel costs	5,515
Cash payments during the period	(2,444)
Balance as of September 30, 2024	**$ 4,098**

5 CSL Behring collaboration

On June 24, 2020, uniQure biopharma B.V. entered into a commercialization and license agreement with CSL Behring (the "CSL Behring Agreement"), pursuant to which CSL Behring received exclusive global rights to HEMGENIX®.

The transaction became fully effective on May 6, 2021.

License revenue

The Company recognized $2.1 million and $5.2 million of royalty revenue in the three and nine months ended September 30, 2024, respectively, compared to $0.5 million and $1.3 million of royalty revenue in the three and nine months ended September 30, 2023, respectively. Royalties on the sale of HEMGENIX® are recorded once earned and are presented as license revenue.

Manufacturing revenue

The Company recognized nil and $6.1 million of manufacturing revenue in the three and nine months ended September 30, 2024, respectively, compared to $0.3 million and $6.6 million of manufacturing revenue recorded in the three and nine months ended September 30, 2023, respectively. The Company recognized contract manufacturing revenue when ownership transferred to CSL Behring.

Following the Closing of the Lexington Transaction, title to HEMGENIX® supply directly passes from the contract manufacturer, Genezen, to CSL Behring. The Company does not control HEMGENIX® before it is transferred to CSL Behring. The Company arranges for HEMGENIX® to be provided by Genezen to CSL Behring. The Company determined that it is an agent in the sale of HEMGENIX® to CSL Behring.

In accordance with ASC 330 *Inventory*, at Closing, the Company recognized a liability of $ 8.8 million related to the expected net losses from the resale of HEMGENIX® to be purchased pursuant to its contractual minimum commitments. As a result of the Company being an agent, the Company recognizes corresponding costs related to the purchase of HEMGENIX® from Genezen net of income from the sales of HEMGENIX® to CSL Behring and income related to the release of liabilities associated with expected net losses in Other expense within the Company's Consolidated Statements of Operations and Comprehensive Loss.

Collaboration revenue

The Company recognized $0.2 million and $10.6 million of collaboration revenue in the three and nine months ended September 30, 2024, respectively, compared to $0.6 million and $1.3 million of collaboration revenue in each of the three and nine months ended September 30, 2023. In accordance with the DCSA, certain development and other services rendered by the Company are reimbursed by CSL Behring.

Accounts receivable

As of September 30, 2024, the Company had accounts receivable of $5.0 million from CSL Behring related to collaboration services and royalty revenue.

As of December 31, 2023, the Company recorded accounts receivable of $4.0 million from CSL Behring related to collaboration services, contract manufacturing revenue and royalty revenue.

6 Investment securities

The following tables summarize the Company's investments in sovereign debt as of September 30, 2024 and December 31, 2023:

	At September 30, 2024			
	Amortized cost	Gross unrealized holding gains	Gross unrealized holding losses	Estimated fair value
	(in thousands)			
Current investments:				
Government debt securities (held-to-maturity)	$ 183,615	$ 250	$ —	$ 183,865
Total	**$ 183,615**	**$ 250**	**$ —**	**$ 183,865**

	At December 31, 2023			
	Amortized cost	Gross unrealized holding gains	Gross unrealized holding losses	Estimated fair value
	(in thousands)			
Current investments:				
Government debt securities (held-to-maturity)	$ 376,532	$ 139	$ —	$ 376,671
Total	**$ 376,532**	**$ 139**	**$ —**	**$ 376,671**

The Company invests in short-term U.S. and European government bonds with the highest investment credit rating. The U.S. and European government bonds are U.S. dollar and euro denominated, respectively.

Investment securities with original maturities of 90 days or less when purchased are presented within cash and cash equivalents and measured at amortized cost (September 30, 2024: $44.6 million, December 31, 2023: nil).

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

7 Inventories, net

The following table summarizes the inventories, net balances as of September 30, 2024 and December 31, 2023:

	September 30, 2024	December 31, 2023
	(in thousands)	
Raw materials	$ —	$ 7,157
Work in progress	—	4,109
Finished goods	—	758
Inventories	**$ —**	**$ 12,024**

The Company recorded write downs to net realizable value of $0.5 million and $6.3 million in the three and nine months ended September 30, 2024, respectively, compared to nil in the same periods in 2023. The costs are recognized as Cost of Contract Manufacturing Revenues. At September 30, 2024, and December 31, 2023, the Company recorded an allowance for inventory of nil and $1.6 million, respectively. The Company sold its inventories as part of the divestment of its commercial manufacturing activities (refer to Note 3 "*Divestiture of commercial manufacturing activities*" and Note 4 "*Restructuring*").

8 Fair value measurement

The Company measures certain financial assets and liabilities at fair value, either upon initial recognition or for subsequent accounting or reporting. *ASC 820, Fair Value Measurements and Disclosures* requires disclosure of methodologies used in determining the reported fair values and establishes a hierarchy of inputs used when available. The three levels of the fair value hierarchy are described below:

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

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

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

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

The carrying amount of cash and cash equivalents, accounts receivable from licensing and collaboration partners, 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, 2024 and December 31, 2023:

	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, 2023					
Assets:					
Cash and cash equivalents	$ 241,360	$ —	$ —	$241,360	Cash and cash equivalents
Restricted cash	3,184	—	—	3,184	Other non-current assets
Total assets	**$ 244,544**	**$ —**	**$ —**	**$244,544**	
Liabilities:					
Contingent consideration	—	—	43,006	43,006	Contingent consideration
Consideration for post-acquisition services	—	—	457	457	Other non-current liabilities
Total liabilities	**$ —**	**$ —**	**$ 43,463**	**$ 43,463**	
At September 30, 2024					
Assets:					
Cash and cash equivalents	$ 251,626	$ —	$ —	$251,626	Cash and cash equivalents
Restricted cash	1,453	—	—	1,453	Other non-current assets
Total assets	**$ 253,079**	**$ —**	**$ —**	**$253,079**	
Liabilities:					
Contingent consideration	—	—	41,414	41,414	Contingent consideration
Consideration for post-acquisition services	—	—	415	415	Other non-current liabilities
Total liabilities	**$ —**	**$ —**	**$ 41,829**	**$ 41,829**	

Contingent consideration

The Company is required to pay up to EUR 178.8 million (or $199.6 million based on the foreign exchange rate on September 30, 2024) to the former shareholders of uniQure France SAS (formerly Corlieve Therapeutics SAS) upon the achievement of contractually defined milestones in connection with the Company's July 2021 acquisition of uniQure France SAS.

The fair value of the contingent consideration as of September 30, 2024 was $ 41.4 million (December 31, 2023: $43.0 million) using discount rates of approximately 14.4% to 15.4% (December 31, 2023: 15.3% to 15.6%). The Company assumes the probability of achieving a EUR 30.0 million (or $33.5 million based on the foreign exchange rate on September 30, 2024) milestone payment following the dosing of the first patient in Phase I/II clinical trial of AMT-260 to be 100%.

If, as of September 30, 2024, the Company had assumed a 100% likelihood of AMT-260 advancing into a Phase III clinical study, then the fair value of the contingent consideration would have increased to $68.5 million. If as of September 30, 2024 the Company had assumed that it would discontinue development of the AMT-260 program, then the contingent consideration would have been released to income.

The following table presents the changes in fair value of contingent consideration between December 31, 2023 and September 30, 2024:

	Amount of contingent consideration
	2024
	(in thousands)
Balance at December 31, 2023	**$ 43,006**
Change in fair value (presented within research and development expenses)	(2,031)
Currency translation effects	439
Balance at September 30, 2024	**$ 41,414**

As of September 30, 2024, the Company classified $29.2 million (December 31, 2023: $28.2 million) of the total contingent consideration of $41.4 million (December 31, 2023: $43.0 million) as current liabilities. The balance sheet classification between current and non-current liabilities is based upon the Company's best estimate of the timing of settlement of the remaining relevant milestones.

Investment securities

Refer to Note 6 "*Investment securities*" for the fair value of the investment securities as of September 30, 2024 and December 31, 2023.

9 Accrued expenses and other current liabilities

Accrued expenses and other current liabilities include the following items:

	September 30, 2024	December 31, 2023
	(in thousands)	
Personnel related accruals and liabilities	$ 15,438	$ 16,263
Accruals for goods received from and services provided by vendors-not yet billed	12,350	12,834
Current portion of firm purchase commitment liability	2,428	-
Liability owed to the Purchaser pursuant to the Royalty Financing Agreement	2,085	1,437
Total	**$ 32,301**	**$ 30,534**

10 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, January 2021, December 2021 (the "2021 Restated Facility"), and on May 12, 2023 (the "2023 Amended Facility") and July 22, 2024 (the "2024 Amended Facility").

On July 19, 2024, in connection with the Closing of the Lexington Transaction and the amendment of the 2023 Amended Facility, the Company prepaid $50.0 million of the $100.0 million of principal outstanding as well as $3.1 million in end-of-term fees.

The 2023 Amended Facility extended the maturity date and interest-only period from December 1, 2025 to January 5, 2027 (the "Maturity Date").

The total principal outstanding as of September 30, 2024 under the 2024 Amended Facility was $ 50.0 million.

The Company is required to repay the residual principal balance of $50.0 million on the Maturity Date. The interest rate is adjustable and is the greater of (i) 7.95% and (ii) 7.95% plus the prime rate less 3.25% per annum. Pursuant to the terms of the 2024 Amended Facility, the Company owes a back-end fee of $2.4 million on December 1, 2025 and a back-end fee of $0.6 million on the Maturity Date.

The amortized cost (including interest due presented as part of accrued expenses and other current liabilities) was $51.7 million as of September 30, 2024, compared to $ 102.9 million as of December 31, 2023, and is recorded net of discount and debt issuance costs. The foreign currency gain on the facility in the three months ended September 30, 2024 was $2.6 million and the foreign currency loss on the facility in the nine months ended September 30, 2024 was $0.4 million compared to a foreign currency loss of $ 3.0 million and $1.4 million, respectively, during the same periods in 2023.

Interest expense during the three and nine months ended September 30, 2024 was $ 3.7 million and $11.1 million, respectively, compared to $3.7 million and $10.9 million during the same periods in 2023.

Under the 2024 Amended Facility, the Company must remain current in its periodic reporting requirements and is required to keep a minimum cash balance deposited in bank accounts in the U.S. equivalent to the lesser of (i) 65% of the outstanding balance of principal due or (ii) 100% of worldwide cash and cash equivalents. This restriction on cash and cash equivalents only relates to the location of the cash and cash equivalents, and such cash and cash equivalents can be used at the discretion of the Company. Beginning on April 1, 2024, the Company is required to keep a minimum of unrestricted cash equal to at least 30% of the loan amount outstanding. In combination with other covenants, the 2024 Amended Facility restricts the Company's ability to, among other things, incur future indebtedness and obtain additional debt financing, to make investments in securities or in other companies, to transfer assets, to perform certain corporate changes, to make loans to employees, officers, and directors, and to make dividend payments and other distributions to its shareholders. The Company secured the facilities by directly or indirectly pledging its total assets of $645.8 million, less $1.2 million of cash and cash equivalents and other current assets held by the Company, and $ 89.7 million of other current assets and investment held by uniQure France SAS as well as receivables sold to the Purchaser.

Under the 2024 Amended Facility, the occurrence of a material adverse effect, as defined therein, would entitle Hercules to declare all principal, interest and other amounts owed by the Company immediately due and payable. As of September 30, 2024, the Company was in material compliance with all covenants and provisions.

11 Royalty Financing Agreement

On May 12, 2023, the Company entered into a royalty purchase agreement (the "Royalty Financing Agreement") with HemB SPV, L.P. (the "Purchaser"). Under the terms of the Royalty Financing Agreement the Company received an upfront payment of $375.0 million in exchange for its rights to the lowest royalty tier on CSL Behring's worldwide net sales of HEMGENIX® for certain current and future royalties due to the Company. The Company is also eligible to receive an additional $25.0 million milestone payment under the Royalty Financing Agreement if 2024 net sales of HEMGENIX® exceed a pre-specified threshold, as set forth in the Royalty Financing Agreement. The Purchaser will receive 1.85 times the upfront payment (or $693.8 million) and 1.85 times the $25.0 million milestone payment (if paid) until June 30, 2032 ("First Hard Cap Date") if such thresholds are met or, if such cap is not met by June 30, 2032, up to 2.25 times of the upfront and milestone payment (if paid) through December 31, 2038. If 2024 net sales do not exceed a pre-specified threshold, the Company will be obligated to pay $25.0 million to the Purchaser but only to the extent that the Company achieves a future sales milestone under the CSL Behring Agreement. If such milestone payment is not due from CSL Behring, the Company is not obligated to pay any amounts to the Purchaser.

The Company has retained the rights to all other royalties, as well as contractual milestones totaling up to $ 1.3 billion, under the terms of the CSL Behring Agreement.

Net proceeds from the Royalty Financing Agreement, after deducting professional and financial advisory fees related to the transaction of $4.9 million, were $370.1 million. The Company initially recorded these net proceeds as "Liability from royalty financing agreement" at their fair market value on its consolidated balance sheet as of closing of the transaction on June 5, 2023. Following the initial recognition, the Company records the debt at amortized cost.

The Company expects to satisfy its commitment to the Purchaser prior to the First Hard Cap Date. The Company will record the difference of $323.7 million between the total expected payments of $693.8 million to the Purchaser and the $370.1 million net proceeds as interest expense using the effective interest rate method. The Company determined the effective interest rate based on the projected cash flows up to the First Hard Cap Date. Based on the Company's projections the effective interest rate is expected to be within a range of 12.0% per annum to 13.5% per annum. Interest expense during the three and nine months ended September 30, 2024 was $12.8 and $37.7 million, respectively, compared to $11.8 million and $14.9 million, during the same period in 2023. The Company would have recorded between $37.4 million and $42.3 million of interest expense through the nine months ended September 30, 2024 ($12.9 million and $14.6 million, respectively, for the three months ended September 30, 2024) if it had used 12.0% or 13.5% instead. The Company will prospectively update the effective interest rate at each reporting date based on updated projections.

The liability was initially recognized at fair value and inputs were considered Level 3 inputs.

The following table presents the movement in the liability related to the Royalty Financing Agreement between the December 31, 2023 and September 30, 2024:

	Amount of liability
	(in thousands)
Balance as of December 31, 2023 (includes $1.4 million presented as "Accrued expenses and other current liabilities)	$ **395,678**
Royalty payments to Purchaser	(4,577)
Liability owed to the Purchaser (presented as "Accrued expense and other current liabilities")	(2,085)
Interest expense for the period	37,671
Liability related to the royalty financing agreement	**$ 426,687**

12 Share-based compensation

The Company's share-based compensation plans include the amended and restated 2014 Share Incentive Plan (as amended, 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 2024, the Company's shareholders approved an increase in the number of ordinary shares authorized for issuance under the 2014 Plan from 14,351,471 to 15,851,471.

In June 2018, the Company's shareholders adopted and approved an employee share purchase plan (the "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, as amended. 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,	
	2024	2023	2024	2023
	(in thousands)		(in thousands)	
Cost of manufacturing services revenue	$ —	$ 315	$ 1,035	$ 477
Research and development	1,413	5,638	7,694	14,675
Selling, general and administrative	2,025	5,144	8,780	12,900
Total	**$ 3,438**	**$ 11,097**	**$ 17,509**	**$ 28,052**

Share-based compensation expense / (income) recognized by award type for the 2014 Plans as well as the ESPP was as follows:

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
	(in thousands)		(in thousands)	
Award type/ESPP				
Share options	$ 2,003	$ 3,497	$ 7,576	$ 10,256
Restricted share units	1,615	5,293	10,199	15,311
Performance share units	(180)	2,299	(276)	2,461
Employee share purchase plan	—	8	10	24
Total	**$ 3,438**	**$ 11,097**	**$ 17,509**	**$ 28,052**

As of September 30, 2024, the unrecognized share-based compensation expense related to unvested awards under the 2014 Plans were:

	Unrecognized share-based compensation expense (in thousands)	Weighted average remaining period for recognition (in years)
Award type		
Share options	$ 13,083	2.21
Restricted share units	15,113	1.67
Performance share units	20	0.04
Total	**$ 28,216**	**1.92**

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.

The Company will account for the forfeitures of awards to employees impacted by the August 2024 restructuring as of the date employment with the Company ends, which is expected to occur between November 2024 and June 2025. The Company expects this to reduce the unrecognized share-based compensation expense by approximately $3.2 million.

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% of each grant 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 2014 Plans for the nine months ended September 30, 2024:

	Options	
	Number of ordinary shares	Weighted average exercise price
Outstanding at December 31, 2023	**4,974,030**	**23.25**
Granted	1,093,080	$ 5.47
Forfeited	(285,065)	$ 16.05
Expired	(352,570)	$ 29.90
Exercised	(3,900)	$ 8.22
Outstanding at September 30, 2024	**5,425,575**	**$ 19.63**
Thereof, fully vested, and exercisable on September 30, 2024	3,233,831	$ 24.50
Thereof, outstanding and expected to vest after September 30, 2024	2,191,744	$ 12.43

Total weighted average grant date fair value of options issued during the period (in $ millions)	$ 3.5

As a result of the August 2024 restructuring, 67,755 options are expected to be forfeited between November 2024 and June 2025.

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,	
	2024	2023	2024	2023
Assumptions				
Expected volatility	70%	70%	70%	70%
Expected terms	10 years	10 years	10 years	10 years
Risk free interest rate	4.32%	3.71% - 4.00%	4.32%	3.71% - 4.10%
Expected dividend yield	0%	0%	0%	0%

RSUs

The following table summarizes the RSU activity for the nine months ended September 30, 2024:

	RSUs	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2023	**2,264,369**	**$ 18.07**
Granted	1,311,360	$ 5.49
Vested	(890,994)	$ 19.98
Forfeited	(703,206)	$ 12.49
Non-vested at September 30, 2024	**1,981,529**	**$ 10.85**
Total weighted average grant date fair value of RSUs granted during the period (in $ millions)		$ 7.2

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

As a result of the August 2024 restructuring, 229,113 RSUs are expected to be forfeited between November 2024 and June 2025.

PSUs

The following table summarizes the PSU activity for the nine months ended September 30, 2024:

	PSUs	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2023	**222,550**	**$ 28.09**
Forfeited	(52,270)	$ 28.04
Non-vested at September 30, 2024	**170,280**	**$ 27.88**

The Company granted ordinary shares to certain employees in December 2021 and at various dates during the year ended December 31, 2022 that will be earned upon achievement of defined milestones. Earned ordinary shares will vest upon the later of a minimum service period of one year or three years, or the achievement of defined milestones, subject to the grantee's continued employment. In addition, portions of the ordinary shares granted in December 2021 to executives and other members of senior management are subject to achieving a minimum total shareholder return relative to the NASDAQ Biotechnology Index. The Company recognizes the compensation cost related to these grants to the extent it considers achievement of the milestones to be probable. As of September 30, 2024, three milestones had been achieved. Additionally, another milestone was achieved in October 2024.

ESPP

During the nine months ended September 30, 2024, 10,150 ordinary shares were issued under the ESPP compared to 12,270 during the same period in 2023. As of September 30, 2024, 86,712 ordinary shares remain available for issuance under the ESPP compared to a total of 103,790 as of September 30, 2023.

13 Income taxes

The Company recorded $0.0 million deferred tax benefit and $1.6 million deferred tax expense in relation to its operations in the U.S. during the three and nine months ended September 30, 2024, respectively. The Company recorded $0.1 million and $1.1 million deferred tax benefit in relation to its operations in the U.S. and France during the three and nine months ended September 30, 2023, respectively.

The effective income tax rate of (0.1%) and 1.0% during the three and nine months ended September 30, 2024 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 and a partial a valuation allowance against its net deferred tax assets in France. The effective income tax rate during the three and nine months ended September 30, 2023 was (0.1%) and (0.5%), respectively, as the Company had recorded a valuation allowance against its net deferred tax assets in the Netherlands.

14 Basic and diluted earnings per share

Diluted earnings per share are calculated by adjusting the weighted average number of ordinary shares outstanding, assuming conversion of all potentially dilutive ordinary shares. As the Company has incurred a loss in the three and nine months ended September 30, 2024, all potentially dilutive ordinary shares 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, 2024. The ordinary shares are presented without giving effect to the application of the treasury method or exercise prices that would be above the share price as of September 30, 2024 and September 30, 2023, respectively.

The potentially dilutive ordinary shares are summarized below:

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
Anti-dilutive ordinary share equivalents				
Stock options under 2014 Plans and previous plan	5,425,575	5,411,599	5,425,575	5,411,599
Non-vested RSUs and PSUs	2,151,809	2,749,755	2,151,809	2,749,755
ESPP	—	2,857	—	2,857
Total anti-dilutive ordinary share equivalents	**7,577,384**	**8,164,211**	**7,577,384**	**8,164,211**

15 Subsequent events

None.

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

The following discussion of our results of operations and financial condition should be read in conjunction with our unaudited consolidated financial statements and the accompanying notes thereto and other disclosures included in this Quarterly Report on Form 10-Q, including the disclosures under Part II, Item 1A "Risk Factors," and our audited financial information and the notes thereto included in our Annual Report on Form 10-K (the "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, seeking to deliver to patients suffering from rare and other devastating diseases single treatments with potentially curative results. We are advancing a focused pipeline of innovative gene therapies, including our clinical candidates for the treatment of Huntington's disease, amyotrophic lateral sclerosis caused by mutations in superoxide dismutase 1 ("SOD1-ALS"), refractory mesial temporal lobe epilepsy ("mTLE") and Fabry disease.

Business Developments

Huntington's disease program (AMT-130) updated interim clinical data

AMT-130 is our novel gene therapy candidate for the treatment of Huntington's disease, which 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 multi-center randomized, controlled Phase I/II clinical trial for AMT-130 in the U.S. ("US study") as well as an open-label Phase Ib/II study in Europe with the same early-manifest criteria for Huntington's disease as the U.S. study ("European study"). We completed the enrollment of all 26 patients in the first two cohorts of our US study in March 2022 and the enrollment of 13 patients in the two cohorts of our European study in June 2023.

In November 2023, we initiated patient dosing in a third cohort of up to 12 patients across both U.S. and U.K. sites to further investigate both doses of AMT-130 in combination with perioperative immunosuppression. Patient enrollment is ongoing in this cohort with a focus on evaluating near-term safety and tolerability.

In June 2024, we announced that the U.S. Food and Drug Administration ("FDA") granted Regenerative Medicine Advanced Therapy ("RMAT") designation for AMT-130 based on the potential of AMT-130 to address the major unmet medical need among patients with Huntington's disease. The designation follows the FDA's review of interim Phase I/II clinical data for AMT-130 announced in December 2023 and is based on an analysis comparing these 24-month clinical data to a non-concurrent criteria-matched natural history cohort.

In July 2024, we announced updated interim clinical data including up to 24 months of follow-up data from 29 treated patients enrolled in the ongoing U.S. and European Phase I/II clinical trials of AMT-130 for the treatment of Huntington's disease.

In conjunction with the July 2024 update, we conducted a post-hoc statistical analysis of clinical outcomes for the 21 treated patients at 24 months compared to an expanded, propensity-weighted external control developed in collaboration with the Cure Huntington's Disease Initiative (CHDI) using data from the TRACK-HD, TRACK-ON and PREDICT-HD natural history studies. The external control includes 154 patients that met the Phase I/II clinical trial eligibility criteria, and whose data contributions were statistically weighted using propensity scoring to closely match the baseline characteristics of patients treated with AMT-130. Disease-related outcomes for these well-balanced cohorts were then compared after 24 months follow-up and are summarized below. Measures of statistical significance in this analysis were based on nominal p values and are unadjusted.

- A statistically significant, dose-dependent, slowing in disease progression measured by the composite Unified Huntington's Disease Rating Scale (cUHDRS) was observed through 24 months in patients receiving the high dose of AMT-130.
    - At 24 months, the mean change in cUHDRS for patients receiving the high-dose of AMT-130 was -0.2 compared to -1.0 for patients in the propensity score-weighted external control, representing an 80% slowing of disease progression (p=0.007).
    - At 24 months, the mean change in cUDHRS for patients receiving the low-dose of AMT-130 was -0.7 compared to -1.0 for patients in the propensity score-weighted external control, representing a 30% slowing of disease progression (p=0.21).
    - cUHDRS has been demonstrated to be the most sensitive measurement of clinical progression in Huntington's disease patients.
- Trends in measurements of motor and cognitive function showed near-baseline stability throughout the 24 months of follow-up in patients receiving the high dose of AMT-130.
- A statistically significant reduction of neurofilament light chain (NfL) in cerebrospinal fluid (CSF) was observed in patients treated with AMT-130.
    - Patients treated with AMT-130 had a mean reduction in CSF NfL of 11% compared to baseline (p=0.02) at 24 months.
    - Mean CSF NfL levels for both high and low doses were below baseline at 24 months.
    - CSF NfL is a biomarker of neurodegeneration that has been shown to be associated with the clinical severity of Huntington's disease. An independent natural history study demonstrated a 26% increase in CSF NfL at 24 months in patients with early manifest Huntington's disease (n=19).

Based on data observed as of the July 2024 interim update, AMT-130 remains generally well-tolerated, with a manageable safety profile at both doses. There were no new AMT-130-related serious adverse events reported.

Based on the granting of the RMAT designation, we have scheduled a Type B, multi-disciplinary meeting with the U.S. Food and Drug Administration (FDA) in late November 2024 at which we plan to present the most recent clinical data and initiate discussions regarding the potential for an expedited development pathway for AMT-130. We will also discuss with the FDA a future communication plan that is expected to include additional sub-disciplinary meetings to take place in the first half of 2025.

Sale of commercial manufacturing activities

On June 29, 2024, our affiliates, uniQure Inc. and uniQure biopharma B.V., entered into an asset purchase agreement (the "APA") with Genezen Holdings Inc. and its subsidiary, Genezen MA, Inc. (together "Genezen") to sell certain assets and assume certain liabilities related to uniQure's manufacturing facility (the "Lexington Facility") and operations in Lexington, Massachusetts (the "Lexington Transaction"). The Lexington Transaction closed on July 22, 2024 (the "Closing"). Our Chief Executive Officer, Matthew Kapusta, joined the board of directors of Genezen in connection with the Closing.

In conjunction with the Lexington Transaction, Genezen extended offers of employment to a significant majority of our employees located at the Lexington Facility, with the remaining employees terminated effective August 30, 2024.

As consideration for the Lexington Transaction, we received (i) shares of newly issued Series C preferred stock of Genezen Holdings Inc. valued at $12.5 million, which are convertible into common stock and will accrue an 8.0% per annum cumulative dividend, (ii) a convertible promissory note with a nominal amount of $12.5 million, bearing interest at 8.0% per annum and maturing 63 months following the date of issuance and (iii) a right to purchase HEMGENIX® at terms considered favorable to market terms (the "Consideration").

In connection with the Closing, we, Genezen and the landlord of the Lexington Facility entered into an agreement for us to assign and Genezen to assume the existing lease agreement between us and the landlord. We also amended our original July 2013 guarantee to continue guaranteeing rental payments owed by Genezen until the end of the current term on May 31, 2029. In the event of Genezen's default related to rental payments owed to the landlord, we are entitled to terminate the assignment agreement and step into the original lease agreement.

At the Closing, we entered into a commercial supply agreement ("CSA") with Genezen. Pursuant to the terms of the CSA, the parties agreed to subcontract the manufacturing of HEMGENIX® to Genezen. The CSA includes a minimum term of three years and minimum purchase commitments of HEMGENIX® commercial supplies of $43.3 million over the first three years, unless certain contractual provisions are triggered. Our obligations with respect to the supply of HEMGENIX® to CSL Behring remain in effect notwithstanding the subcontracting to Genezen.

We recorded a $1.2 million gain from the divestment. We paid a total of $8.3 million to Genezen and a third party related to adjustments of working capital and to obtain consent to proceed with the divestment.

Additionally, we entered into a development and other manufacturing services agreement ("DMSA") with Genezen at Closing. Pursuant to the DMSA, we are entitled to preferred customer status to receive manufacturing and development services to support our investigational gene therapy programs and other services related to HEMGENIX® (other than our manufacturing and supply obligations under the CSA). The DMSA has a minimum term of three years and requires us to purchase services for a total minimum of $14.0 million.

Hercules Loan Repayment and Amendment

In connection with the Closing on July 22, 2024, we and Hercules amended the 2023 Amended Facility ("2024 Amended Facility"). As a condition to Hercule's consent to the Lexington Transaction, on July 19, 2024 we prepaid $50.0 million of the total $100.0 million principal outstanding. The remaining $50.0 million principal outstanding will need to be repaid on January 5, 2027 (the "Maturity Date").

Results of the business review

On July 23, 2024, we announced the Closing and on August 1, 2024, we announced an organizational restructuring (the "Restructuring"). These actions were the outcome of a recently completed, comprehensive review of our operations with the goals of conserving capital and streamlining the organization. As part of these changes, we eliminated approximately 300 positions or 65% of our workforce. We estimate that we will incur costs in the range of $6.5 million to $7.5 million related to employee severance costs depending on whether or not employees continue to provide services through the residual service periods. The Restructuring was subject to the review by our Amsterdam-based works council, which was completed in the third quarter of 2024. We expect the Restructuring to be substantially completed by the end of 2024 with some employees continuing through second quarter 2025.

Recent Developments of other Product Candidates

Temporal lobe epilepsy program (AMT-260)

In August 2023, the FDA cleared the IND application for AMT-260, our investigational gene therapy candidate for refractory MTLE. AMT-260 is comprised of an AAV9 vector that locally delivers two engineered miRNAs designed to degrade the GRIK2 gene and suppress the aberrant expression of glutamate receptor subtype GLUK2 that is believed to trigger seizures in patients with refractory MTLE.

We are initiating a Phase I/IIa clinical trial that will be conducted in the United States and consist of two parts. The first part is a multicenter, open-label trial with two dosing cohorts of six patients each to assess safety, tolerability, and first signs for efficacy of AMT-260 in patients with refractory MTLE. The second part is expected to be a randomized, controlled trial to generate proof of concept ("POC") data. The first patient has been enrolled into the observational phase of the Phase I/II clinical trial of AMT-260 for the treatment of mTLE. The FDA-approved study protocol provides that the first three patients to be enrolled in the study are required to have MRI-confirmed unilateral, hippocampal sclerosis. Due to the more restrictive inclusion criteria for these sentinel patients, enrollment has taken longer than expected. We are rapidly activating recruitment sites with 10 centers currently open and an additional two sites expected to be activated by the end of 2024.

Fabry disease program (AMT-191)

AMT-191 is our investigational gene therapy candidate for the treatment of Fabry disease. AMT-191 is comprised of an AAV5 capsid that incorporates the α-galactosidase A ("GLA") transgene and a proprietary, highly potent, liver-specific promoter. In November 2023 we announced that the FDA had cleared the IND application for AMT-191.

In August 2024, we announced that the first patient has been dosed in a Phase I/IIa clinical trial of AMT-191 for the treatment of Fabry disease. The multicenter, open-label clinical trial consists of two dose-escalating cohorts of up to six adult male patients each to assess safety, tolerability, and early signs of efficacy of AMT-191 in patients with Fabry disease.

In September 2024, we announced the FDA has granted Orphan Drug Designation to AMT-191 and in October 2024, the FDA granted Fast Track Designation to AMT-191.

Amyotrophic Lateral Sclerosis (AMT-162)

AMT-162 is our investigational gene therapy candidate for a one-time, intrathecally administered investigational gene therapy for SOD1-ALS. AMT-162 is comprised of a recombinant AAVrh10 vector that expresses a miRNA designed to knock down the expression of SOD1 with the goal of slowing down or potentially reversing the progression of ALS in patients with SOD1 mutations. The FDA has cleared the IND application for AMT-162 and has granted Orphan Drug and Fast Track Designation.

In October 2024, we announced the first patient has been dosed in a Phase I/IIa clinical trial of AMT-162 for the treatment of SOD1-ALS. The first-in-human Phase I/II clinical trial is a U.S.-based, multi-center, open-label trial consisting of three cohorts with up to four patients each receiving a one-time intrathecal infusion with immunosuppression. Safety, tolerability and early signs of efficacy will be evaluated in the study.

Financial Overview

Key components of our results of operations include the following:

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
	(in thousands)		(in thousands)	
Total revenues	$ 2,287	$ 1,407	$ 21,898	$ 9,154
Cost of license revenues	(264)	—	(648)	—
Cost of contract manufacturing revenues	(757)	(1,006)	(17,060)	(4,793)
Research and development expenses	(30,595)	(65,400)	(104,942)	(172,245)
Selling, general and administrative expenses	(11,575)	(18,074)	(41,279)	(57,103)
Net loss	(44,378)	(89,571)	(166,295)	(235,272)

As of September 30, 2024 and December 31, 2023, we had cash and cash equivalents and investment securities of $435.2 million and $617.9 million, respectively. We had a net loss of $44.4 million and $166.3 million in the three and nine months ended September 30, 2024, respectively, compared to a net loss of $89.6 million and $235.3 million for the same periods in 2023. As of September 30, 2024 and December 31, 2023, we had accumulated deficits of $1,056.7 million and $890.4 million, respectively.

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

Critical Accounting Policies and Estimates

In preparing our consolidated financial statements in accordance with U.S. GAAP and pursuant to the rules and regulations promulgated by the Securities and Exchange Commission (the "SEC") we make assumptions, judgments and estimates that can have a significant impact on our net loss and affect the reported amounts of certain assets, liabilities, revenue and expenses, and related disclosures. We base our assumptions, judgments and estimates on historical experience and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not clear from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies. A summary of our critical accounting policies as well as a discussion of our critical accounting estimates are presented in our Annual Report. There were no material changes to our critical accounting policies during the nine months ended September 30, 2024 with the exception of determining the valuation of the intangible asset with favorable terms recorded as part of the Lexington Transaction.

Intangible asset

We entered into the APA with Genezen on June 29, 2024 to divest our commercial manufacturing activities in return for the Consideration. The Lexington Transaction closed on July 22, 2024. Part of the Consideration received was a right, with an estimated fair market value of $16.7 million, to purchase HEMGENIX® from Genezen up to the termination of our supply agreement with CSL Behring at terms considered favorable to market terms. The determination of the fair market value required us to estimate the current and future commercial supply prices of HEMGENIX® to compare these to the contractually agreed terms. Prices for the commercial supply of HEMGENIX® are not readily observable in the market. Therefore, our estimate of the commercial supply price was based on what a market participant would be willing to pay in a comparable transaction, using industry benchmarks and relevant market data as reference points.

If the estimated commercial supply price used in the valuation had increased by 5% per drug product batch, then the fair market value of the intangible asset and the consideration received as well as the gain recorded on the divestment would have been increased by $3.0 million. If the estimated commercial supply price used in the valuation had been decreased by 5% per drug product batch, then the fair market value of the intangible asset and the consideration received on the divestment would have been decreased by $2.9 million. This would have resulted in a loss on divestment of $1.7 million instead of the $1.2 million gain presented.

Cost of contract manufacturing

We entered into a development and commercial supply agreement with CSL Behring in June 2020. Prior to Closing, we recognized the cost to manufacture HEMGENIX® under such agreement as cost of contract manufacturing.

Research and development expenses

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

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense;
- costs incurred for laboratory research, preclinical and nonclinical studies, clinical trials, statistical analysis and report writing, and regulatory compliance costs incurred with clinical research organizations and other third-party vendors;
- costs incurred to conduct consistency and comparability studies;
- costs incurred for the development and improvement of our manufacturing processes and methods;
- costs associated with research activities for enabling technology platforms;
- costs associated with the rendering of collaboration services;
- payments related to identifiable intangible assets without an alternative future use;
- payments to our licensors for milestones that have been achieved related to our product candidates;
- 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 uniQure France SAS.

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

- the scope, rate of progress and expense of our research and development activities;
- clinical trial protocols, speed of enrollment and resulting data;
- the effectiveness and safety of our product candidates; and
- the timing of regulatory approvals.

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

Selling, general and administrative expenses

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

Other items, net

Our other income primarily consists of the net gain resulting from the sale of the commercial manufacturing activities located in Lexington, MA in July 2024, payments received to subsidize our research and development efforts, and income from the subleasing of our Amsterdam facility and our Lexington, MA research and development facility which, commenced in September 2024.

Our other expense primarily consists of costs incurred under our commercial supply agreement with Genezen. These include costs related to the purchase of HEMGENIX® from Genezen net of income from the sales of HEMGENIX® to CSL Behring, amortization of the intangible asset for our favorable supply terms under the CSA and credits from the release of liabilities related to expected net losses associated with minimum purchase commitments under the CSA. Additionally, other expense also consists of expenses we incur in relation to our subleasing income.

Results of Operations

Comparison of the three months ended September 30, 2024 and 2023

The following table presents a comparison of our results of operations for the three months ended September 30, 2024 and 2023.

	Three months ended September 30,		
	2024	2023	2024 vs 2023
		(in thousands)	
Total revenues	$ 2,287	$ 1,407	$ 880
Operating expenses:			
Cost of license revenues	(264)	—	(264)
Cost of contract manufacturing	(757)	(1,006)	249
Research and development expenses	(30,595)	(65,400)	34,805
Selling, general and administrative expenses	(11,575)	(18,074)	6,499
Total operating expenses	**(43,191)**	**(84,480)**	**41,289**
Other income	2,591	1,424	1,167
Other expense	(1,915)	(228)	(1,687)
Loss from operations	**(40,228)**	**(81,877)**	**41,649**
Other non-operating items, net	(4,181)	(7,763)	3,582
Net loss before income tax expense	**$ (44,409)**	**$ (89,640)**	**$ 45,231**
Income tax benefit	31	69	(38)
Net loss	**$ (44,378)**	**$ (89,571)**	**$ 45,193**

Revenues

Our revenues for the three months ended September 30, 2024 and 2023 were as follows:

	Three months ended September 30,		
	2024	2023	2024 vs 2023
		(in thousands)	
License revenues	$ 2,111	$ 497	$ 1,614
Contract manufacturing revenues	—	349	(349)
Collaboration revenues	176	561	(385)
Total revenues	**$ 2,287**	**$ 1,407**	**$ 880**

License revenues

We recognize license revenues from CSL Behring, related to royalty payments owed on HEMGENIX® sales, when earned. For the three months ended September 30, 2024, we recognized $2.1 million of license revenues, compared to $0.5 million for the same period in 2023.

Contract manufacturing revenues

We recognized contract manufacturing revenues related to contract manufacturing HEMGENIX® for CSL Behring prior to the Closing of the Lexington Transaction. Contract manufacturing revenues were realized when earned upon sales of HEMGENIX® drug product to CSL Behring. We recognized nil contract manufacturing revenues in the three months ended September 30, 2024, compared to $0.3 million for the same period in 2023.

Collaboration revenues

We provide services to CSL Behring in accordance with the CSL Behring Agreement. Collaboration revenue related to these contracted services is recognized when the performance obligations are satisfied.

For the three months ended September 30, 2024 and 2023 we recognized $0.2 million and $0.6 million of collaboration revenue for CSL Behring, respectively.

Cost of contract manufacturing

We incurred $0.8 million of cost of contract manufacturing related to the manufacture of HEMGENIX® prior to the Closing of the Lexington Transaction in the three months ended September 30, 2024, compared to $1.0 million cost of contract manufacturing in the three months ended September 30, 2023.

R&D expenses

R&D expenses for the three months ended September 30, 2024 were $30.6 million, compared to $65.4 million for the same period in 2023. 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,		
	2024	2023	2024 vs 2023
	(in thousands)		
Huntington's disease (AMT-130)	$ 4,470	$ 3,116	$ 1,354
Temporal lobe epilepsy (AMT-260)	1,606	4,662	(3,056)
Programs in preclinical development and platform related expenses	965	3,104	(2,139)
Amyotrophic lateral sclerosis (AMT-162)	910	2,420	(1,510)
Fabry disease (AMT-191)	792	358	434
Total direct research and development expenses	**$ 8,743**	**$ 13,660**	**$ (4,917)**
Employee and contractor-related expenses	9,967	19,431	(9,464)
Facility expenses	3,839	6,652	(2,813)
Severance costs	3,378	—	3,378
Share-based compensation expense	1,413	5,638	(4,225)
Disposables	1,013	4,694	(3,681)
Fair value changes related to contingent consideration	(410)	14,229	(14,639)
Other expenses	2,652	1,096	1,556
Total other research and development expenses	**$ 21,852**	**$ 51,740**	**$ (29,888)**
Total research and development expenses	**$ 30,595**	**$ 65,400**	**$ (34,805)**

Direct research and development expenses

Huntington’s disease (AMT-130)

In the three months ended September 30, 2024 and September 30, 2023, we incurred costs of $4.5 million and $3.1 million respectively. Our external costs for the development of AMT-130 were primarily related to the execution of our Phase I/II clinical trials in the U.S. and in Europe. We completed enrollment of the first two cohorts in the U.S. in March 2022 and in Europe in June 2023.

Temporal lobe epilepsy (AMT-260)

In the three months ended September 30, 2024 and September 30, 2023, we incurred costs of $1.6 million and $4.7 million respectively, for the development of AMT-260. In August 2023, the FDA cleared our IND application, and we continue to incur costs for the preparation of a Phase I clinical trial.

Preclinical programs and platform development

In the three months ended September 30, 2024 and September 30, 2023, we incurred $1.0 million and $3.1 million of costs, respectively, primarily related to our preclinical activities associated with product candidates for various other research programs and technology innovation projects.

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

On January 31, 2023, we entered into a global licensing agreement with Apic Bio for AMT-162. In the three months ended September 30, 2024 and September 30, 2023, we incurred costs of $0.9 million and $2.4 million, respectively, to initiate a Phase I/II clinical trial.

Fabry disease (AMT-191)

In the three months ended September 30, 2024 and September 30, 2023, we incurred costs of $0.8 million and $0.4 million, respectively, related to our development of AMT-191. In November 2023, the FDA cleared the IND application, and we started incurring additional costs for the Phase I/II clinical trial preparation.

Other research & development expenses

- We incurred $10.0 million in personnel and contractor-related expenses in the three months ended September 30, 2024, compared to $19.4 million for the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities as well as a reduction in expense from the restructuring that occurred in October 2023;
- We incurred $3.8 million in operating expenses and depreciation expenses related to our rented facilities in Amsterdam and Lexington, Massachusetts in the three months ended September 30, 2024, compared to $6.7 million in the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities as well as the subleasing of our 20 Maguire facility;
- We incurred $2.7 million of other expenses for the three months ended September 30, 2024, compared to $1.1 million for the same period in 2023;
- We incurred $1.4 million in share-based compensation expenses in the three months ended September 30, 2024, compared to $5.6 million for the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities, a reduction in expense from the restructuring that occurred in October 2023 and a decrease in the fair value of the awards granted;
- We incurred $1.0 million in disposable costs in the three months ended September 30, 2024, compared to $4.7 million for the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities as well as a reduction in expense from the restructuring that occurred in October 2023;
- We included $3.4 million of severance costs related to the divestment of our commercial manufacturing activities and the organizational restructuring in the three months ended September 30, 2024 with no such cost in the same period in 2023; and
- We recognized a $0.4 million gain in the three months ended September 30, 2024 related to a decrease in the fair value of contingent consideration associated with the acquisition of uniQure France SAS, compared to a loss of $14.2 million related to the increase in fair value for the same period in 2023.

Selling, general and administrative expenses

Selling, general and administrative expenses for the three months ended September 30, 2024 were $11.6 million, compared to $18.1 million for the same period in 2023.

- We incurred $5.5 million in personnel and contractor-related expenses in the three months ended September 30, 2024, compared to $6.4 million in the same period in 2023;
- We incurred $2.0 million in share-based compensation expenses in the three months ended September 30, 2024, compared to $5.1 million in the same period in 2023. The decrease was primarily related to the divestment of our Lexington Facility, a reduction in expense from the restructuring that occurred in October 2023 and a decrease in the fair value of the awards granted;
- We incurred $1.5 million in professional fees in the three months ended September 30, 2024, compared to $2.8 million in the same period in 2023. We regularly incur accounting, audit and legal fees associated with operating as a public company;
- We incurred $0.9 million in other expenses in the three months ended September 30, 2024, compared to $2.8 million in the same period in 2023; and
- We incurred $0.7 million of severance costs related to the organizational restructuring in the three months ended September 30, 2024 with no such cost in the same period in 2023.

Other items, net

We recognized $1.2 million net gain resulting from the sale of the commercial manufacturing activities located in Lexington, MA in July 2024 in other income.

We recognized $1.5 million net in other expenses during the three months ended September 30, 2024 (nil in three months ended September 30, 2023) related to the purchase of HEMGENIX® from Genezen net of income from the sales of HEMGENIX® to CSL Behring, amortization of the intangible asset for our favorable supply terms under the CSA and credits from the release of liabilities related to expected net losses associated with minimum purchase commitments under the CSA.

We recognized $1.1 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, 2024, compared to $1.4 million for the same period in 2023.

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

Other non-operating items, net

Our other non-operating items, net, for the three months ended September 30, 2024 and 2023 were as follows:

	Three months ended September 30,		
	2024	2023	2024 vs 2023
		(in thousands)	
Interest income	$ 4,866	$ 7,495	$ (2,629)
Interest expense	(16,611)	(15,444)	(1,167)
Foreign currency gains, net	7,564	186	7,378
Total non-operating expense, net	**$ (4,181)**	$ **(7,763)**	$ **3,582**

We recognize interest income associated with our cash and cash equivalents, investment securities and convertible promissory note. We recognized $4.9 million in interest income in the three months ended September 30, 2024, compared to $7.5 million in the same period in the prior year. Our interest income decreased by $2.6 million due to less interest income earned on investment securities during the three months ended September 30, 2024.

We recognized $16.6 million in interest expense for the three months ended September 30, 2024 and $15.4 million for the three months ended September 30, 2023. Our interest expense in 2024 increased due to an increase of $1.0 million in non-cash interest expense related to the Royalty Financing Agreement that we entered into in May 2023.

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, the Royalty Financing Agreement and our cash and cash equivalents and investment securities as well as loans between entities within the uniQure group, of $7.6 million during the three months ended September 30, 2024, compared to a net gain of $0.2 million during the same period in 2023.

Income tax benefit

We recognized $0.0 million of deferred tax benefit in the three months ended September 30, 2024, and $0.1 million of deferred tax benefit for the same period in 2023.

Comparison of the nine months ended September 30, 2024 and 2023

The following table presents a comparison of our results of operations for the nine months ended September 30, 2024 and 2023:

	Nine months ended September 30,		
	2024	2023	2024 vs 2023
	(in thousands)		
Total revenues	$ 21,898	$ 9,154	$ 12,744
Operating expenses:			
Cost of license revenues	(648)	—	(648)
Cost of contract manufacturing	(17,060)	(4,793)	(12,267)
Research and development expenses	(104,942)	(172,245)	67,303
Selling, general and administrative expenses	(41,279)	(57,103)	15,824
Total operating expenses	**(163,929)**	**(234,141)**	**70,212**
Other income	5,950	4,537	1,413
Other expense	(2,385)	(673)	(1,712)
Loss from operations	**(138,466)**	**(221,123)**	**82,657**
Non-operating expense, net	(26,256)	(15,262)	(10,994)
Loss before income tax benefit	$ **(164,722)**	$ **(236,385)**	**71,663**
Income tax (expense) / benefit	(1,573)	1,113	(2,686)
Net loss	**$ (166,295)**	**$ (235,272)**	**$ 68,977**

Revenue

Our revenue for the nine months ended September 30, 2024 and 2023 was as follows:

	Nine months ended September 30,		
	2024	2023	2024 vs 2023
	(in thousands)		
License revenues	$ 5,182	$ 1,290	$ 3,892
Contract manufacturing revenues	6,114	6,596	(482)
Collaboration revenues	10,602	1,268	9,334
Total revenues	**$ 21,898**	**$ 9,154**	**$ 12,744**

License revenues

We recognize license revenues from CSL Behring, related to royalty payments owed on HEMGENIX® sales, when earned. For the nine months ended September 30, 2024, we recognized $5.2 million of license revenues, compared to $1.3 million for the same period in 2023.

Contract manufacturing revenues

We recognized contract manufacturing revenues related to contract manufacturing HEMGENIX® for CSL Behring prior to the Closing of the Lexington Transaction. Contract manufacturing revenues were realized when earned upon sales of HEMGENIX® drug product to CSL Behring. We recognized $6.1 million contract manufacturing revenues in the nine months ended September 30, 2024, compared to $6.6 million for the same period in 2023.

Collaboration revenues

We provide services to CSL Behring in accordance with the CSL Behring Agreement. Collaboration revenue related to these contracted services is recognized when the performance obligations are satisfied.

For the nine months ended September 30, 2024 and 2023 we recognized $10.6 million and $1.3 million of collaboration revenue for CSL Behring, respectively. The increase in collaboration revenue of $9.3 million in the nine months ended September 30, 2024 compared to the same period in 2023 was primarily related to additional development and other services provided to CSL Behring in relation to the CSL Behring Agreement.

Cost of contract manufacturing

We incurred $17.1 million of cost of contract manufacturing related to the manufacture of HEMGENIX® prior to the Closing of the Lexington Transaction in the nine months ended September 30, 2024, compared to $4.8 million cost of contract manufacturing in the nine months ended September 30, 2023. The increase in cost of $12.3 million in 2024 is primarily related to expensing costs that could not be recovered from selling HEMGENIX® under the terms of our development and commercial supply agreement with CSL Behring.

R&D expense

R&D expenses for the nine months ended September 30, 2024 were $104.9 million, compared to $172.2 million for the same period in 2023. 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,		
	2024	2023	2024 vs 2023
		(in thousands)	
Huntington's disease (AMT-130)	9,790	11,093	(1,303)
Temporal lobe epilepsy (AMT-260)	5,858	11,970	(6,112)
Amyotrophic lateral sclerosis (AMT-162)	$ 4,539	$ 13,048	$ (8,509)
Fabry disease (AMT-191)	3,617	1,846	1,771
Programs in preclinical development and platform related expenses	2,312	7,246	(4,934)
Etranacogene dezaparvovec (AMT-060/061)	—	(1,336)	1,336
Total direct research and development expenses	**$ 26,116**	**$ 43,867**	**$ (17,751)**
Employee and contractor-related expenses	39,926	55,894	(15,968)
Facility expenses	16,910	21,114	(4,204)
Share-based compensation expense	7,694	14,675	(6,981)
Other expenses	7,499	6,779	720
Severance costs	4,475	—	4,475
Disposables	4,354	14,475	(10,121)
Fair value changes related to contingent consideration	(2,032)	15,441	(17,473)
Total other research and development expenses	**$ 78,826**	**$ 128,378**	**$ (49,552)**
Total research and development expenses	**$ 104,942**	**$ 172,245**	**$ (67,303)**

Direct research and development expenses

Huntington’s disease (AMT-130)

In the nine months ended September 30, 2024 and September 30, 2023, we incurred costs of $9.8 million and $11.1 million respectively. Our external costs for the development of AMT-130 were primarily related to the execution of our Phase I/II clinical trials in the U.S. and in Europe. We completed enrollment of the first two cohorts in the U.S. in March 2022 and in Europe in June 2023. This resulted in a $1.3 million reduction of cost in 2024 compared to the prior year as we typically incur higher costs per patient during the first six months of enrollment compared to the follow-up period thereafter.

Temporal lobe epilepsy (AMT-260)

In the nine months ended September 30, 2024 and September 30, 2023, we incurred costs of $5.9 million and $12.0 million respectively, for the development of AMT-260. In August 2023, the FDA cleared our IND application, and we continue to incur costs for the preparation of a Phase I clinical trial.

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

On January 31, 2023, we entered into a global licensing agreement with Apic Bio for AMT-162. In the nine months ended September 30, 2024, we incurred $4.5 million of costs to initiate a Phase I/II clinical trial in 2024. In the nine months ended September 30, 2023 we incurred $3.1 million of costs to initiate the Phase I/II clinical trial as well as $10.0 million related to the upfront consideration paid to Apic Bio for the global licensing rights to AMT-162.

Fabry disease (AMT-191)

In the nine months ended September 30, 2024 and September 30, 2023, we incurred costs of $3.6 million and $1.8 million, respectively, related to our development of AMT-191. In November 2023, the FDA cleared the IND application, and we started incurring additional costs for the Phase I/II clinical trial preparation.

Preclinical programs & platform development

In the nine months ended September 30, 2024 and September 30, 2023, 2023, we incurred $2.3 million and $7.2 million of costs, respectively, primarily related to our preclinical activities associated with product candidates for various other research programs and technology innovation projects.

Etranacogene dezaparvovec (AMT-060/061)

We transitioned activities related to the clinical trial and long-term follow-up of patients to CSL Behring in December 2022. Direct research and development expenses related to clinical development and other regulatory activities and commercialization expenses incurred in the nine months ended September 30, 2024 and September 30, 2023 are presented net of reimbursements due from CSL Behring and include settlement amounts from the transition.

Other research & development expenses

- We incurred $39.9 million in personnel and contractor-related expenses in the nine months ended September 30, 2024, compared to $55.9 million for the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities as well as a reduction in expense from the restructuring that occurred in October 2023;
- We incurred $16.9 million in operating expenses and depreciation expenses related to our rented facilities in Amsterdam and Lexington, Massachusetts in the nine months ended September 30, 2024, compared to $21.1 million in the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities;
- We incurred $7.7 million in share-based compensation expenses in the nine months ended September 30, 2024, compared to $14.7 million for the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities, a reduction in expense from the restructuring that occurred in October 2023 and a decrease in the fair value of the awards granted;
- We incurred $7.5 million of other expenses for the nine months ended September 30, 2024, compared to $6.8 million for the same period in 2023;
- We incurred $4.5 million of severance costs related to the divestment of our commercial manufacturing activities and the organizational restructuring in the nine months ended September 30, 2024 with no such cost in the same period in 2023;
- We incurred $4.4 million in disposable costs in the nine months ended September 30, 2024, compared to $14.5 million for the same period in 2023. The decrease was primarily related to the divestment of our commercial manufacturing activities as well as a reduction in expense from the restructuring that occurred in October 2023; and
- We recognized a $2.0 million gain in the nine months ended September 30, 2024 related to a decrease in the fair value of contingent consideration associated with the acquisition of uniQure France SAS, compared to $15.4 million loss related to an increase in fair value for the same period in 2023.

Selling, general and administrative expenses

Selling, general and administrative expenses for the nine months ended September 30, 2024 were $41.3 million, compared to $57.1 million for the same period in 2023.

- We incurred $17.4 million in personnel and contractor-related expenses in the nine months ended September 30, 2024, compared to $18.8 million in the same period in 2023. The decrease was primarily related to the reduction in personnel and contractors as a result of the Lexington Transaction and the October 2023 and August 2024 reorganizations;
- We incurred $8.8 million in share-based compensation expenses in the nine months ended September 30, 2024, compared to $12.9 million in the same period in 2023. The decrease was primarily related to the Lexington Transaction, the October 2023 and August 2024 organizational restructurings, and a decrease in the fair value of the awards granted;
- We incurred $5.7 million in professional fees in the nine months ended September 30, 2024, compared to $8.5 million in the same period in 2023. We regularly incur accounting, audit and legal fees associated with operating as a public company. In 2024, we incurred professional fees related to the Lexington Transaction. There was a partial offset as in the prior period we incurred professional fees related to our global licensing agreement with Apic Bio;
- We incurred $5.7 million in other expenses in the nine months ended September 30, 2024, compared to $9.0 million in the same period in 2023. The $3.3 million decrease was primarily related to a reduction of expenses for information technology;
- We incurred $1.4 million in intellectual property fees including registration and professional fees in the nine months ended September 30, 2024 compared to $3.3 million in the same period in 2023. The decrease mainly related to an decrease in professional fees;
- We incurred $1.0 million of severance costs related to the Lexington Transaction and August 2024 organizational restructuring in the nine months ended September 30, 2024 with no such cost in the same period in 2023; and
- We incurred nil in financial advisory fees in relation to our licensing transaction with CSL Behring in the nine months ended September 30, 2024, compared to $3.8 million in 2023.

Other items, net

We recognized $1.2 million net gain resulting from the sale of the commercial manufacturing activities located in Lexington, MA in July 2024.

We recognized $1.5 million in net other expenses during the nine months ended September 30, 2024 (nil in same period in 2023) related to the purchase of HEMGENIX® from Genezen net of income from the sales of HEMGENIX® to CSL Behring, amortization of the intangible asset for our favorable supply terms under the CSA and credits from the release of liabilities related to expected net losses associated with minimum purchase commitments under the CSA.

We recognized $4.0 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, 2024, compared to $3.9 million for the same period in 2023.

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

Other non-operating items, net

Our other non-operating items, net, for the nine months ended September 30, 2024 and 2023 were as follows:

	Nine months ended September 30,		
	2024	2023	2024 vs 2023
	(in thousands)		
Interest income	$ 17,179	$ 12,393	$ 4,786
Interest expense	(48,865)	(25,846)	(23,019)
Foreign currency gains / (losses), net	5,430	(1,809)	7,239
Total non-operating expense, net	**$ (26,256)**	**$ (15,262)**	**$ (10,994)**

We recognize interest income associated with our cash and cash equivalents, investment securities and convertible note. We recognized $17.2 million in interest income in the nine months ended September 30, 2024, compared to $12.4 million in the same period in the prior year. Our interest income increased by $4.8 million due to the interest income earned on investment securities as well as cash on hand during the nine months ended September 30, 2024.

We recognized $48.9 million in interest expense for the nine months ended September 30, 2024 and $25.8 million for the nine months ended September 30, 2023. Our interest expense in 2024 mainly increased due to an increase of $22.7 million in non-cash interest expense related to the Royalty Financing Agreement that we entered into in May 2023.

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, the Royalty Financing Agreement and our cash and cash equivalents and investment securities as well as loans between entities within the uniQure group, of $5.4 million during the nine months ended September 30, 2024, compared to a net loss of $1.8 million during the same period in 2023.

Income tax benefit

We recognized $1.6 million of deferred tax expense in the nine months ended September 30, 2024 , and $1.1 million of deferred tax benefit for the same period in 2023.

Financial Position, Liquidity and Capital Resources

As of September 30, 2024, we had cash and cash equivalents, restricted cash and investment securities of $436.7 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. Based on our current operating plan, research and development plans and our timing expectations related to the progress of our programs, we believe that our cash and cash equivalents and investment securities will fund our operations through the end of 2027. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. We expect that we will require additional funding if we decide to advance AMT-130 for our Huntington's disease gene therapy program or any of our other product candidates into late-stage clinical development. Our material cash requirements include the following contractual and other obligations:

Debt

As of September 30, 2024, we had an outstanding loan amount owed to Hercules Capital, Inc. ("Hercules") for an aggregate principal amount of $50.0 million. On July 19, 2024, in connection with the closing of the Lexington Transaction, we repaid $50.0 million of the $100.0 million of principal outstanding as well as $3.1 million in end-of-term fees. Future interest payments and financing fees associated with the loan total $18.2 million, with $6.5 million payable within 12 months. We are contractually required to repay the $50.0 million in full in January 2027.

Leases

We entered into lease arrangements for facilities, including corporate, manufacturing and office space. As of September 30, 2024, we had fixed lease payment obligations of $25.3 million, with $4.3 million payable within 12 months. Following the closing of the Lexington Transaction on July 22, 2024 we assigned our lease for the Lexington Facility to Genezen. This reduced our fixed lease payment obligations by $21.8 million, including $4.4 million payable within 12 months. We continue to guarantee such payments until the end of the lease term in May 2029.

Commitments related to uniQure France SAS acquisition (nominal amounts)

In relation to our acquisition of uniQure France SAS in 2021, we entered into commitments to make payments to the former shareholders upon the achievement of certain contractual milestones. The commitments include payments related to post-acquisition services that we agreed to as part of the transaction. In September 2023, we made a payment of EUR 10.0 million ($10.6 million) to the former shareholders of uniQure France SAS following the FDA's clearance of the IND application for AMT-260. As of September 30, 2024, our remaining commitment amounts include a EUR 30.0 million ($33.5 million) milestone payment due upon treating the first patient in a Phase I/II clinical trial for AMT-260 and EUR 160.0 million ($178.6 million) in potential milestone payments associated with Phase III development and the approvals of AMT-260 in the U.S. and European Union. The timing of achieving these milestones and consequently the timing of payments, as well as whether the milestones 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, 2024, of $1.12/€1.00. As of September 30, 2024, we expect these obligations will become payable between 2024 and 2033. If and when due, up to 25% of the milestone payments can be settled with our ordinary shares.

Commitments related to licensors and financial advisors

We have obligations to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones (such as the start of a clinical trial, filing of a BLA, approval by the FDA or product launch) or as a result of collecting payments related to our sale of the exclusive global rights of HEMGENIX® to CSL Behring. We also owe payments to a financial advisor related to certain payments we will collect under the CSL Behring Agreement.

Commitments related to the CSA and DMSA with Genezen

Our CSA with Genezen requires us to take or pay contract manufacturing services for HEMGENIX® during a three-year period ending July 22, 2027. As of September 30, 2024, our remaining minimum purchase commitments to Genezen amount to $39.9 million, with $14.7 million to be paid within the next 12 months. CSL Behring's minimum purchase commitments to us over the next 12 months are $11.9 million.

Our DMSA with Genezen requires us to take or pay contract development services during a three-year period ending July 22, 2027. As of September 30, 2024 our remaining minimum purchase commitments amount to $13.3 million with $3.5 million to be paid within the next 12 months.

The table below summarizes our consolidated cash flow data for the nine months ended September 30, 2024 and 2023:

	Nine months ended September 30,	
	2024	2023
	(in thousands)	
Cash, cash equivalents and restricted cash at the beginning of the period	$ 244,544	$ 231,173
Net cash used in operating activities	(129,884)	(96,388)
Net cash generated from / (used in) investing activities	189,592	(265,248)
Net cash (used in) / generated from financing activities	(52,969)	362,675
Foreign exchange impact	1,796	424
Cash, cash equivalents and restricted cash at the end of period	**$ 253,079**	$ **232,636**

We had previously incurred losses and cumulative negative cash flows from operations since our business was founded by our predecessor entity AMT Therapeutics 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 $44.4 million and $166.3 million in the three and nine months ended September 30, 2024, respectively, compared to a net loss of $89.6 million and $235.3 million during the same periods in 2023. As of September 30, 2024, we had an accumulated deficit of $1,056.7 million.

Sources of liquidity

From our first institutional venture capital financing in 2006 through the current period, we funded our operations primarily through private and public placements of equity securities, debt securities, payments from our collaboration partners as well as from selling a portion of royalties due from our collaboration partner CSL Behring. We collected $100.0 million in July 2023 related to the first sale milestone of HEMGENIX® in the U.S., and are eligible to receive additional milestone payments, as well as royalties (to the extent not owed to settle the liability from royalty financing) on net sales of HEMGENIX®.

On May 12, 2023 we and Hercules amended the 2021 Restated Facility. The 2023 Amended Facility extended the maturity date and interest-only period from December 1, 2025 to January 5, 2027. In connection with the closing of the Lexington Transaction on July 22, 2024 we amended the 2023 Amended Facility and repaid $50.0 million of the principal. We are required to repay the remaining principal balance of $50.0 million on the Maturity Date. The interest rate is adjustable and is the greater of (i) 7.95% and (ii) 7.95% plus the prime rate less 3.25% per annum. Under the 2024 Amended Facility, we owe a back-end fee of $2.4 million on December 1, 2025 and a back-end fee of $0.6 million on the maturity date.

We are subject to certain covenants under the 2024 Amended Facility and may become subject to covenants under any future indebtedness that could limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends, which could adversely impact our ability to conduct our business. In addition, our pledge of assets as collateral to secure our obligations under the 2024 Amended Facility may limit our ability to obtain debt financing. The 2024 Amended Facility permits us to issue up to $500.0 million of convertible debt.

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 financing, 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 $129.9 million for the nine months ended September 30, 2024 and consisted of net loss of $166.3 million adjusted for non-cash items, including depreciation and amortization expense of $8.3 million, amortization of the discount on investment securities of $8.5 million, share-based compensation expense of $17.5 million, $37.7 million of interest expense related to the Royalty Financing Agreement, a change in deferred taxes of $1.6 million, changes in the fair value of contingent consideration of $2.0 million, a provision for inventory write-downs of $6.3 million and unrealized foreign exchange gains of $5.7 million. Net cash used in operating activities also included unfavorable changes in operating assets and liabilities of $16.2 million. There was a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $5.8 million. There was an increase in inventory balances of $3.9 million. There was a net decrease in accounts payable, accrued expenses, other liabilities, and operating leases of $6.6 million.

Net cash used in operating activities was $96.4 million for the nine months ended September 30, 2023 and consisted of net loss of $235.3 million adjusted for non-cash items, including depreciation and amortization expense of $7.7 million, amortization of the premium/discount on investment securities of $6.5 million, share-based compensation expense of $28.1 million, changes in the fair value of contingent consideration of $15.4 million, unrealized foreign exchange losses of $3.1 million, $14.9 million of interest expense related to the Royalty Financing Agreement and a change in deferred taxes of $1.1 million. Net cash used in operating activities also included favorable changes in operating assets and liabilities of $77.0 million. There was a net decrease in accounts receivable, prepaid expenses, and other current assets and receivables of $96.6 million, primarily related to the collection of the $100.0 million milestone due from CSL Behring in July 2023. There was an increase in inventory balances of $8.7 million.

There was a net decrease in accounts payable, accrued expenses, other liabilities, and operating leases of $10.8 million, primarily related to a decrease of $4.8 million in accounts payable and a decrease of $6.0 million related to various accruals. Net cash used in operating activities also includes a payment for a contingent consideration milestone of $1.9 million.

Net cash generated from / (used in) investing activities

In the nine months ended September 30, 2024, we generated $189.6 million in our investing activities compared to using $265.2 million for the same period in 2023.

	Nine months ended September 30,	
	2024	2023
	(in thousands)	
Proceeds from maturity of debt securities	$ 480,806	$ 106,307
Investment in debt securities	(279,586)	(366,439)
Divestment of commercial manufacturing facility	(8,300)	—
Capital expenditures - Amsterdam site	(1,743)	(2,161)
Capital expenditures - Lexington site	(1,585)	(2,955)
Net cash generated from / (used in) investing activities	**$ 189,592**	**$ (265,248)**

During the nine months ended September 30, 2024, we received $480.8 million from the repayment of previous investments into euro and U.S. dollar denominated government bonds ($106.3 million for nine months ended September 30, 2023).

During the nine months ended September 30, 2024, we invested $279.6 million of our cash on hand into euro and dollar denominated government bonds ($366.4 for the nine months ended September 30, 2023).

During the nine months ended September 30, 2024 we incurred a cash outflow of $8.3 million related to the divestment of our commercial manufacturing facility.

We invested $1.7 million and $1.6 million, respectively, into our Amsterdam, Netherlands and Lexington, Massachusetts sites during the nine months ended September 30, 2024, compared to $2.2 million and $3.0 million for the same period in 2023.

Net cash generated from / (used in) financing activities

In the nine months ended September 30, 2024, we used $53.0 million in financing activities compared to generating $362.7 million for the same period in 2023.

	Nine months ended September 30,	
	2024	2023
	(in thousands)	
Cash flows from financing activities		
Proceeds from royalty financing agreement, net of debt issuance costs	$ —	$ 370,062
Proceeds from issuance of ordinary shares related to employee stock option and purchase plans	81	262
Contingent consideration payment	—	(7,649)
Repayment of long-term debt	(53,050)	—
Net cash (used in) / generated from financing activities	**$ (52,969)**	**$ 362,675**

In June 2023, we received $370.1 million net proceeds from the Royalty Financing Agreement.

During the nine months ended September 30, 2024, we received $0.1 million from the exercise of options to purchase ordinary shares in relation to our 2014 Plans, compared to $0.3 million for the same period in 2023.

In September 2023, following the FDA's clearance of the IND application for AMT-260, we made a contingent consideration payment of $9.5 million to the former shareholders of uniQure France SAS related to a contractually defined milestone, of which $7.6 million was classified as cash flows from financing activities and $1.9 million was classified as a net cash flow used in operating activities. We made nil payments for the period ended September 30, 2024.

During the nine months ended September 30, 2024 we repaid $50.0 million of the $100.0 million of principal outstanding of the Hercules debt as well as $3.1 million in end-of-term fees.

Funding requirements

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

- contractual milestone payments and royalties we might be owed in accordance with the CSL Behring Agreement;
- earnout payments we might owe the former shareholders of uniQure France SAS, which are subject to the achievement of specific development and regulatory milestones;
- the scope, timing, results, and costs of our current and planned clinical trials, including those for funding late-stage clinical development of AMT-130 in Huntington's disease;
- the scope, obligations and restrictions on our business related to our existing equity, debt or royalty monetization financings and underlying agreements;
- the extent to which we acquire or in-license other businesses, products, product candidates or technologies;
- the amount and timing of revenue, if any, we receive from manufacturing products for CSL Behring;
- the scope, timing, results and costs of preclinical development and laboratory testing of our additional product candidates;
- the need for additional resources and related recruitment costs to support the preclinical and clinical development of our product candidates;
- the need for any additional tests, studies, or trials beyond those originally anticipated to confirm the safety or efficacy of our product candidates and technologies;
- the cost, timing and outcome of regulatory reviews associated with our product candidates;
- our ability to enter into collaboration arrangements in the future; and
- 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.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

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

Our market risks and exposures to such market risks during the nine months ended September 30, 2024, 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, 2024. Based on such evaluation, our CEO and CFO concluded that as of September 30, 2024, 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 period covered by this Quarterly Report on Form 10-Q, there were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Part II – OTHER INFORMATION

Item 1. Legal Proceedings

None.

Item 1A. Risk Factors

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

Summary Risk Factors

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

- We are dependent on the success of our lead product candidate in clinical development, AMT-130 for the treatment of Huntington's disease. A failure of AMT-130 in clinical development, challenges associated with its regulatory pathway, or its inability to demonstrate sufficient efficacy to warrant further clinical development or accelerated approval pathways could adversely affect our business.
- 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.
- Our progress in early-stage clinical trials may not be predictive of long-term efficacy in late-stage clinical trials, and our progress in trials for one product candidate may not be predictive of progress in trials for other product candidates.
- Interim or preliminary data from studies or trials announced or published from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- Data analyses conducted on a post-hoc basis and using external, historical controls may not be accepted as a basis for regulatory approval.
- We may use certain specialized pathways and designations to develop our product candidates or to seek regulatory approval. Even if one or more of our product candidates receives such a designation or is permitted pursue such a pathway, we may be unable to obtain and maintain the benefits associated with such designations and pathways. These designations and pathways may not lead to a faster development or regulatory review or approval process, and may not increase the likelihood that our product candidates will receive marketing approval.
- The Lexington Transaction may not yield the benefits that we expect and may result in additional risks to our business.
- Our future success depends on our ability to retain key executives, technical staff, and other employees and to attract, retain and motivate qualified personnel.
- Actions that we have taken or may take in the future to restructure our business in alignment with our strategic priorities may not be as effective as anticipated, may not result in cost savings to us and could disrupt our business.
- Gene therapies are complex, expensive and difficult to manufacture. We, Genezen or any third-party manufacturer that we engage could experience capacity, production or technology transfer challenges that could result in delays in our development or commercialization schedules or otherwise adversely affect our business.

- We will need to raise additional funding in order to advance the development of our product candidates, 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 had net losses in the years ended December 31, 2023 and 2022, have 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.
- The price of our ordinary shares has been and may in the future be volatile and fluctuate substantially.
- If we do not achieve our projected development and financial 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.
- 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 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.
- 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 in the conduct and completion of such trials or failing to comply with regulatory requirements.
- 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 collaborations or other contractual arrangements, our business could be adversely affected.
- We face substantial competition, and others may discover, develop, or commercialize competing products before or more successfully than we do.

Risks Related to the Development of Our Product Candidates

We are dependent on the success of our lead product candidate in clinical development, AMT-130 for the treatment of Huntington's disease. A failure of AMT-130 in clinical development, challenges associated with its regulatory pathway, or its inability to demonstrate sufficient efficacy to warrant further clinical development or accelerated approval pathways could adversely affect our business.

We have invested a significant portion of our development efforts and financial resources in the development of our lead clinical product candidate, AMT-130. In July 2024, we announced updated interim data from our ongoing clinical trials of AMT-130, a one-time administered investigational gene therapy for the treatment of Huntington's disease. The interim data included follow-up data from patients enrolled in our two ongoing multi-center, dose-escalating Phase I/II clinical trials in the U.S. and Europe as of a March 31, 2024 cut-off date. Among other data in this interim update, we reported a statistically significant, dose-dependent, slowing in disease progression measured by composite Unified Huntington's Disease Rating Scale (cUHDRS) observed through 24 months in patients receiving the high dose of AMT-130. We also reported a statistically significant reduction of neurofilament light chain (NfL) in cerebrospinal fluid (CSF) observed in patients treated with AMT-130, a key biomarker for neurodegeneration. These interim data follow notification from the FDA in June 2024 that the agency had granted Regenerative Medicine Advanced Therapy ("RMAT") designation for AMT-130 based on AMT-130's potential to address the major unmet medical need among patients with Huntington's disease.

There are numerous factors that could impede or otherwise negatively impact our further development of AMT-130, including, but not limited to, patient safety issues, our failure to demonstrate sufficient clinical efficacy or durability of response data to warrant further development, delays in our ability to enroll patients or challenges with potential development partners, clinical trials or regulatory authorities. Any one or combination of these factors could force us to halt or discontinue the ongoing clinical trials of AMT-130. Certain of these risk factors are heightened in the context of drug development for rare diseases like Huntington's disease and novel investigational products like gene therapies in which non-traditional study designs are utilized to demonstrate efficacy and safety, including open-label studies, single arm studies, studies utilizing active comparators or natural history data, biomarkers or other forms of surrogate endpoints, which may be utilized due to the challenges inherent in designing and conducting clinical trials for severe diseases that progress slowly and that affect small patient populations. For example, in the course of our interactions with the FDA and EMA, the regulatory authorities may disagree with our interpretation of the interim safety and efficacy data we have received to date, including our determinations of statistical significance and the utility of post hoc analyses we conduct with respect to interim clinical data. Since AMT-130 is based on our novel gene therapy technology, we are unable to predict how regulatory authorities will interpret our data or whether they will agree with our interim conclusions or trial design or whether those data may be utilized in later-stage or registrational trials. We may be required by such regulatory authorities to conduct additional randomized studies of AMT-130 beyond our existing planned clinical trials, which would be costly and would significantly delay the potential approval of AMT-130. We may not be able to commit sufficient capital to support additional clinical studies of AMT-130, in which case we may need to secure a development partner for AMT-130. Such partnerships may not be available, in which case we may not be able to fully fund the AMT-130 program through to regulatory approval.

If AMT-130 fails in development as a result of any underlying problem with our technology, then we may be required to discontinue development of other product candidates that are based on the same novel therapeutic approach. We cannot be certain that AMT-130, or any of our product candidates, will be successful in clinical trials or receive regulatory approval. If we were required to, or if we chose to, discontinue development of AMT-130 or any other current or future product candidates, or if any of them were to fail to receive regulatory approval or achieve sufficient market acceptance, we could be prevented from or significantly delayed in achieving profitability and our business would be adversely affected.

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.

Drug development is expensive, time-consuming, and uncertain as to the outcome. Our product candidates are in different stages of clinical or preclinical development, and there is a significant risk of failure or delay in each of these programs. We are currently conducting Phase I/II clinical trials in the U.S. and Europe for AMT-130, our investigational gene therapy for the treatment of Huntington's disease. We are also advancing three other product candidates into clinical development – AMT-260 for the treatment of refractory mesial temporal lobe epilepsy, AMT-162 for the treatment of SOD1-ALS and AMT-191 for the treatment of Fabry disease.

We have experienced clinical setbacks in the past and may experience setbacks in the future. For example, we experienced an immaterial but unexpected delay when our clinical trials of HEMGENIX® were placed on clinical hold by the FDA from December 2020 to April 2021 following a preliminary diagnosis of hepatocellular carcinoma in one patient. Similarly, we experienced an unexpected delay in the enrollment of our Phase Ib/II clinical trial of AMT-130 for the treatment of Huntington's disease between July and October 2022 due to our voluntary postponement and comprehensive safety investigation into suspected unexpected serious adverse reactions in three patients.

A failure of one or more clinical trials can occur at any stage and for a variety of reasons that we cannot predict with accuracy and that are out of our control. 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;
- insufficient number of patients treated with the product candidate or an insufficient study period for assessing the effectiveness of the product candidate;
- failures or delays in reaching agreement with regulatory agencies on study design, particularly with respect to our novel gene therapies for which regulatory pathways remain untested;
- failures or delays in hiring sufficient personnel with the requisite expertise to execute multiple clinical programs simultaneously;

- failures or delays in reaching agreement on acceptable terms with clinical research organizations ("CROs") and clinical trial sites;
- failures or delays in patient recruiting into clinical trials or in the addition of new investigators;
- delays in receiving regulatory authorization to conduct our clinical trials or a regulatory authority decision that the clinical trial should not proceed;
- failures or 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 or testing;
- 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, our chosen bases for comparison as it relates to clinical efficacy, our interpretation and analyses 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;
- delays or deviations in the testing, validation, manufacturing, and delivery of our product candidates to the clinical sites;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a study;
- the number of patients required for clinical trials of our product candidates being larger than we anticipate;
- clinical trials producing negative or inconclusive results, or our studies failing to reach the necessary level of statistical significance, requiring that we conduct additional clinical trials or abandon product development programs;
- interruptions in manufacturing clinical supply of our product candidates or issues with manufacturing product candidates that meet the necessary quality requirements;
- unanticipated clinical trial costs or insufficient funding, including paying substantial application user fees;
- emergence of new information about or impacting our product candidates or the field of gene therapy;
- determinations that there are issues with our third-party manufacturing facilities or processes; or
- changes in regulatory requirements and guidance, as well as new, revised, postponed, or frozen regulatory requirements (such as the EU Clinical Trials Regulation), that require amending or submitting new clinical protocols, undertaking additional new tests or analyses, or submitting new types or amounts of clinical data.

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

If the results of our clinical trials are inconclusive, or fail to meet the level of statistical significance required for regulatory approval or if there are safety concerns, concerns around efficacy or durability of response or other 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, safety warnings, labeling statements or contraindications;
- be subject to changes in the way our products are 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 legal action or other challenges; 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 for which we may not be able to meet the regulatory authorities' standards.

Our ability to recruit patients for our clinical trials is heavily reliant on third parties, such as clinical trial sites. Clinical trial sites may not have the adequate infrastructure established to handle the administration of our gene therapy products, related surgeries or other means of product administration, or may have difficulty finding eligible patients to enroll into a clinical trial, which may delay or impede our planned trials. In addition, we or any of our collaborators may not be able to locate and enroll enough eligible patients to participate in these trials as required by the FDA, the EMA or similar regulatory authorities outside the U.S. and the European Union. This may result in our failure to initiate or continue clinical trials for our product candidates or may cause us to abandon one or more clinical trials altogether. Because our programs are focused on the treatment of patients with rare or orphan or ultra-orphan diseases, our ability to enroll eligible patients in these trials may be limited or slower than we anticipate considering the small patient populations involved and the specific age range required for treatment eligibility in some indications. In addition, our potential competitors, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, may seek to develop competing therapies, which would further limit the small patient pool available for our studies. Also, patients may be reluctant to enroll in gene therapy trials where there are other therapeutic alternatives available or that may become available for various reasons, including, but not limited to, 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 predictive of long-term efficacy in late-stage clinical trials, and our progress in trials for one product candidate may not be predictive of progress in trials for other product candidates.

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. For example, the interim results from our ongoing Phase I/II clinical trials of AMT-130, our product candidate targeting Huntington's disease, may not be predictive of the results of future interim analyses or later-stage trials. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Moreover, should there be an issue with the design of any of our clinical trials, our results may be impacted. We may not discover such a flaw until the clinical trial is at an advanced stage. Changes to product candidates, whether as a result of regulatory feedback or changes in clinical trial procedures and protocols, 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 our clinical trials, if the results are not reproducible or if our products show diminishing activity over time, our product candidates may not receive approval from the FDA, EMA or comparable regulatory authorities. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections because of many factors, including changes in regulatory policy during the period of product development. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our products in later-stage clinical trials with larger patient populations could have a material adverse effect on our business, financial condition, and results of operations.

Additionally, we are currently conducting and may in the future conduct clinical trials that utilize an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational therapeutic candidate (as opposed to an existing approved drug or placebo). Open-label trials typically test only the investigational therapeutic candidate and sometimes may do so at different dose levels. For example, our ongoing Phase I/II clinical trial of AMT-130 is designed as an open-label trial following a 12-month core study period during which certain patients received a sham surgical procedure. Certain of these patients have crossed over to treatment and are now subject to long-term, unblinded follow-up monitoring for a period of five years. Open-label trials are subject to various limitations that may bias the interpretation of the data. Open-label trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Accordingly, the results from our open-label trials, including early indications of potential efficacy, may not be predictive of future clinical trial results.

Interim or preliminary data from studies or trials announced or published from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we publicly disclose interim, preliminary or other data from preclinical studies and clinical trials, which are based on a preliminary and sometimes post hoc analysis of data. With respect to interim and preliminary data, the results and related findings and conclusions are subject to change following a more comprehensive review of the data, the particular study, or trial. We also make assumptions, estimations, calculations, and conclusions as part of our preliminary or interim analyses of data, and we may not have received or had the opportunity to evaluate all data at that time. As a result, the interim or preliminary data that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, preliminary or interim data should be viewed with caution until the final data are available.

For example, in December 2023, we announced updated interim data from our ongoing Phase I/II clinical trials of AMT-130, along with our expectation that we will present additional clinical updates with respect to AMT-130 in the future. We announced additional interim data from the ongoing AMT-130 trials in July 2024. Interim data from clinical trials and our analyses of that data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available after longer time on study. Significant differences between interim data and final data could change the nature of any interim conclusions we may report and could seriously harm our business.

We may also disclose data based on post-hoc analyses, the pooling of data from multiple studies, or using statistical assessments or comparisons, including comparisons to historical controls and calculations of nominal p-values, that regulatory authorities may not agree with. By example, the FDA may not agree with our pooling of the data from our U.S. and European studies of AMT-130. FDA may also find that statistical significance calculations using nominal p-values are not sufficiently reliable or subject to certain statistical limitations and, as a result, regulatory authorities may give such calculations less regulatory weight. The FDA may not view post-hoc analyses, analyses of exploratory endpoints, or comparisons to external controls to be sufficient to provide substantial evidence of efficacy, with the outcomes typically being viewed as hypothesis generating. FDA and other regulatory authorities may form a different or unfavorable view of our data, which could negatively impact our ability to obtain marketing approval.

Accordingly, third parties, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. For example, following receipt of RMAT designation for AMT-130, we expect to hold a Type B, multi-disciplinary RMAT meeting with FDA to present our updated interim data and discuss potential expedited clinical development pathways and accelerated approval. The FDA and other regulatory authorities may not agree with the assumptions, estimates, calculations, conclusions or analyses underlying the interim data from our ongoing clinical trial of AMT-130 or any of our future proposals regarding the ongoing development of AMT-130. Even if the data supporting such regulatory interactions are suggestive of clinical responses, the durability of response may not be sustained over time or may not be sufficient to support regulatory approval.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or interim data that we report differ from final results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could seriously harm our business.

Data analyses conducted on a post-hoc basis and using external, historical controls may not be accepted as a basis for regulatory approval.

We have in the past and may in the future undertake certain analyses to further understand the data and potential reasons for the study results, including retrospective, post-hoc, and subgroup analyses. Because these analyses are not pre-planned and studies may not be adequately designed for these analyses, they may not be a reliable nor an acceptable basis for regulatory approval. For example, in conjunction with our July 2024 interim data update for AMT-130, we conducted a post-hoc analysis of clinical outcomes for the 21 treated patients at 24 months compared to an expanded, propensity-weighted external control consisting of 154 patients. Among other conclusions in this interim update, we reported, based on this analysis, a statistically significant, dose-dependent, slowing in disease progression measured by cHUDRS observed through 24 months in patients receiving the high dose of AMT-130. We also reported a statistically significant reduction of CSF NfL observed in patients treated with AMT-130.

Some of our favorable statistical data from these trials also are based on nominal p-values. Nominal p-values are subject to certain limitations, and because of these limitations, regulatory authorities may give less weight to nominal p-values, compared to standard p-values. The FDA could find that our reliance on nominal p-values for some of our statistical data is insufficient to support accelerated or standard approval of AMT-130 or any other product candidate we choose to advance. An unfavorable view of our data and analyses by regulatory authorities could negatively impact our ability to obtain or maintain marketing authorizations, which would have a material adverse effect on our revenue and would materially harm our business, financial results and results of operations.

We are making use of exploratory biomarkers and other data that are not scientifically validated, and our reliance on these data may lead us to direct our resources inefficiently.

We are making use of experimental biological markers, or biomarkers, in an effort to facilitate our drug development and to optimize our clinical trials. Biomarkers are proteins or other substances which can serve as an indicator of specific cell processes or as evidence of a patient's biological response to drug product administration. For example, with respect to our ongoing clinical trials of AMT-130, we are measuring NfL in CSF as a potential indicator of neurodegeneration, as well as changes in total brain volume of patients treated with AMT-130.

While we believe that these biomarkers and data may serve useful purposes for us, including in the evaluation of whether our product candidates are having their intended effects through their assumed mechanisms of action, improving patient selection and monitoring patient compliance with trial protocols, these biomarkers and data have not been scientifically validated and are considered experimental as used in our trials. If our understanding and use of biomarkers is inaccurate or flawed, or if our reliance on specific biomarkers such as CSF NfL is otherwise misplaced, then we may fail to realize any benefits from using these data and may also be led to invest time and financial resources inefficiently in attempting to develop inappropriate drug candidates.

We may not be successful in our efforts to use our gene therapy technology platform to build a pipeline of additional product candidates or otherwise leverage our research and technology to remain competitive.

An element of our strategy is to use our gene therapy technology platform to expand our product pipeline and to progress our product candidates through preclinical and clinical development ourselves or together with collaborators. To date, we have only been successful in obtaining regulatory approval for one product, HEMGENIX®, our gene therapy for the treatment of hemophilia B, which was approved for commercialization by the FDA and the EMA in November 2022 and February 2023, respectively. AMT-130 is our investigational gene therapy candidate for the treatment of Huntington's disease that utilizes our proprietary, gene-silencing miQURE platform and incorporates an AAV vector carrying a miRNA specifically designed to silence the huntingtin gene and the potentially highly toxic exon 1 protein fragment, which is currently in ongoing Phase I/II studies in the U.S. and Europe. In addition to AMT-130, we are also developing other investigational gene therapies, including AMT-260 for the treatment of MTLE, AMT-162 for the treatment of SOD1-ALS and AMT-191 for the treatment of Fabry disease. Although we currently have a pipeline of programs at various stages of development, including an approved product, 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. Due to the significant resources required for the development of our product candidates, we must decide which product candidates to pursue and advance and the resources to allocate to each. For example, as a result of prior restructuring efforts, we discontinued investments in certain of our prior research and development programs, including AMT-210 for the treatment of Parkinson's disease, and certain other technology projects, prioritizing instead our early clinical-stage programs, including AMT-130, AMT-260, AMT-162 and AMT-191. Even though we have focused our efforts on advancing these four clinical programs, we may not be able to successfully develop all of them or our business strategy and objectives could change.

Our decisions concerning the allocation of research, development, collaboration, management, and financial resources toward particular programs and product candidates, including the decisions stemming from our prior restructuring efforts, may not lead to the development of any viable commercial product and may divert resources away from better opportunities. 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 business development strategy depends on our ability to obtain rights to key technologies through in-licenses and support the development of our product pipeline through out-licenses, and those efforts may not be successful.

We may expand our product pipeline from time to time through strategic transactions that involve in-licensing the rights to key technologies, including those related to gene delivery, genes, and gene cassettes. For example, in July 2021, we acquired uniQure France (formerly Corlieve Therapeutics SAS) and its lead program, now known as AMT-260, to treat refractory MTLE. AMT-260 is being developed based on exclusive licenses to certain patents uniQure France obtained from two French research institutions that continue to collaborate with us. uniQure France also obtained an exclusive license from Regenxbio, Inc. to use AAV9 in connection with the delivery of any sequence that affects the expression of the GRIK2 gene in humans. Notwithstanding prior efforts to expand our product pipeline, the cost of drug development is high as is the rate of failure in the drug development process. In order to fund the development of some of our existing product candidates, including potential late-stage development of AMT-130 if required by regulators, we may seek to out-license some of our product candidates or technologies to other pharmaceutical or biotechnology companies or other third parties. The aim of such out-licensing would be generate non-dilutive funds in the form of up-front or milestone payments or royalties. Such decisions will be taken on a case-by-case basis, as the opportunity arises or is required.

The future success of our business will depend in significant part on our business development efforts with respect to existing and future product candidates, including our ability to in-license or otherwise acquire the rights to additional product candidates or technologies, particularly through our collaborations with academic research institutions, and our ability to out-license product candidates and technologies for which collaboration with external parties forms a part of our business strategy or is necessary to cover certain development costs. 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 gene therapy 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.

Similarly, there is no guarantee that we will generate product candidates that are suitable for out-licensing or attractive to potential collaborators, and even if we do, there is no guarantee that we will be successful in identifying potential licensees and successfully negotiating such collaborations on agreeable terms if and when required. Any failure with respect to our business development efforts may materially affect our ability to finance our business and support the development of our product pipeline.

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.

Gene therapy remains a novel technology. Our technology utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Public perception may be influenced by claims that gene therapies are unsafe, and gene therapies may not ultimately gain the acceptance of the public or the medical community. The risk of cancer remains a concern for gene therapy, and we cannot guarantee that patients treated in any of our planned or future clinical studies will not develop cancer or experience other adverse events as a result of being treated with our product candidates. 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.

Public and medical community adoption of any of our gene therapies will depend on other factors, including the ease of administration in comparison to other therapeutics and the extent to which our therapies are successful in slowing disease progression if not acting as a cure for the disease. For example, the need for lengthy and 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 products prescribing treatments that involve the use of our products 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 regulation of gene therapies or negative public opinion may 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. A small number of patients have experienced serious adverse events during our clinical trials of AMT-060 (HEMGENIX®), etranacogene dezaparvovec (AMT-061), and AMT-130. However, adverse events in our clinical trials or those conducted by third 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 require medical devices for administration, such as AMT-130 and AMT-260, each of which requires a stereotactic, magnetic resonance imaging guided catheter. 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. In addition, certain of our product candidates, including AMT-130 and AMT-260, may require the use of immunosuppressive agents to reduce the inflammatory responses associated with administration.

It is possible that our product candidates would be deemed to be combination products, potentially necessitating compliance with the FDA's investigational device regulations, separate marketing application submissions for the medical device component, a demonstration that our product candidates are safe and effective when used in combination with the medical devices, cross-labeling with the medical device, and compliance with certain of the FDA's device regulations. If we are not able to comply with the FDA's device regulations, if we are not able to effectively partner with the applicable medical device manufacturers, if we or any partners are not able to obtain any required FDA clearances or approvals of the applicable medical devices, or if we are not able to demonstrate that our product candidates are safe and efficacious when used with the applicable medical devices, we may be delayed in or may never obtain FDA approval for our product candidates, which would materially harm our business.

Moreover, certain of our delivery modalities, such as direct delivery of product candidates to the brain, may require significant time and 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, or if there is reluctance to administer immunosuppressive agents that are outside of the standard of care to treat immune responses from the administration of our therapies, 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 the Manufacturing of our Products and Product Candidates

The Lexington Transaction may not yield the benefits that we expect and may result in additional risks to our business.

In June 2024 we entered into the APA with Genezen pursuant to which we agreed to sell to Genezen and Genezen agreed to purchase certain assets and assume certain liabilities related to the Lexington Facility and our prior manufacturing operations in Lexington, Massachusetts. Pursuant to the APA, Genezen agreed to acquire the manufacturing equipment and related manufacturing operations along with certain other assets associated with the Lexington Facility and to extend offers of employment to a majority of the uniQure employees located at the Lexington Facility. The Lexington Transaction closed in July 2024.

In connection with the closing of the Lexington Transaction, we and Genezen entered into certain additional agreements, including (i) a commercial supply agreement pursuant to which Genezen will manufacture and supply for our requirements of HEMGENIX® pursuant to our manufacturing and supply obligations to CSL Behring, (ii) a development and other manufacturing services agreement pursuant to which Genezen will manufacture, supply and provide certain development services to support the requirements of our investigational gene therapy programs and for other services related to the manufacture of HEMGEMIX®, (iii) a transition services agreement pursuant to which each party will provide transitional services to the other related to the operation of the Lexington Facility for a period following the closing of the Lexington Transaction, and (iv) an assignment and assumption of the lease agreement for the Lexington Facility, along with other customary agreements. As a component of our broader efforts to focus our business and reduce operating expenses, the Lexington Transaction is expected to reduce our cash burn as a result of a reduction in facility and personnel-related costs, among others.

The Lexington Transaction may not ultimately reduce our operating expenses to a magnitude consistent with our expectations. In addition, we may be exposed to additional costs and risks related to or as a result of the Lexington Transaction, including, without limitation (i) additional expenses associated with outsourcing certain manufacturing and development services, as well as our contractual obligations and minimum financial commitments to Genezen under the CSA and the DMSA, (ii) supply-related risks related Genezen's ability and capacity to satisfy our continued obligations to CSL Behring and the supply of our other product candidates, including AMT-130, (iii) contractual default under our agreements with Genezen or with CSL Behring, and (iv) other third-party risks relative to our partnership with Genezen (see "—Risks Related to our Dependence on Third Parties"). The occurrence of any of the foregoing or any other risks as a result of or related to the Lexington Transaction could considerably harm our business and impact our financial condition and results of operations.

Gene therapies are complex, expensive and difficult to manufacture. We, Genezen or any third-party manufacturer that we engage could experience capacity, production or technology transfer challenges that could result in delays in our development or commercialization schedules or otherwise adversely affect our business.

Our proprietary manufacturing processes leveraging insect cells and baculoviruses to produce AAV-based gene therapies is highly complex and is regularly subject to variation or production difficulties. Issues with any of our manufacturing processes, even minor deviations from our standard processes, could result in insufficient yield, product deficiencies or manufacturing or supply failures that could result in adverse patient reactions, lot failures, insufficient inventory, product recalls and product liability claims. Additionally, we and our third-party manufacturers, including Genezen, may not be able to scale up some or all our manufacturing processes as necessary and on our desired timelines to meet the demands of our clinical product pipeline, which may result in delays in regulatory approvals, inability to produce sufficient amounts of clinical or commercial product, or otherwise adversely affect our business.

Factors common to the manufacturing process associated with most biologics and drugs could also cause production interruptions for us or our third-party manufacturers, including, without limitation, raw materials shortages and other supply chain challenges, raw material failures, limited control over pricing of raw materials, growth media failures, equipment malfunctions, costs associated with servicing real property lease and other contractual obligations, facility contamination, labor problems, natural disasters, disruption in utility services, public health crises, terrorist activities, war or cases of force majeure and other events beyond our control. We or our third-party manufacturers also may encounter problems in hiring and retaining the experienced and specialized personnel needed to evaluate and supervise manufacturing and quality operations and, in the case of our contract manufacturers, operate manufacturing facilities, processes and testing, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. Following the Lexington Transaction, Genezen may experience the same personnel-related challenges resulting in the same delays and compliance issues.

Prior to the Lexington Transaction, we manufactured HEMGENIX® at the Lexington Facility, which is optimized to meet HEMGENIX® product specifications and the commercial manufacturing and supply obligations under our collaboration with CSL Behring. Following the Lexington Transaction, Genezen is responsible for the manufacturing and supply of HEMGENIX® at the Lexington Facility, though we remain contractually obligated to CSL Behring consistent with the terms of the collaboration. While uniQure will have priority and preferential status with Genezen, Genezen may not have sufficient capacity to support our other development programs or those of its other customers, which may negatively impact our business and ability to advance development goals unrelated to HEMGENIX® and our obligations to CSL Behring. The manufacturing of HEMGENIX® pursuant to our obligations under the CSL Behring Agreement is expensive and requires the dedication of significant resources, notwithstanding the Lexington Transaction and our subcontracting to Genezen. In September 2022, CSL Behring notified us of its intent to transfer manufacturing technology in the coming years related to HEMGENIX® to a third-party contract manufacturer to be designated by CSL Behring in the future. Until CSL Behring identifies and designates a new manufacturer capable of supporting the commercial requirements of HEMGENIX®, we will continue to incur significant costs associated with the manufacturing and supply of HEMGENIX®. Moreover, as Genezen will be the party engaged in the manufacture of HEMGENIX®, should Genezen encounter a manufacturing issues or if Genezen is unable to provide a sufficient supply of HEMGENIX® consistent with agreed-upon forecasting mechanisms, we may be unable to fulfil our contractual commitments to CSL Behring and may, thus, face contractual liabilities.

Following the Lexington Transaction, Genezen may experience challenges in adapting the Lexington Facility to meet the manufacturing and supply needs for products other than HEMGENIX® as a result of excess capacity or the ability to adapt to new processes, among other challenges. Any problems or limitations with respect to our manufacturing processes or facilities, including the existing commercial supply and manufacturing obligations to CSL Behring, could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs or sources of capital, result in delays in our clinical development or marketing schedules and materially harm our business.

We currently rely and expect to continue to rely on third parties to conduct product manufacturing for our product candidates, and these third parties may not perform satisfactorily.

We currently rely, and expect to continue to rely, on third parties for the production of our preclinical study and planned clinical trial materials and, therefore, we can control only certain aspects of their activities. Prior to the Lexington Transaction, we manufactured HEMGENIX® in-house at the Lexington Facility. Following the Lexington Transaction, we rely on Genezen for the production of HEMGENIX® and will have preferential access to the Lexington Facility for the production of materials related to AMT-130 and AMT-191 programs under separately negotiated development and supply arrangements. The facilities used by Genezen and our other contract manufacturers to manufacture certain of our product candidates must be reviewed by the FDA pursuant to inspections that will be conducted after we submit a BLA to the FDA. We do not control the manufacturing process of, and are completely dependent on, Genezen and our other contract manufacturing partners for compliance with the cGMP for the manufacture of our products and product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory bodies, we will not be able to obtain and/or maintain regulatory approval for our products manufactured by third parties. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative third-party manufacturers, which may not be available and which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

The manufacturing of our products and product candidates are subject to significant government regulations and approvals. If we or third-party manufacturers fail to comply with these regulations or maintain these approvals, our business could be materially harmed.

With the exception of AMT-260 and AMT-162 and prior to the Lexington Transaction, we produced our gene therapies at the Lexington Facility using a proprietary baculovirus expression vector system. The Lexington Facility is and will continue to be subject to ongoing regulation and periodic inspection by the FDA, EU member state, and other regulatory bodies to ensure compliance with cGMP and other requirements. Any failure to follow and document our adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical study, may result in the termination of or a hold on a clinical study, or may delay or prevent filing or approval of marketing applications for our products.

Failure to comply with applicable regulations could also result in the FDA, EU member state, or other applicable authorities taking various actions, including:

- taking enforcement actions or 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, or conduct new or additional 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; or
- 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 the Lexington Facility or the manufacturing facilities of any third-party manufacturer we may engage is not able to meet regulatory requirements, we or they 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, Genezen or our other third-party manufacturers are not able to manufacture a sufficient amount of our product candidates for clinical studies or eventual commercialization, or if Genezen is unable to satisfy our manufacturing and supply obligations to CSL Behring, our development programs and commercial prospects will be harmed. If Genezen cannot produce an adequate amount of our drug substance and product in compliance with the applicable regulatory requirements, we may need to contract with another third party to do so, and there is not guarantee that such third-party manufacturers will be available to us and able to manufacture on favorable terms or at all. 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.

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

Our development and manufacturing processes and those of our third-party contract manufacturers involve the use of viruses, chemicals, other potentially hazardous materials and produce waste products. Accordingly, we and our third-party manufacturers are subject to national, federal, state, and local laws and regulations in the U.S. and Europe governing the use, manufacture, distribution, storage, handling, treatment, and disposal of these materials. In addition to ensuring the safe handling of these materials, these laws and regulations impose 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 or our third-party contract manufacturers 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 business may be adversely affected if we or third-party manufacturers of our product candidates are unable to validate our manufacturing processes and methods or develop new processes and methods to meet our product supply needs and obligations.

The manufacture of our AAV gene therapies is complex and requires significant expertise. Even with the relevant experience and expertise, manufacturers of gene therapy products often encounter difficulties in production, particularly in scaling out and validating initial production and ensuring that the product meets required specifications. These problems include difficulties with production costs and yields, quality control, including stability and potency of the product, quality assurance testing, instances of operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state, and foreign regulations. In the past and prior to the Lexington Transaction, we have manufactured certain batches of product candidates intended for nonclinical, clinical and process validation purposes that have not met all our pre-specified quality parameters. To meet our expected future production needs and our regulatory filing timelines for gene therapy product candidates, Genezen will need to complete the validation of our manufacturing processes and methods for each program, and we may need to develop and validate new or larger scale manufacturing processes and methods to meet our needs. If Genezen or any other third-party manufacturer we engage is 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 our product candidates.

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

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

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

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

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, which are and will be applicable to our product candidates. 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. Experiences with existing gene therapies, including any emergent adverse effects, could also impact how the FDA and the EMA view our products and product candidates, making it harder to obtain or maintain regulatory approvals.

Regulatory requirements affecting gene therapy have changed frequently and continue to evolve, and agencies at both the U.S. federal and state level, as well as congressional committees and foreign governments, have sometimes expressed interest in further regulating biotechnology. In the U.S., there have been a number of changes relating to gene therapy development. By example, FDA issued a number of 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.

We may use certain specialized pathways and designations to develop our product candidates or to seek regulatory approval. Even if one or more of our product candidates receives such a designation or is permitted pursue such a pathway, we may be unable to obtain and maintain the benefits associated with such designations and pathways. These designations and pathways may not lead to a faster development or regulatory review or approval process and may not increase the likelihood that our product candidates will receive marketing approval.

In June 2024, the FDA granted RMAT designation for AMT-130 based on AMT-130's potential to address the major unmet medical need among patients with Huntington's disease. The designation followed the FDA's review of interim Phase I/II clinical data for AMT-130 announced in December 2023 and was based on an analysis comparing 24-month clinical data from the AMT-130 trials to a non-concurrent criteria-matched natural history cohort. In the future, we may seek additional product designations intended to facilitate the development or regulatory review or approval process for our product candidates, such as fast-track designations, breakthrough therapy designation, RMAT designation, PRIME scheme access or priority review designation for our product candidates.

A fast-track product designation is designed to facilitate the clinical development and expedite the review of drugs intended to treat a serious or life-threatening condition and which demonstrate the potential to address an unmet medical need. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. An RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to accelerate the FDA marketing application review timeframe for drug products that treat a serious condition and that, 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 (in the case of AMT-130), or breakthrough therapies, or granted access to the PRIME scheme, more frequent 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 a designation. In any event, the receipt of such a designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional regulatory procedures and does not assure ultimate marketing approval by the agency. In addition, the FDA may later decide that the products no longer meet the applicable conditions for qualification as either a fast-track product, RMAT, or a breakthrough therapy or, for priority review products, decide that the period for FDA review or approval will not be shortened. Moreover, in the U.S., the FDA expects that sponsors with products under these programs will be prepared for a more rapid pace of development, including with respect to manufacturing or any combination medical devices, such as companion diagnostics. If we are unable to meet these expectations, we may not be able to fully avail ourselves of certain advantages of these programs.

Biologics studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may also receive accelerated approval by the FDA, meaning the agency may approve the product candidate based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. There is no guarantee that we would be able to obtain accelerated approval as FDA may disagree with our surrogate endpoint or may find that such endpoint is not met. Even if we do qualify for accelerated approval, we may be unsuccessful in meeting post-marketing compliance requirements, or fail to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, which could result in the FDA withdrawing our product from the market. In recent years, the accelerated approval pathway has come under significant FDA and public scrutiny. Accordingly, it is uncertain whether the FDA may be more conservative in granting accelerated approval or, if granted, more apt to withdraw approval if clinical benefit is not confirmed. There is no guarantee that regulatory interactions with FDA or comparable foreign authorities will result in our ability to avail ourselves of any specialized approval pathways for our product candidates.

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

Regulatory authorities in some jurisdictions, including the U.S. and the European Union, may designate drugs for relatively small patient populations as orphan drugs. While certain of our product candidates, including AMT-130 and AMT-191, have received orphan drug designation, there is no guarantee that we will be able to receive such designations in the future. The FDA may grant orphan designation to multiple sponsors for the same compound or active molecule and for the same indication. If another sponsor receives FDA approval for such product before we do, we would be prevented from launching our product in the U.S. for the orphan indication for a period of at least seven years unless we can demonstrate clinical superiority.

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

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

Our focus on developing gene therapies makes it difficult to determine the availability and utility of the orphan drug regime to our product candidates. Regulatory criteria with respect to orphan products are evolving, especially in gene therapy. By example, in the U.S., whether two gene therapies are considered to be the same for the purpose of determining clinical superiority was updated via a final guidance document specific to gene therapies, and depends on a number of factors, including the expressed transgene, the vector, and other product or product candidate features. Depending on the products, whether two products are ultimately considered to be the same may be determined by FDA on a case-by-case basis, making it difficult to make predictions regarding when the FDA might be able to make an approval of a product effective and whether periods of exclusivity will effectively block competitors seeking to market products that are the same or similar to ours for the same intended use. Accordingly, whether any of our gene therapies will be deemed to be the same as another product or product candidate is uncertain.

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

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

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

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

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

Following any regulatory approval, the FDA and the EMA may impose certain post-approval requirements related to a product. Specifically, any approved products will be subject to continuing and comprehensive regulation concerning the product's design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution. Regulatory authorities may also require post-marketing testing, known as Phase 4 testing, a risk evaluation and mitigation strategy, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Failure to comply with any of these requirements could result in regulatory, administrative, or other enforcement action, which 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 on the Internet and social media. Approved products may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Failure to comply with regulatory promotional standards could result in actions being brought against us by these agencies.

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

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

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

In addition, the manufacture, testing, packaging, labeling, and distribution of products after approval will need to continue to conform to cGMPs. Drug and biological product manufacturers, including us, 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. If we or any of our contractors are unable to comply with the requirements that are applicable to drug manufacturers, we or they may be subject to regulatory enforcement, or may need to conduct a recall or take other corrective actions, which could result in material harm to us or our products.

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

Risks Related to Commercialization

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

Our ability to generate revenues from our product candidates 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 completion of preclinical studies and clinical trials, and other work required by regulators;
- receipt and maintenance of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and non-patent, exclusivities for our product candidates;
- maintaining regulatory approvals using our manufacturing facility in Lexington, Massachusetts;
- launch and commercialization of our products, if approved, whether alone or in collaboration with others;
- identifying and engaging effective distributors or resellers on acceptable terms in jurisdictions where we plan to utilize third parties for the marketing and sales of our product candidates;
- acceptance of our products, if approved, by patients, the medical community, and third-party payers;
- effectively competing with existing therapies and gene therapies based on safety and efficacy profiles;
- the strength of our marketing and distribution;
- the achievement 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 healthcare coverage and adequate reimbursement of our products;
- any price concessions, rebates, or discounts we may need to provide;
- complying with any applicable post-approval commitments and requirements, and maintaining a continued acceptable overall safety profile; and
- obtaining adequate reimbursement for the total patient population and each subgroup to sustain a viable commercial business model in U.S. and EU markets.

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 ("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 and may change. The total addressable market opportunities for these therapies will 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, among other factors.

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. For example, the addressable markets for certain of our 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 might not be eligible for administration of a gene therapy that includes this particular capsid. Moreover, neutralizing antibodies may be developed by a patient following administration of the product, which may render the patient ineligible for subsequent dosing. The use of such data to support addressable market estimates involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies and information 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.

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

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

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

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

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

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

Ethical, legal, and social issues associated with genetic testing 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 patient's underlying genetic information. For example, concerns have been expressed that insurance carriers and employers may use these tests to discriminate based on 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 partners, obtain approval to commercialize any of our product candidates outside of the U.S., a variety of risks associated with international operations could materially adversely affect our business.

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

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

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 current and future product candidates from large and specialty pharmaceutical companies and biotechnology companies worldwide, who, like us, currently market and sell products or are pursuing the development of products for the treatment of rare diseases. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. In recent years, there has been a significant increase in commercial and scientific interest and financial investment in gene therapy as a therapeutic approach, which has intensified the competition in this area.

We face worldwide competition from larger pharmaceutical companies, specialty pharmaceutical companies and biotechnology firms, universities and other research institutions and government agencies that are developing and commercializing pharmaceutical products. Our key competitors focused on developing therapies in various indications, include among others, Pfizer, Freeline Therapeutics, Intellia Therapeutics, Sangamo Biosciences, Voyager Therapeutics, Passage Bio, Roche, PTC Therapeutics, Prilenia Therapeutics, CombiGene, Caritas Therapeutics, Alnylam, Wave Life Sciences, Bayer AG (AskBio), Amicus Therapeutics, 4D Molecular Therapeutics, Sanofi, Idorsia, Amicus, Spark, Takeda, Chiesi, CANbridge, Abeona, Annexon, Vico, Alexion (AZ), Neurona, Combigene, NeuExcell, EpiBlok, Biogen, Ionis Pharmaceuticals, Eisai and Lexeo.

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. For example, in April 2024, the FDA approved Pfizer's Beqvez (fidanacogene elaparvovec-dzkt), a one-time gene therapy to treat adults with moderate to severe hemophilia B and a direct competitor to HEMGENIX.

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. Moreover, actions taken in connection with our prior restructuring efforts to streamline our product portfolio may hamper our ability to remain competitive. 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.

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 in the conduct and completion of such trials or failing to comply with regulatory requirements.

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

In addition, we will be required to report on 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 costs and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, if we need to enter into alternative arrangements, it could delay our product development activities and adversely affect our business. Though we carefully manage our relationships with our third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects, and results of operations.

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

We rely on third parties for important aspects of our development programs. If these parties do not perform successfully or if we are unable to enter into or maintain key collaborations 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 we enter into 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, may be open to multiple interpretations 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 are 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, or have otherwise given up the right, to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we own or 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 which may materially impact any revenue that may be due to us in connection with such patents. 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 or may otherwise result in reputational damage to our business. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or amended agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

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

We rely, in part, upon a combination of forms of intellectual property, including in-licensed and owned patents to protect our intellectual property. Our success depends in large part on our ability to obtain and maintain this protection in the U.S., the European Union, and other countries, in part by filing patent applications related to our novel technologies and product candidates. Our patents may not provide us with any meaningful commercial protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The patents we own currently are and may become subject to future patent opposition or similar proceedings. Additionally, the patent prosecution process is expensive, time-consuming, and uncertain, and in certain instances we have chosen, and in the future we may choose, not to file and prosecute all necessary or desirable patent applications. For example, our defense of certain patent cases in each of Canada, the United Kingdom, the Netherlands and the U.S. pertaining to licensed rights of etranacogene dezaparvovec was assumed by CSL Behring in October 2023. These oppositions and future patent oppositions may result in loss of scope of some claims or the entire patent and, with respect to our rights under the CSL Agreement, could affect CSL Behring's successful commercialization of HEMGENIX® and, in turn, could negatively impact our financial position. Additionally, 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 or the ability of our licensees 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.

It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Additionally, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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

Competitors may infringe on 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 a more narrowly amended form or interpreted narrowly.

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

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

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

For example, we are aware of patents or patent applications 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 positions will be needed. In addition, in some cases, we believe that the claims of these patents are invalid or not infringed or will expire before commercialization. However, if such patents are needed and found to be valid and infringed, we could be required to obtain licenses, which might not be available on commercially reasonable terms, or to cease or delay commercializing certain product candidates, or to change our programs to avoid infringement.

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

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

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

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

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

In addition, these agreements typically restrict the ability of our collaborators, advisors, and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, if we are notified in advance and may delay publication for a specified time to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Some courts inside and outside the U.S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those with whom they communicate, from using that technology or information to compete with us.

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

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

- others may be able to make gene therapy products that are similar to our product candidates or utilize similar gene therapy technology but that are not covered by the claims of the patents that we own or have licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered issued patents or pending patent applications that we own or have licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

The occurrence of any of these events could seriously harm our business.

Risks Related to Pricing and Reimbursement

We and our commercial partner face uncertainty related to insurance coverage of, and pricing and reimbursement for, HEMGENIX® and other product candidates for which we may receive marketing approval.

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

Government authorities and other third-party payers, such as private health insurers and health maintenance organizations, decide for which medications they will pay and, subsequently, establish reimbursement levels. Reimbursement systems vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. Government authorities and third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and procedures and negotiating or requiring payment of manufacturer rebates. Increasingly, third party payers require drug companies to provide them with predetermined discounts from list prices, are exerting influence on decisions regarding the use of particular treatments and are limiting covered indications.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient assistance programs. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (with the maximum fair prices for the first year of the negotiation program being initially applicable in 2026), with prices that can be negotiated subject to a cap; imposes rebates for certain drugs under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures and could seriously harm our business.

Individual states in the U.S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could seriously harm our business. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. Prescription drugs and biological products that are in violation of these requirements will be included on a public list. These reforms could reduce the ultimate demand for our product candidates or put pressure on our product pricing and could seriously harm our business.

In the EU, similar political, economic, and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the U.S. and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or judicial action in the U.S., the EU, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

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

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

The relatively small market size for orphan indications and the potential for long-term therapeutic benefit from a single administration present challenges for 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 many 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 net losses in the years ended December 31, 2023 and 2022, have 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 $166.3 million in the nine months ended September 30, 2024, and a net loss of $308.5 million in the year ended December 31, 2023. We incurred a gain of $329.6 million in year ended December 31, 2021; however, such gain was primarily attributable to one-time license revenue from CSL Behring. We incurred significant losses in the years prior to 2021. As of September 30, 2024, we had an accumulated deficit of $1,056.7 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 2024 and through the end of 2027 primarily from our existing cash, cash equivalents, and cash resources. 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 for the foreseeable future, and our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that we will continue to incur net losses for the foreseeable future as we:

- continue to fund AMT-130 in its ongoing clinical trials and advance our other product candidates into clinical development;
- incur the costs associated with the manufacturing of preclinical, clinical and commercial supplies of our product candidates through our partnership with Genezen and other third-party manufacturers;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain personnel to support our business;
- enhance our operational, financial and management information systems and personnel; and
- incur legal, accounting and other expenses operating as a public company.

We may never succeed in materially reducing our operating expenses and, even if we do, may never generate revenues that are sufficient to achieve or sustain profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to generate value for our shareholders could impair our ability to raise capital, maintain our research and development efforts, diversify our product offerings, or even continue our operations.

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

We expect to incur significant expenses in connection with our ongoing activities and we will need to obtain substantial additional funding in order to fund the development of our product pipeline and support 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 additional debt financing may be limited by covenants we have made under our 2024 Amended Facility with Hercules and our pledge to Hercules of substantially all our assets as collateral. Our ability to obtain additional equity financing may be limited by our shareholders' willingness to approve the issuance of additional share capital. 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, 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 or successfully pursue strategic partnerships where necessary, we could be forced to delay, reduce, or further 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, 2024, we had $50.0 million of outstanding principal of borrowings under the 2024 Amended Facility. In July 2024, in connection with the closing of the Lexington Transaction, we repaid $50.0 million of the principal outstanding. We are required to repay the outstanding principal balance of $50.0 million upon the maturity date of the 2024 Amended Facility in January 2027. We may not be able to finance our operations from our existing cash, cash equivalents, and cash resources consistent with our expectations if we are not able to refinance the 2024 Amended Facility prior to the January 2027 maturity date. We could in the future incur additional debt obligations beyond our borrowings from Hercules. Our existing loan obligations with Hercules, 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 2024 Amended Facility could result in an event of default and acceleration of amounts due. Under the 2024 Amended Facility, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets, or condition is an event of default. If an event of default occurs and the lender accelerates the amounts due, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all our assets.

Our 2024 Amended Facility bears a variable interest rate with a fixed floor. The U.S. Federal Reserve has raised, and may in the future further raise, interest rates to combat the effects of high inflation. An increase in interest rates by the Federal Reserve has and could in the future cause the prime rate to increase, which has and could in the future increase our debt service obligations. Significant increases in such obligations could have a negative impact on our financial position or operating results, including cash available for servicing our indebtedness, or result in increased borrowing costs in the future.

We may not realize the intended financial benefits of, or achieve the intended goals or outlooks with respect to, our business development and strategic initiatives, including divestitures, acquisitions or other potential transactions.

We have recently and historically pursued various strategic initiatives, transactions and business arrangements, including the July 2024 Lexington Transaction and the July 2021 acquisition of uniQure France and its lead program (AMT-260). We may, from time to time, enter into strategic transactions consistent with our business development and financial objectives. Implementing these and other strategic initiatives has included, and may in the future include, divestitures, acquisitions, asset purchases, partnerships, collaborations, joint ventures and other investments. Certain of these transactions and arrangements have been and may in the future be material to us both from a strategic and financial perspective. These initiatives, whether successful or not, have been, and may continue to be, complex, time-consuming and expensive, may divert management's attention, and could expose us to operational challenges and potential inefficiencies. We may miscalculate the risks associated with our strategic initiatives at the time they are made or may not have the resources or ability to access all the relevant information to evaluate them properly, including with regard to the research and development-related risks, manufacturing and compliance issues, or the outcome of ongoing legal and other proceedings. There can be no assurance that we will be able to achieve all of our intended goals with respect to such strategies within the anticipated timeframes, if at all, or fully realize the expected benefits of any such transactions or arrangements.

Divestitures (including the Lexington Transaction), product rationalizations or asset sales could result in asset impairments, or reductions to the size or scope of our business, our market share in particular markets or our opportunities and ability to compete with respect to certain markets, therapeutic areas or products. We may not be successful in separating divested businesses or assets, which could negatively impact our ongoing and future operations. For example, the Lexington Transaction may result in continued financial and operational exposure related to the divested assets or businesses, through guarantees or other financial arrangements, indemnification obligations, continued manufacturing and supply and transition services obligations to the divested businesses, or potential litigation. In addition, we may also not be able to realize the intended or anticipated benefits from such transactions, such as realizing the anticipated cost savings, maintaining employee morale and retaining key management and other employees to meet our transition service obligations and to operate our retained business, or may be unable to realize the intended or expected goals, outlooks, synergies or operating efficiencies with respect to such transactions.

The overall execution of our strategic initiatives may result in material unanticipated problems, expenses, liabilities, competitive responses, operational inefficiencies, adverse tax consequences, impairment or restructuring charges, loss of important third-party relationships, difficulty attracting and retaining qualified employees, and diversion of management's and/or employee's attention, among other potential adverse consequences. In addition, we may have to terminate a strategic alliance, agreement or arrangement, or our partners may be unable to fulfill their collaboration. Any of the risks described above could have a material adverse effect on our reputation, business, financial condition, results of operations, cash flows, ability to pay dividends and/or share price.

Risks Related to Other Legal Compliance Matters

Our relationships with employees, customers and third parties are subject to applicable laws and regulations, the non-compliance of any of which could have a material adverse effect on our business, financial condition, and results of operations.

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

Efforts to ensure that our business arrangements with third parties will comply with applicable laws and regulations could involve substantial costs. If our operations, or the activities of our collaborators, distributors or other third-party agents are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs and the curtailment or restructuring of our operations.

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

The costs associated with an alleged or actual violation of any of the foregoing could be substantial and could cause irreparable harm to our reputation or otherwise have a material adverse effect on our business, financial condition, and results of operations.

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

Many national, international, 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 EU General Data Protection Regulation that took effect in May 2018. The UK has, following its exit from the EU, substantially adopted the EU General Data Protection Regulation into its domestic law through the UK General Data Protection Regulation (collectively with the EU General Data Protection Regulation, and related EU and UK e-Privacy laws, the "GDPR"). The GDPR, together with the national legislation of the UK (including the Data Protection Act 2018) and EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, use, analyze and transfer personal information, including health data from clinical trials and adverse event reporting.

GDPR obligations applicable to us may include, in many circumstances, obtaining the (opt-in) consent of the individuals to whom the personal data relates; providing GDPR-prescribed data processing notices to individuals; complying with restrictions regarding the transfer of personal data out of the EU or the UK (as applicable) (including to the US); implementing and maintaining data protection policies and procedures; restrictions regarding the use of certain innovative technologies; providing data security breach notifications to supervisory authorities and affected individuals under tight timescales; and implementing security and confidentiality measures. Supervisory authorities in the different EU member states and the UK may interpret the GDPR and national laws differently and impose additional requirements. Guidance on implementation and compliance practices are often updated or otherwise revised. All of this adds to the complexity of processing personal information and remaining compliant with the GDPR.

The GDPR allows EU and UK supervisory authorities to impose penalties for non-compliance of up to the greater of EUR 20.0 million and 4% of annual worldwide gross revenue of the corporate group in question. (There are similar caps in GBP under the UK GDPR.). Supervisory authorities in the EU and UK may potentially levy such fines directly upon on the non-compliant entity and/or on the parent company of the non-compliant entity. Supervisory authorities also possess other wide-ranging powers, including conducting unannounced inspections of our facilities and system (so-called "dawn raids"), and issuing "stop processing" orders to us. Separate from regulatory enforcement actions, individuals may bring private actions (including potentially group or representative actions) against us. There is no statutory cap in the GDPR on the amount of compensation or the damages which individuals may recover.

Overall, the significant costs of GDPR compliance, risk of regulatory enforcement actions and private litigation 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 or the procedures used to administer them to patients 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.

Depending upon the country where the clinical trial is conducted, we currently hold coverages ranging from EUR 500,000 to EUR 10,000,000 per occurrence. Such coverage may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials. In addition, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. In the event insurance coverage is insufficient to cover liabilities that we may incur, it could have a material adverse effect on our business, financial condition, and results of operations.

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

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

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, Congress subsequently has extended the period over which these reductions are in effect. While President Biden previously signed legislation temporarily to eliminate this reduction through the end of 2021, a 1% payment adjustment was implemented from April 1 – June 30, 2022, and a 2% payment adjustment took effect beginning July 1, 2022. 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 118th U.S. Congress and under the Biden Administration. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Our future growth may depend, in part, on our ability to penetrate markets outside of the U.S. and Europe where we would be subject to additional regulatory burdens and other risks and uncertainties.

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

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

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

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. We may need to devote significant resources to protect against security breaches or to address problems caused by a cyber-attack or security breach. 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.

See Part I, Item 1C, *Cybersecurity*, in our Annual Report for more information regarding our cybersecurity risk management, strategy and governance.

Climate change as well as corporate responsibility initiatives, including environmental, social and governance (ESG) matters, may impose additional costs on our business and expose us to new risks.

Greenhouse gases may have an adverse effect on global temperatures, weather patterns, and the frequency and severity of extreme weather and natural disasters. Such events could have a negative effect on our business. Concern over the impact of climate change may result in new or additional legislative and regulatory requirements to reduce or mitigate the effects of climate change on the environment, which could result in increases in taxes, transportation costs and utilities, among other expenses. Moreover, natural disasters and extreme weather conditions may impact the productivity of our facilities, the ability of the patients in our clinical trials to maintain compliance with trial protocols or access clinical trial sites, the operation of our supply chain, or consumer buying patterns. The occurrence of any of these events could have a material adverse effect on our business.

ESG and sustainability initiatives continue to attract political and social attention have resulted in both existing and pending international agreements and national, regional, and local legislation, regulatory measures, reporting obligations and policy changes. There is increasing societal pressure in some of the countries in which we operate to limit greenhouse gas emissions as well as other global initiatives focused on climate change. These agreements and measures, including the Paris Climate Accord, may require, or could result in future legislation, regulatory measures or policy changes that would require operational changes, taxes, or purchases of emission credits to reduce emission of greenhouse gases from our operations, which may require the that we dedicate additional resources toward compliance with these measures and result in substantial capital expenditures. Furthermore, increasing attention on ESG matters has resulted in governmental investigations, and public and private litigation, which could increase our costs or otherwise adversely affect our business or results of operations.

In addition, organizations that provide information to investors on corporate governance and related matters have developed ratings processes for evaluating companies and investment funds based on ESG and sustainability metrics. Such ratings are used by investors to inform their investment and voting decisions. Unfavorable ESG ratings may lead to increased negative investor sentiment toward us, which could have a negative impact on the price of our securities and our access to and costs of capital. In addition, investors, particularly institutional investors, use these scores to benchmark companies against their peers and if a company is perceived as lagging, take actions to hold these companies and their boards of directors accountable. Board diversity is an ESG topic that is, in particular, receiving heightened attention by investors, stockholders, lawmakers and listing exchanges. Certain states have passed laws requiring companies to meet certain gender and ethnic diversity requirements on their boards of directors. We may face reputational damage in the event our corporate responsibility initiatives or objectives, do not meet the standards set by our investors, stockholders, lawmakers, listing exchanges or other constituencies, or if we are unable to achieve an acceptable ESG or sustainability rating from third-party rating services.

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

Risks Related to Employee Matters and Managing Our 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.

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 the 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.

Actions that we have taken or may take in the future to restructure our business in alignment with our strategic priorities may not be as effective as anticipated, may not result in cost savings to us and could disrupt our business.

In October 2023, we commenced a restructuring of our business to reprioritize our portfolio of development candidates, conserve financial resources and better align our workforce with current business needs. In June 2024, we announced the sale of the Lexington Facility and related manufacturing assets in conjunction with our broader efforts to reduce operating expenses and cash burn. In addition, in August 2024, we announced the outcome of our strategic review intended to conserve capital, streamline operations and ensure sufficient cash resources to advance multiple clinical-stage programs through potentially meaningful milestones. This restructuring, inclusive of the sale of our Lexington facility and associated employee transitions to Genezen, involved the elimination of approximately 65% of our global workforce, or approximately 300 roles across the company. We expect the Restructuring to be substantially completed by the end of 2024 with some employees continuing through second quarter 2025. We may encounter challenges in the execution of these and any future restructuring efforts, and these challenges could impact our financial results.

Although we believe that these actions will reduce operating costs, we cannot guarantee that these restructuring efforts will achieve or sustain the targeted benefits, or that the benefits, even if achieved, will be adequate to meet our long-term expectations and the needs of our business. As a result of these restructuring efforts, we will incur additional costs in the near term, including cash expenditures for employee transitions, notice periods and severance payments, costs associated with employee benefit programs and related restructuring facilitation and transaction costs. Additional risks associated with the continuing impact of these restructuring efforts include employee attrition beyond our intended reduction in force and adverse effects on employee morale (which may be exacerbated by actual or perceived declining value of equity awards), diversion of management attention, adverse effects to our reputation as an employer (which could make it more difficult for us to hire and retain new employees in the future), potential understaffing and potential failure or delays to meet development targets due to the loss of qualified employees or other operational challenges. If we do not realize the expected benefits of our restructuring efforts on a timely basis or at all, our business, results of operations and financial condition could be adversely affected.

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 31, 2024 the sale price of our ordinary shares ranged from a high of $82.49 to a low of $3.73. The closing price on October 31, 2024 was $5.72 per ordinary share.

In recent years, the stock market in general and the market for shares of smaller biopharmaceutical companies in particular have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. 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 and market reaction to our interim data from clinical trials;
- public perception of gene therapy;
- interactions with the FDA on the design of our clinical trials and regulatory endpoints;
- regulatory delays and greater government regulation of potential products due to adverse events;
- regulatory or legal developments in the EU, the U.S., and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- changes to our business, including pipeline reprioritizations and restructurings;
- 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;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

Following periods of such market volatility, securities class actions have been brought against companies experiencing such volatility in the price of their securities. Because of the potential volatility of our ordinary share price, we may become the target of securities litigation in the future. In addition, notwithstanding protective provisions in our articles of association and available to us under Dutch corporate law, market volatility may lead to increased shareholder activism if we experience a market valuation that activist investors believe is not reflective of the intrinsic value of our ordinary shares. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition. Securities litigation or shareholder activism could result in substantial costs and divert management’s attention and resources from our business.

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 25.9% of our issued share capital (including such shares to be issued upon the exercise options to purchase ordinary shares) as of September 30, 2024. 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 shareholders, if they choose to act together, could control the election of the board of 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.

Under Dutch law, various protective measures are possible and permissible within the boundaries set by Dutch statutory and case law. 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:

- the staggered three-year terms of our non-executive directors as a result of which only approximately one-third of our non-executive directors may be subject to election or re-election in any one year;

- a provision that our directors may only be dismissed or suspected at a general meeting of shareholders by a two-thirds majority of votes cast representing more than half of our outstanding ordinary shares;
- a provision that our executive directors may only be appointed upon binding nomination of the non-executive directors, which can only be overruled by the general meeting of shareholders with a two-thirds majority of votes cast representing at least 50% of our outstanding ordinary shares; 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.

Moreover, according to Dutch corporate law, our board can invoke a cooling-off period of up to 250 days in the event of an unsolicited takeover bid or certain shareholder activism. During a cooling-off period, our general meeting of shareholders would not be able to dismiss, suspend or appoint directors (or amend the provisions in our articles of association dealing with those matters) except at the proposal of our board.

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

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

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

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

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

A corporation organized outside the U.S. generally will be classified as a passive foreign investment company ("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. Based on our average value of our gross assets, our cash and cash equivalents as well as the price of our ordinary shares, we expect to be classified as a PFIC for U.S. federal income tax for 2023. Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will continue to qualify as a PFIC in future taxable years. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate, and may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were considered a PFIC for the current taxable year or any future taxable year, a U.S. holder would be required to file annual information returns for such year, whether the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year. In certain circumstances a U.S. holder may be able to make certain tax elections that would lessen the adverse impact of PFIC status; however, to make such elections the U.S. holder will usually have to have been provided information about the company by us, and we do not intend to provide such information.

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

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

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

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

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

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

We are a public company (*naamloze vennootschap*) organized under the laws of the Netherlands and 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, it is possible that some of these parties will have interests that are different from, or in addition to, your interests as a shareholder, and our directors may take actions that would be different than those that would be taken by a company organized under the law of some U.S. jurisdictions.

In addition, in accordance with our articles of association, approval of our shareholders is required before our board of directors can authorize the issuance of our ordinary shares in an equity financing. Our shareholders' reluctance to approve such further issuances of ordinary shares could adversely affect our ability to raise capital and fund development programs and continued operations. There can be no assurance that Dutch law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the U.S., which could adversely affect the rights of investors.

We may be adversely affected by unstable market and economic conditions, such as inflation, which may negatively impact our business, financial condition and stock price.

Market conditions such as inflation, volatile energy costs, geopolitical issues, war, unstable global credit markets and financial conditions could lead to periods of significant economic instability, diminished liquidity and credit availability, diminished expectations for the global economy and expectations of slower global economic growth going forward. Our business and operations may be adversely affected by such instability, including any such inflationary fluctuations, economic downturns, volatile business environments and continued unstable or unpredictable economic and market conditions. Inflation in particular has the potential to adversely affect our liquidity, business, financial condition, and results of operations by increasing our overall cost structure. The existence of inflation in the economy has resulted in, and may continue to result in, higher interest rates and capital costs, shipping costs, supply shortages, increased costs of labor, weakening exchange rates and other similar effects. As a result of inflation, we have experienced, and may continue to experience, cost increases across our business. Although we may take measures to mitigate the impact of this inflation, if these measures are not effective our business, financial condition, results of operations and liquidity could be materially adversely affected. Even if such measures are effective, there could be a difference between the timing of when these beneficial actions impact our results of operations and when cost inflation is incurred.

Any such volatility and disruptions may have adverse consequences on us or the third parties on whom we rely. If economic and market conditions deteriorate or do not improve, it may make any future financing efforts more difficult to complete, more costly and more dilutive to our shareholders. Additionally, due to our volatile industry and industry-wide declining stock values, investors may seek to pursue non-biotech investments with steadier returns. Failure to secure any necessary financing in a timely manner or on favorable terms could have a material adverse effect on our operations, financial condition or stock price or could require us to delay or abandon development or commercialization plans.

If securities or industry analysts cease to publish or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrades our common shares or publishes inaccurate or unfavorable research about our business, our share price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our shares could decrease, which might cause our share price and trading volume to decline.

If we do not achieve our projected development and financial 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.

We estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, along with financial and other business-related milestones. From time to time, we publicly announce the expected timing of some of these milestones along with guidance as to our cash runway. These milestones may include the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings and interactions with regulatory authorities, and approval timelines for commercial sales. All these milestones are based on a variety of assumptions that may prove to be untrue. The timing of our actual achievement 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 development and commercialization of our products may be delayed, our business could suffer reputational harm and, as a result, our stock price may decline.

Item 2. Unregistered Sales of Equity Securities, Use of Proceeds, and Issuer Purchases of Equity Securities

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

During the three months ended September 30, 2024, the following officer adopted a " Rule 10b5-1 trading arrangement" (as defined in Item 408(a) of Regulation S-K) that is intended to satisfy the affirmative defense of Rule 10b5-1(c) under the Exchange Act and our policies on insider trading:

Name & Title	Date Adopted[(1)]	Aggregate Number of Ordinary Shares to be Purchased or Sold Pursuant to Trading Arrangement	Expiration Date[(2)]
Matthew Kapusta	August 12, 2024	200,000	August 25, 2025

Mr. Kapusta's Rule 10b5-1 trading arrangement relates exclusively to options to purchase ordinary shares scheduled to expire in the near-term, including 100,000 options scheduled to expire on January 1, 2025 (with an exercise price of $14.71) and 100,000 options schedule to expire on August 25, 2025 (with an exercise price of $23.60).

(1) Date of adoption of this Rule 10b5-1 trading arrangement is in accordance with applicable SEC rules and regulations. The first trade pursuant to this Rule 10b5-1 trading arrangement will be, in accordance with applicable SEC rules and regulations, on a date after the date of adoption of the Rule 10b5-1 trading arrangement, to the extent triggered under its terms.

(2) The Rule 10b5-1 trading arrangement permits transactions through and including the earlier to occur of (a) the completion of all sales or (b) the date listed in the table. The arrangement also provides for automatic expiration in the event of bankruptcy, insolvency, death or mental incapacity of the adopting person.

Other than those disclosed above, none of our directors or officers adopted, modified, or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," in each case as defined in Item 408 of Regulation S-K, during the nine months ended September 30, 2024.

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*	Certification of Chief Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities and Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities and Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
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, 2024, filed with the Securities and Exchange Commission on November 5, 2024, 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, 2024, filed with the Securities and Exchange Commission on November 5, 2024, 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)

Date: November 5, 2024

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 5, 2024

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 5, 2024

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, 2024, 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 5, 2024

By: /s/ CHRISTIAN KLEMT

Christian Klemt
Chief Financial Officer
(Principal Financial Officer)

November 5, 2024

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.