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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 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
(Jurisdiction of incorporation or organization)

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

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

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

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Ordinary shares, par value €0.05 per share	QURE	The Nasdaq Stock Market LLC (The Nasdaq Global Select Market)

Securities registered under Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the voting and non-voting ordinary shares held by non-affiliates of the registrant, computed by reference to the closing price on the Nasdaq Global Select Market as of the last business day of the registrant's most recently completed second fiscal quarter, was approximately $218.15 million.

As of February 24, 2025, the registrant had 54,076,880 ordinary shares, par value €0.05, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for its 2025 Annual Meeting of Shareholders to be filed with the Securities and Exchange Commission no later than April 30, 2025 and are herein incorporated by reference in Part III of this Annual Report on Form 10-K.

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SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K 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 involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. These forward-looking statements include, without limitation, 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; the success of our collaborations with third parties; our ability to identify and develop new product candidates and technologies; our intellectual property position; our commercialization, marketing and manufacturing capabilities and strategy; our ability to identify, recruit and retain key personnel; our financial performance; developments and projections relating to our competitors in the industry; and our liquidity and working capital requirements.

Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, such 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, without limitation, the clinical results and the development and timing of our programs, which may not support further development of our product candidates; actions of regulatory authorities, which may affect the initiation, timing and progress of clinical trials and regulatory submissions; our ability to continue to build and maintain the company infrastructure and personnel needed to achieve our goals; our effectiveness in managing current and future clinical trials and regulatory processes; the continued development and acceptance of gene therapies; our ability to demonstrate the therapeutic benefits of our gene therapy candidates in clinical trials; our ability to obtain, maintain and protect intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; our ability to fund our operations and to raise additional capital as needed; competition from others developing therapies for similar uses; the impact of global economic uncertainty, inflation, interest rates or market disruptions on our business; those factors discussed in Part I, Item 1A "Risk Factors" in this Annual Report on Form 10-K, as well as other factors which may be identified from time to time in our other filings with the Securities and Exchange Commission ("SEC"), 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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.

Summary Risk Factors

An investment in our ordinary shares involves risks. You should consider carefully the following risks, which are discussed more fully in "Item 1.A. Risk Factors", and all of the other information contained in this Annual Report on Form 10-K before investing in our ordinary shares. These risks include, but are not limited to, the following:

- We are dependent on the success of our lead product candidate, AMT-130, for the treatment of Huntington's disease. A failure of AMT-130 in clinical development, including inability to demonstrate sufficient safety or efficacy, or challenges associated with its regulatory approval, manufacturing or commercialization 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.
- If we are unable to successfully commercialize our product candidates or experience significant delays in doing so, our business could be materially harmed.
- Any approved gene therapy we seek to commercialize 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.
- Interim or preliminary results from our clinical trials may change as more data become available, as such data are subject to regulatory audit and verification procedures, and regulatory review, which could result in material changes in the final results and conclusions.
- We cannot predict when or if we will obtain marketing approval to commercialize our product candidates.
- The risks associated with the marketing approval process are heightened by the status of our products as gene therapies.
- We may leverage certain specialized regulatory pathways and designations, such as the FDA's accelerated approval pathway and RMAT designation, to develop our product candidates or to seek licensure. Even if one or more of our product candidates receives such a designation or is permitted to pursue such a pathway, we may be unable to obtain and maintain the benefits associated with such designations and pathways.
- Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage the public perception of our product candidates or adversely affect our ability to conduct our business or obtain marketing approvals for our product candidates.
- Our business development and strategic initiatives, including divestitures such as the Lexington Transaction, acquisitions, partnerships, collaborations or other transactions, may not achieve their intended benefits or goals and may result in additional risks to our business.
- We may not be successful in obtaining rights from external parties to new product candidates and key technologies, or in securing partnerships to support the development or commercialization of our product candidates.
- The Lexington Transaction may not yield the benefits that we expect and may result in additional risks to our business, including those related to Genezen's ability to manufacture HEMGENIX in accordance with regulatory requirements and to meet CSL Behring's supply requirements for commercial product.
- Gene therapies are complex, expensive and difficult to manufacture. 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.
- The manufacturing of our products and product candidates is subject to significant government regulations and approvals. We currently rely and expect to continue to rely on third parties to manufacture our product candidates, and these third parties may not perform satisfactorily or may fail to comply with these regulations or maintain these approvals.
- We had net losses in the years ended December 31, 2024 and 2023, have incurred significant losses in previous years and expect to incur losses in the future, and may never achieve or maintain profitability.

- There may be future changes in legal and regulatory requirements that may materially impact our results of operations.
- The market price of our ordinary shares has been and may in the future be volatile and fluctuate substantially
- We will need to raise additional funding in order to advance the development of our product candidates and support the commercial launch of AMT-130, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations, which could have a material adverse effect on our business, financial condition, results of operations and cash flows.
- Our future success depends on our ability to retain key executives, technical staff, and other employees and to attract, retain and motivate qualified personnel.
- We face substantial competition, and others may discover, develop, or commercialize competing products before or more successfully than we do.

Part I

Unless the context requires otherwise, references in this report to "uniQure," "Company," "we," "us" and "our" and similar designations refer to uniQure N.V. and our subsidiaries.

Item 1. Business.

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 ("ALS") caused by mutations in superoxide dismutase 1 ("SOD 1"), refractory mesial temporal lobe epilepsy ("mTLE"), and Fabry disease.

Recent Product Candidate Developments

Huntington's disease program (AMT-130)

RMAT Designation

In June 2024, we announced that the U.S. Food and Drug Administration ("FDA") granted us 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 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 these 24-month clinical data to a non-concurrent criteria-matched natural history cohort.

Updated Interim Data

In July 2024, we announced updated interim clinical data, including up to 24 months of follow-up data from 29 patients enrolled in the U.S. study and the European study as of a March 31, 2024 cut-off date.

As summary of key observations from the July 2024 interim update is set forth below.

- A statistically significant, dose-dependent, slowing in disease progression measured by composite Unified Huntington's Disease Rating Scale ("cUHDRS") was observed through 24 months in patients receiving the high dose of AMT-130.
- 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.
- Based on data observed as of the July 2024 update, AMT-130 remained generally well-tolerated, with a manageable safety profile at both high and low doses. There were no new AMT-130-related serious adverse events reported.

Regulatory Alignment

In December 2024, following our initial Type B meeting, we announced that we had reached agreement with FDA on key elements of an Accelerated Approval pathway for AMT-130. In correspondence leading up to and following the Type B meeting, FDA agreed that data from the ongoing Phase I/II studies of AMT-130, compared to a natural history external control, may serve as the primary basis for a Biologics License Application, ("BLA"), submission under FDA's accelerated approval pathway. The FDA also agreed that cUHDRS may be used as an intermediate clinical endpoint and that reductions in NfL measured in CSF may serve as supportive evidence of therapeutic benefit in the application for such accelerated approval.

We have initiated BLA-readiness activities and plan to have additional interactions with the FDA to discuss the primary statistical analysis plan and chemistry, manufacturing, and controls ("CMC") requirements for a BLA submission. In addition, we plan to initiate regulatory interactions with the European Medicines Agency ("EMA") in the first half of 2025.

Other clinical candidates

In November 2024, we announced that the that the first patient was dosed in the GenTLE Phase I/IIa clinical trial of AMT-260 for the treatment of refractory mTLE. In addition, the FDA recently approved a protocol amendment expanding the inclusion criteria for certain patients in the first cohort to include patients with non-lesional mesial temporal lobe epilepsy in the non-dominant hemisphere.

In August 2024, we announced that the first patient had been dosed in a Phase I/IIa clinical trial of AMT-191 for the treatment of Fabry disease.

In October 2024, we announced the first patient had been dosed in a Phase I/IIa clinical trial of AMT-162 for the treatment of SOD1-ALS.

Other Business Developments

Sale of commercial manufacturing activities

In June 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 and operations in Lexington, Massachusetts ("Lexington Transaction"). The Lexington Transaction closed in July 2024 ("Closing"). In connection with the Closing, Genezen extended offers of employment to a significant majority of our employees located at the Lexington facility and our Chief Executive Officer, Matthew Kapusta, joined the board of directors of Genezen.

At the Closing, we entered into a commercial supply agreement ("CSA") with Genezen for the commercial manufacture of HEMGENIX®. Pursuant to the CSA, Genezen manufactures and supplies CSL Behring's commercial demand for HEMGENIX® on our behalf. 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.

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.

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

Organizational restructuring

In August, 2024, we announced a global organizational restructuring (the "Restructuring"). These actions were the outcome of a comprehensive review of our operations with the goals of conserving capital and streamlining the organization. As a result of the Restructuring and the Lexington Transaction, we eliminated approximately 300 positions or 65% of our workforce. We substantially completed the Restructuring at the end of 2024. We have incurred $5.2 million employee severance costs in the year ended December 31, 2024 and estimate that we will incur additional costs in the range of $0.5 million to $1.0 million in 2025.

Hercules loan repayment and amendment

In connection with the July 2024 closing of the Lexington Transaction we and Hercules amended our existing term loan facility whereby 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 in January 2027.

Financing

In January 2025, we received net proceeds of $70.1 million, after deducting underwriting discounts and commissions and other offering expenses payable by us, through a follow-on public offering of 4.4 million ordinary shares at a public offering price of $17.00 per ordinary share. In February 2025, we received an additional $10.6 million in net proceeds upon the underwriters' exercise of their option to purchase an additional 0.7 million ordinary shares at the public offering price.

We expect that net proceeds and our existing cash, cash equivalents and investments will be sufficient to fund our operating expenses and capital requirements into the second half of 2027.

Our Mission and Strategy

Our mission is to deliver curative, one-time administered genomic medicines that transform the lives of patients. We aim to build an industry-leading, fully integrated, and global company that leverages its technology and proprietary manufacturing platform to deliver these medicines to patients with serious unmet medical needs. Our strategy to achieve this mission is to:

Advance the development and commercialization of AMT-130, a potential one-time gene-therapy approach for the treatment of Huntington's disease. AMT-130 is the first AAV-based gene therapy for the treatment of Huntington's disease to have entered into clinical development. In November 2024, we aligned with the FDA on core elements of an Accelerated Approval pathway for AMT-130. In 2025, we intend to further engage with the FDA regarding a potential BLA submission and to initiate discussions with EMA regarding the registrational pathway for AMT-130. We also intend to initiate commercial planning and readiness activities in the U.S. in anticipation of a potential Accelerated Approval.

Advance our pipeline of clinical-stage gene therapy candidates. We have dosed the first patients in the clinical studies of our product candidates for the treatment of MTLE (AMT-260), SOD1-ALS (AMT-162), and Fabry disease (AMT-191). We intend to complete enrollment and generate clinical data to assess the safety, tolerability and potential efficacy of these product candidates.

Develop next-generation delivery and cargo technologies. We are developing technologies that have the potential to augment the safety and efficacy of our product candidates and broaden the applicability of our gene therapies to a wider range of diseases and patients. These technologies include next-generation delivery approaches, such as smart AAV capsids potentially capable of improved central nervous system ("CNS") transduction and crossing the blood-brain barrier, as well as novel cargo technologies such as miQURE, our one-time administered gene silencing platform, linkQURE to combine multiple miRNAs to suppress different genes, and goQURE for simultaneous silencing of a disease gene and replacement with a healthy gene.

Central Nervous System Diseases

Huntington's Disease

Huntington's Disease

Huntington's disease is a severe genetic neurodegenerative disorder causing loss of muscle coordination, behavioral abnormalities, and cognitive decline, often resulting in complete physical and mental deterioration over a 12 to 15-year period. The median survival time after onset is 15 to 18 years (range: 5 to >25 years). Huntington's disease is caused by an inherited defect in a single gene that codes for a protein called Huntingtin ("HTT"). The estimated prevalence of Huntington's disease is three to seven per 100,000 in the general population, similar in men and women, and it is therefore considered a rare disease. Huntington's disease mutation carriers can be identified decades before onset. There is currently no available therapy that can delay onset or slow progression of the disease. Although some symptomatic treatments are available, they only are transiently effective despite significant side effects.

Our Development of AMT-130 for Huntington's Disease

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.

Our goal for AMT-130 is to develop a gene therapy with the following profile:

(1) one-time administration of disease-modifying therapy into the striatum, the area of the brain where Huntington's disease is known to manifest;
(2) biodistribution of the therapy in both the deep and cortical structures of the brain via transport of the AAV vector and through secondary exosome-mediated delivery; and
(3) safe, on-target and durable knockdown of HTT and exon 1 HTT.

We are currently conducting a multi-center randomized, controlled Phase I/II clinical trial for AMT-130 in the United States ("U.S. study"), as well as an open-label Phase Ib/II study in Europe ("European study") with the same early-manifest criteria for Huntington's disease as the U.S. study.

We completed the enrollment of all 26 patients in the first two cohorts of the U.S. study in March 2022 and the enrollment of 13 patients in the two cohorts of the European study in June 2023. In the U.S. study, 26 patients with early manifest Huntington's disease were randomized to treatment (six low-dose patients, 10 high-dose patients) or an imitation (sham) surgical procedure (10 patients). The U.S. study consists of a blinded 12-month core patient study period followed by an unblinded long-term follow-up period of five years. Four imitation surgery patients from the U.S. study crossed over to treatment ("Crossover patients"). In the European study, 13 patients were enrolled and treated with AMT-130 (six low-dose patients and seven high-dose patients).

As of February 2025, we have enrolled 12 patients across the U.S. and the U.K. into a third cohort to further investigate both doses of AMT-130 together with perioperative immunosuppression using the current, established stereotactic administration procedure. The focus of this third cohort is to evaluate the near-term safety and tolerability.

In July 2024, we announced updated interim clinical data including up to 24 months of follow-up data from 29 patients enrolled in the U.S. study and the European study as of a March 31, 2024 cut-off date. 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 a propensity-weighted external control developed in collaboration with the Cure Huntington's Disease Initiative 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. Measures of statistical significance in this analysis were based on nominal p values and are unadjusted.

A summary of key observations related to efficacy from the July 2024 interim update is set forth below:

- A statistically significant, dose-dependent, slowing in disease progression measured by 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 cUHDRS 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 NfL in 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 well-characterized biomarker of neurodegeneration that has been shown to be strongly 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 19 patients with early manifest Huntington's disease.

Safety and tolerability

We believe AMT-130 was generally well-tolerated, with a manageable safety profile in patients treated with the lower dose of $6x10^{12}$ vector genomes and the higher dose of $6x10^{13}$ vector genomes. The most common adverse events in the treatment groups were related to the surgical procedure.

There were four serious adverse events (SAE) unrelated to AMT-130 (post-operative delirium, major depression, suicidal ideation and epistaxis) in the low-dose cohort, six unrelated SAEs in the high-dose cohort (back pain, hypothermia, post procedural hematoma, post-lumbar puncture syndrome (n=2), pulmonary embolism), and one SAE (deep vein thrombosis) in the control group. In addition, there were four AMT-130-related SAEs in the high-dose cohort (central nervous system inflammation (n=3), and severe headache (n=1) that, retrospectively, also was attributable to central nervous system inflammation.

Patients with symptomatic central nervous system inflammation improved with glucocorticoid medication. Additionally, six high-dose patients have received preoperative steroids with the administration of AMT-130 to reduce the risk of inflammation.

Temporal Lobe Epilepsy Program (AMT-260)

Temporal Lobe Epilepsy Disease and Market Background

TLE affects approximately 1.0 million people in the U.S. and E.U. alone, of which approximately 0.3 million U.S. patients are inadequately treated through anti-seizure medications and are considered refractory. 240,000 of U.S. refractory TLE patients have a lesion in the mesial temporal lobe (hippocampus), which is expressed as sclerosis, atrophy or scarring. Mesial TLE ("MTLE") is often caused by brain injury, infections or prolonged febrile seizures which can lead to hyperexcitability of the hippocampus and repeated seizures which can further damage the hippocampus over time. Refractory MTLE patients have a poor quality of life and a reduced lifespan. Surgical treatment for refractory patients is lobectomy or laser tissue ablation but only 1-2% of eligible patients undergo surgery.

Our Development of AMT-260 for Temporal Lobe Epilepsy

In July 2021, we acquired uniQure France SAS ("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 SAS obtained following its formation in 2019 from two French research institutions.

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. The use of AAV9 to deliver any sequence that affects the expression of the GRIK2 gene in humans has been exclusively licensed from Regenxbio Inc ("Regenxbio").

In September 2023 we announced that the FDA had cleared the IND application for AMT-260.

We initiated a Phase I/IIa clinical trial that is being 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 data. 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.

In November 2024 we announced that the first patient had been dosed in the GenTLE Phase I/IIa clinical trial of AMT-260 for the treatment of mTLE. In addition, the FDA recently approved a protocol amendment expanding the inclusion criteria for certain patients in the first cohort to include patients with non-lesional mesial temporal lobe epilepsy in the non-dominant hemisphere.

Amyotrophic Lateral Sclerosis ("ALS")

ALS Disease and Market Background

ALS commonly known as Lou Gehrig's disease, is a progressive and fatal neuromuscular disease with the majority of ALS patients dying within 2 to 5 years of receiving a diagnosis. Familial ALS, a hereditary form of the disease, accounts for 5-10% of cases, whereas the remaining cases (sporadic ALS) have no clearly defined etiology. ALS affects persons of all races and ethnicities; however, persons of certain demographics (Caucasians, males, non-Hispanics and persons aged 60 years or older) and those with a family history of ALS are more likely to develop the disease.

ALS affects approximately 17,800 to 31,800 adults in the U.S. and a similar number of adults in Europe. Evidence from prevalence studies suggests that prevalence and incident rates can vary significantly between regions and ethnicities. Most cases are sporadic ("sALS") but approximately 10% are found to have a familial, i.e., dominant genetic causation ("fALS"). fALS can be caused by mutations in various genes including chromosome 9 open reading frame 72, SOD1, tyrosyl-DNA phosphodiesterase 2 and others.

One genetic mutation that causes ALS are pathogenic mutations in the superoxide dismutase enzyme 1("SOD1"). SOD1 is an enzyme that that is responsible for catalyzing toxic superoxide to hydrogen peroxide and dioxygen. While the exact mechanism for disease is not known, it is believed that a toxic gain of function in SOD1 results in oxidative stress and cell death of motor neurons. More than 100 pathogenic SOD-1 have been identified. Mutations are concentrated in a few regions of the protein. Mutations can be both dominant and recessive. Most common mutations occur in the D90A, G93A, A4H and D46R genes.

Patients with different mutations progress at different rates. It is estimated that there are approximately 300 incident cases per year in the U.S. and Europe.

Our Development of AMT-162 for ALS – SOD1

In January 2023 we announced that we entered into a global licensing agreement with Apic Bio for a novel, one-time, intrathecally administered gene therapy for ALS caused by SOD1 mutations (formerly APB-102). The FDA has cleared the IND for APB-102 and has granted it Orphan Drug and Fast Track designation. APB-102 is comprised of a recombinant AAVrh10 vector that expresses a miRNA designed to knock down the expression of SOD1 with the goal of slowing down or potentially reversing the progression of ALS in patients with SOD1 mutations. 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 had been dosed in a Phase I/IIa clinical trial of AMT-162 ("EPISOD1") for the treatment of SOD1-ALS. In January 2025, we announced that the independent data monitoring committee had recommended to proceed with enrollment of the second cohort after a review of the 28-day safety data from the first cohort.

EPISOD1 is a Phase I/II multi-center, open-label trial of AMT-162 for the treatment of SOD1-ALS being conducted in the United States consisting of three dose-escalating cohorts with up to four patients each receiving a short course of immunosuppression prior to and after an intrathecal infusion of AMT-162. The trial will explore the safety and tolerability of AMT-162 and will assess exploratory signs of efficacy by measuring neurofilament light chain, a biomarker of neuronal damage, and SOD1 protein. Additional details are available on www.clinicaltrials.gov (NCT06100276).

Liver-directed diseases

Hemophilia B (HEMGENIX® or etranacogene dezaparvovec)

Hemophilia B Disease and Market Background

Hemophilia B is a rare, lifelong bleeding disorder caused by a single gene defect, resulting in insufficient production of factor IX, a protein primarily produced by the liver that helps blood clots form. Treatments for moderate to severe hemophilia B include prophylactic infusions of factor IX replacement therapy to temporarily replace or supplement low levels of blood-clotting factor and, while these therapies are effective, those with hemophilia B must adhere to strict, lifelong infusion schedules. They may also still experience spontaneous bleeding episodes as well as limited mobility, joint damage or severe pain as a result of the disease. For appropriate patients, HEMGENIX® allows people living with hemophilia B to produce their own factor IX, which can lower the risk of bleeding.

CSL Behring collaboration

In June 2020, we entered into the CSL Behring Agreement pursuant to which CSL Behring received exclusive global rights to HEMGENIX®. The transaction became fully effective in May 2021. Unless earlier terminated as described below, the CSL Behring Agreement will continue on a country-by-country basis until expiration of the royalty term in a country. The royalty term expires in a country on the later of (a) 15 years after the first commercial sale of the Product in such country, (b) expiration of regulatory exclusivity for the Product in such country and (c) expiration of all valid claims of specific licensed patents covering the Product in such country. Either we or CSL Behring may terminate the CSL Behring Agreement for the other party's material breach if such breach is not cured within a specified cure period. In addition, if CSL Behring fails to commercialize the Product in any of a group of major countries for an extended period of time following the first regulatory approval of the Product in any of such group of countries (other than due to certain specified reasons) and such failure has not been cured within a specified cure period, then we may terminate the CSL Behring Agreement. CSL Behring may also terminate the CSL Behring Agreement for convenience.

We and CSL Behring also entered into a development and commercial supply agreement, pursuant to which, among other things, we will supply the Product to CSL Behring. We are contractually obligated to supply the Product until such time that these capabilities are transferred to CSL Behring or its designated contract manufacturing organization. On September 6, 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 designated by CSL Behring.

Fabry disease program (AMT-191)

Fabry Disease and Market Background

Fabry disease is a progressive, inherited, multisystemic lysosomal storage disease characterized by specific neurological, cutaneous, renal, cardiovascular, cochleo-vestibular, and cerebrovascular manifestations. Fabry disease is caused by a defect in a gene that encodes for a protein called α-galactosidase A ("GLA"). The GLA protein is an essential enzyme required to breakdown globotriaosylsphingosine ("Gb3") and lyso-globotriaosylsphingosine ("lyso-Gb3"). In patients living with Fabry disease, Gb3 and lyso-Gb3 accumulate in various cells throughout the body causing progressive clinical signs and symptoms of the disease. Current treatment options, which consist of bi-weekly intravenous enzyme replacement therapy, typically have no therapeutic benefit in patients with advanced renal or cardiac disease. Studies have also shown that a majority of male patients develop antibodies that inhibit the GLA protein and interfere with therapeutic efficacy.

Fabry disease has two major disease phenotypes: the type 1 “classic” and type 2 “later-onset” subtypes. Both lead to renal failure, and/or cardiac disease, and early death. Type 1 males have little or no functional a-Gal A enzymatic activity (<1% of normal mean) and marked accumulation of GL-3/Gb3 and related glycolipids in capillaries and small blood vessels which cause the major symptoms in childhood or adolescence. In contrast, males with the type 2 “later-onset” phenotype (previously called cardiac or renal variants) have residual a-Gal A activity, lack GL-3/Gb3 accumulation in capillaries and small blood vessels, and do not manifest the early manifestations of type 1 males. They experience an essentially normal childhood and adolescence. They typically present with renal and/or cardiac disease in the third to seventh decades of life. Most type 2 later-onset patients have been identified by enzyme screening of patients in cardiac, hemodialysis, renal transplant, and stroke clinics and recently by newborn screening. Fabry disease occurs in all racial and ethnic populations and affects males and females. It is estimated that type 1 classic Fabry disease affects approximately one in 40,000 males and approximately one in 20,000 females. The type 2 later-onset phenotype is more frequent, and in some populations may occur as frequently as about 1 in 1,500 to 4,000 males.

Our Development of AMT-191 for Fabry Disease

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 FDA had cleared the investigation new drug application (“IND”) for AMT-191. We are conducting a Phase I/IIa clinical trial in the United States. The multicenter, open-label clinical trial consists of two dose-escalating cohorts of three patients each to assess safety, tolerability, and efficacy of AMT-191 in patients with Fabry disease. Three patients will be dosed in the initial dose. If no dose-limiting toxicology is identified, the dose will be escalated. If dose-limiting toxicology occurs in one of the three initial patients, three additional patients will be enrolled at the same dose level. If no additional patients in the cohort experience a dose-limiting toxicology, the dose will be escalated. Assessments will be made at three- and six-months post-treatment.

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.

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

In February 2025, we announced the completion of enrollment in the first cohort of the Phase I/IIa trial. Additionally, the Independent Data Monitoring Committee reviewed safety data from the initial two patients enrolled in the first cohort. The IDMC’s review did not identify any significant safety concerns and recommended proceeding with enrollment in the second cohort.

New Technology Development

We are seeking to develop next-generation technologies with the goal of further improving the potential of AAV-based gene therapies to treat patients suffering from debilitating diseases. We are focused on innovative technologies across each of the key components of an AAV-based gene therapy, including: (i) the capsid, or the outer viral protein shell that encloses the target deoxyribonucleic acid (“DNA”); (ii) the cargo, including the transgene or therapeutic gene, and promoters, or the DNA sequence that drives the expression of the transgene; and (iii) administration techniques.

We dedicate significant effort to designing and screening novel AAV capsids with the potential for (i) higher biological potency; (ii) improved biodistribution including greater cell transduction and increased cellular specificity; (iii) enhanced safety; and (iv) manufacturing efficiency. We believe we have significant expertise in vector engineering and have created promising genetically engineered capsids using both rational and directed evolution approaches.

We have also demonstrated the ability to deliver engineered DNA constructs that can silence or suppress disease-causing genes. Our miQURE gene silencing platform, based on exclusively licensed technology from Cold Spring Harbor Laboratory ("CSHL"), is designed to degrade mutated genes without off-target toxicity and induce silencing of the mutated gene in the entire target organ through secondary exosome-mediated delivery. miQURE-based gene therapy candidates, such as AMT-130, incorporate proprietary, therapeutic miRNA constructs that can be delivered using AAVs to potentially provide long-lasting activity. Preclinical studies of miQURE-based gene therapies have demonstrated several important advantages, including enhanced tissue-specificity, improved nuclear and cytoplasmic gene lowering and no off-target effects associated with impact to the cellular miRNA or messenger RNA transcriptome. The existing miQURE gene silencing strategy was expanded by linking several miRNA molecules in a single construct, resulting in the new linQURE platform.

Our Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including by seeking and maintaining patent protection in the U.S., Europe, and other jurisdictions for novel components of our gene therapies, the chemistries of and processes for manufacturing these gene therapies, the use of these components in gene therapies, our technology platform, and other inventions and related technology. We also rely on trade secrets, security measures and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We expect that our probability of success will be significantly enhanced by our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of AAV-based gene therapies.

In some cases, we are dependent on the patented or proprietary technology of third parties to develop and commercialize our products. We must obtain licenses from such third parties on commercially reasonable terms, or our business could be harmed, possibly materially. For example, we license from third parties essential parts of the therapeutic gene cassettes as well as the principal AAV vectors we use and key elements of our manufacturing process. We anticipate that we will require licenses to additional technology in the future.

Because most patent applications throughout the world are confidential for 18 months after the earliest claimed priority date, and since the publication of discoveries in the scientific and patent literature often lags actual discoveries, we cannot be certain that we were the first to invent or file applications for the inventions covered by our pending patent applications. Moreover, we may have to participate in post-grant proceedings in the patent offices of the U.S. or foreign jurisdictions, such as oppositions, reexaminations, or interferences, in which the patentability or priority of our inventions are challenged. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us. For more information regarding the risks related to our intellectual property, please see Item 1A., *Risk factors—Risks Related to Our Intellectual Property*, in this Annual Report on Form 10-K.

Our intellectual property portfolio consists of owned and in-licensed patents, copyrights, licenses, trademarks, trade secrets and other intellectual property rights.

Patent Portfolio

Our gene therapy programs are protected by patents and patent applications directed to various aspects of our technology. For example, our gene therapy programs are protected by patents and patent applications with composition of matter or method of use claims that cover the therapeutic gene, the promoter, the viral vector capsid, or other specific parts of these technologies. We also seek protection of core aspects of our manufacturing process, particularly regarding our baculovirus expression system for AAV vectors in insect cells. In addition, we have filed manufacturing patent applications with claims directed to alternative compositions of matter and manufacturing processes to seek better protection from competitors.

We file the initial patent applications for our commercially important technologies in Europe and/or the U.S. For the same technologies, we typically file international patent applications under the Patent Cooperation Treaty (PCT) within one year. After the PCT phase, we file patent applications in Europe (EPO) or the U.S., as applicable based on the jurisdiction in which we file the first patent application. We also may seek, usually on a case-by-case basis, local patent protection in Canada, Australia, Japan, China, India, Israel, South Africa, New Zealand, South Korea, and Eurasia, as well as South American jurisdictions such as Brazil and Mexico. During prosecution of the patent applications, we may file divisional applications at the EPO or divisionals or continuations in the U.S. prior to the grant or issue of the patent. For patent families which are considered particularly important, we may also file divisional applications in other jurisdictions.

As of December 31, 2024, our fully owned intellectual property portfolio included 128 issued patents (including 27 U.S. patents and 15 patents granted by the European Patent Office ("EPO")) and 127 (published) pending patent applications (including 27 U.S. patent applications and 27 patent applications pending at the EPO). These patents relate to a variety of technologies including our product candidates that are in development as well as to our manufacturing and technology platforms.

We own three published patent families directed to gene therapy treatment of Huntington's disease, including AMT-130 and its formulation. AMT-130 is a miQURE®-based gene-transcript silencing technology designed to degrade disease-causing gene transcripts without off-target toxicity while inducing silencing throughout the entire target organ through secondary exosome-mediated delivery. We co-own two patent families, and fully own one patent family, directed to gene therapy-mediated treatment of TLE, including our product candidate AMT-260. Of the two co-owned patent families, the co-owners have exclusively licensed their rights to us. Additionally, we are the exclusive licensee to two other patent families directed to the Gluk2/Gluk5 antagonists and their use in TLE. We have obtained an exclusive license to two patent families directed to gene therapy treatment of ALS, including our product candidate AMT-162. We own a patent family directed to potent liver-specific promoters, including the promoter present in our product candidate AMT-191. Additionally, we own a patent family directed to the formulation of AMT-191 for intravenous infusion.

Licenses

We have obtained exclusive or non-exclusive rights from third parties under a range of patents and other technology that we use in our product and development programs, as described below. Our agreements with these third parties generally grant us a license to make, use, sell, offer to sell, and import products covered by the licensed patent rights in exchange for our payment of some combination of an upfront amount, annual fees, royalties, a percentage of amounts we receive from our licensees and payments upon the achievement of specified development, regulatory or commercial milestones. Some of the agreements specify the extent of the efforts we must use to develop and commercialize licensed products. The agreements generally expire upon expiration of the last-to-expire valid claim of the licensed patents. Each licensor may terminate the applicable agreement if we materially breach our obligations and fail to cure the breach within a specified cure period.

Licensed Technology Used for Multiple Programs

We are exploiting technology from third-party sources described below in more than one of our programs.

Cold Spring Harbor Laboratory

In 2015, we entered into a license agreement with CSHL in which CSHL granted to us an exclusive, sublicensable license to develop and commercialize certain of CSHL's patented RNAi-related technology for use in connection with the treatment or prevention of Huntington's disease. We expanded the scope of the license agreement with CSHL in 2018 beyond Huntington's disease to include the diagnosis, treatment, or prevention of all CNS diseases in the field. Under the amended license agreement CSHL granted to us an exclusive license to develop and commercialize therapeutic products for the additional disease classifications in the field of liver diseases, neuromuscular diseases, and cardiovascular diseases, and we have subsequently added such products to our pipeline.

Under this license agreement, as amended, annual fees, development milestone payments and future single-digit royalties on net sales of a licensed product are payable to CSHL. The standard 20-year patent term for the licensed patents expires in 2031.

Protein Sciences

In 2016, we revised our existing license contract with Protein Sciences Corporation for the use of its *expresSF+* insect cell line and associated technology for human therapeutic and prophylactic uses (except influenza) to provide us with a royalty free, perpetual right and license to the technology in the field of AAV-based gene therapy.

Technology Used for Specific Development Programs

Temporal Lobe Epilepsy (AMT-260)

Regenxbio

In June 2020, uniQure France SAS entered into an agreement, subsequently amended in June 2021, with Regenxbio for an exclusive (in the field of using AAV9 to expression of the *GRIK2* gene in humans (the "Field")), sublicensable, royalty-bearing, worldwide license under Regenxbio's interest in EU patent application 19185533.7 (the "Foreground Patents") and related patents, as well as patents covering inventions developed during the collaboration and certain patents and know-how relating to AAV9. The license also includes non-exclusive rights to exploit the licensed Foreground Patents and certain related patents know-how developed in collaboration pursuant to the license agreement outside the Field. The license also includes retained and license back rights that permit Regenxbio and its upstream licensors to exploit for any research, development, commercialization, or other purposes certain patents, inventions and know-how (other than the Foreground Patents) subject to or created pursuant to the license agreement.

Payment obligations under the agreement provide for royalty payments on net sales in the mid-single digit to low-double digits, and milestone payments to Regenxbio in the mid-tens of millions of dollars related to clinical trials, commercialization, and net sales. The agreement also calls for sublicense fees in the low-double digit range. The royalty is paid on sales of license products using any of licensed patents or know-how for as long as the agreement is in effect. Royalty and milestone payments may continue to be owed under the license following termination of the agreement if licensed products are sold following termination of the license. Under the agreement, uniQure France SAS has certain diligence obligations and Regenxbio has certain obligations related to the pre-clinical development of manufacturing technology.

Inserm Transfert

In January 2020, uniQure France SAS entered into license agreement with Inserm Transfert SA (also acting as a delegate for the French National Institute of Health and Medical Research) and La societe SATT Aquitaine (the counterparties collectively referred to as "Inserm Transfert"). Under the license agreement, uniQure France SAS is granted an exclusive, sublicensable, royalty-bearing, worldwide license under European Patent ("EP") patent application 13306265.3 in the field of the prevention and treatment of epilepsy, and in Inserm Transfert's share in EP patent application 19185533.7 (which is co-owned by Regenxbio) in the field of all human use. uniQure France SAS also is granted a non-exclusive, sublicensable, royalty-bearing, worldwide license under certain know-how in the fields that may be developed by Inserm pursuant to the agreements. Under the agreements, Inserm retains certain rights for teaching, academic and/or research purposes.

Payment obligations under the agreements include a royalty on the net sales of license products in the low single digits, milestone payments associated with clinical trial and regulatory approval milestones of multiple licensed products totaling in the low-single digit millions of Euros. The agreement also calls for sublicense fees in the low to mid double-digit range depending on the timing of such sublicense. The obligation to pay royalties extends until the later of the expiration of the patent rights, any regulatory exclusivity period, and 10 years from the first commercial sale of a licensed product.

Amyotrophic Lateral Sclerosis (AMT-162)

In January 2023, we announced that we had entered into a global licensing agreement with Apic Bio for a one-time, intrathecally administered investigational gene therapy for ALS caused by mutations in SOD-1, pursuant to which we acquired an exclusive global license (including a sublicense of rights granted to Apic Bio pursuant to an exclusive license agreement with a certain U.S.-based academic institution) to Apic Bio's rights under certain licensed technology to develop, manufacture, and commercialize any product incorporating a licensed construct (including APB-102, certain constructs expressing a SOD1-targeting microRNA or AAV that codes for a microRNA that silences SOD1 expression), in any dosage strength, formulation, concentration or method of delivery in the applicable field. We made an initial cash payment of $10.0 million to Apic Bio. In addition, we will pay Apic Bio up to $43.0 million in milestones upon achievement of regulatory approvals in the U.S. and Europe and pre-specified annual net sales, and a tiered royalty on net sales ranging from the mid-single digits to low double digits.

Trade Secrets

In addition to patents and licenses, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, significant aspects of the process by which we manufacture our gene therapies are based on unpatented trade secrets and know-how. We seek to protect our proprietary technology and processes and obtain and maintain ownership of certain technologies, in part, through confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial collaborator. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Trademarks

We have a number of material registered trademarks, including "uniQure", that we have registered in various jurisdictions including the U.S. and the EU. We may seek trademark protection for other product candidates and technologies as and when appropriate.

Competition

The biotechnology and pharmaceutical industries, including in the gene therapy field, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic and other research institutions and governmental agencies and public and private research institutions that are developing and commercializing pharmaceutical products that may be competitive with ours.

Our key competitors focused on developing therapies in various indications, include among others, PTC Therapeutics, Roche, Wave Life Sciences, Alnylam Pharmaceuticals, Regeneron Pharmaceuticals and Skyhawk Therapeutics (for Huntington's disease), Neurona Therapeutics and CombiGene (for TLE), Biogen, Ionis Pharmaceuticals, Neurimmune, Regeneron Pharmaceuticals, Alnylam Pharmaceuticals and Voyager Therapeutics (for ALS) and Amicus Therapeutics, Sanofi, Takeda, Chiesi, Idorsia, Sangamo Therapeutics, 4D Molecular Therapeutics, Skyline Pharmaceuticals and CANbridge (for Fabry disease).

We also compete with existing standards of care, therapies, and symptomatic treatments, as well as any new therapies and novel technologies, that may become available in the future for the indications we are targeting.

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

The key competitive factors affecting the success of all our programs are likely to be their efficacy, safety, convenience, price, and the availability of reimbursement from government and other third-party payers. We also believe that, due to the small size of the patient populations in the orphan indications we target, being first to market will be a significant competitive advantage. We believe that our advantages in vector and manufacturing technology will enable us to reach market in a number of indications ahead of our competitors, and to potentially capture the markets in these indications either by being first or in those markets with larger populations having a differentiated product.

Government Regulation and Reimbursement

Government authorities in the U.S., EU and other countries extensively regulate, among other things, the approval, research, development, nonclinical and clinical testing, manufacture (including any manufacturing changes), packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, reimbursement, and import and export of pharmaceutical products, biological products, and medical devices. We believe that all our product candidates will be regulated as biological products, or biologics, and in particular, as gene therapies, and will be subject to such requirements and regulations under U.S. and foreign laws. If we fail to comply with applicable regulatory requirements, we may be subject to, among other things, civil penalties, refusal to approve pending applications, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

Regulation in the United States

In the U.S., the FDA regulates biologics under the Public Health Service Act ("PHSA") and the Federal Food, Drug, and Cosmetic Act ("FDCA") and regulations and guidance implementing these laws. These laws and regulatory guidance are continually evolving. By example, various actions have been taken by the U.S. Congress and President over recent years with respect to drug shortage prevention and reporting, supply chain security, and the promotion of U.S. domestic manufacturing. The FDA also continually issues nonbinding guidance documents that provide the FDA's interpretation of its laws and regulations, as well as the FDA's approach to scientific issues and questions.

Obtaining regulatory approvals and ensuring compliance with applicable statutes and regulatory requirements entails the expenditure of substantial time and financial resources, including payment of user fees for applications to the FDA. All our current product candidates are subject to regulation by the FDA as biologics. An applicant seeking approval to market and distribute a new biologic in the U.S. must typically undertake the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's current Good Laboratory Practice regulations;
- submission to the FDA of an IND application which allows human clinical trials to begin unless the FDA objects within 30 days; the sponsor of an IND or its legal representative must be based in the U.S.;
- approval by an independent institutional review board ("IRB") and, for some studies, Institutional Biosafety Committee ("IBC") before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with the FDA's cGCP to establish substantial evidence of the safety and efficacy for the proposed biological product for each indication;
- preparation and submission to the FDA of a Biologics License Application ("BLA");
- satisfactory completion of one or more FDA inspections or remote regulatory assessments of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practice ("cGMP") requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity, as well as selected clinical trial sites and investigators to determine cGCP compliance;
- approval of the BLA by the FDA, in consultation with an FDA advisory committee, if deemed appropriate by the FDA; and
- compliance with any post-approval commitments, including Risk Evaluation and Mitigation Strategies ("REMS"), and post-approval studies required by the FDA.

Human Clinical Studies in the United States under an IND

Before initiating clinical studies in the U.S. or under an IND, investigational product sponsors must first complete nonclinical studies. Nonclinical studies include laboratory evaluation of chemistry, pharmacology, toxicity, and product formulation, as well as animal studies to assess potential safety and efficacy. Such studies must generally be conducted in accordance with the FDA's GLPs.

Clinical trials involve the administration of the investigational biologic to human subjects under the supervision of qualified investigators in accordance with current GCP requirements, which includes requirements for informed consent, study conduct, and IRB review and approval. Special clinical trial ethical considerations also must be considered if a study involves children. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of an IND. Sponsors will be required to provide the FDA with diversity action plans. INDs include nonclinical study reports, together with manufacturing information, analytical data, any available clinical data, or literature, and proposed clinical study protocols among other things. A clinical trial may not proceed in the U.S. unless and until an IND becomes effective, which is 30 days after its receipt by the FDA. The FDA may raise concerns or questions related to one or more components of an IND and place the IND on clinical hold if during its review the FDA determines that study subjects would be exposed to significant risk of illness or injury. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance.

The protocol and informed consent documents, as well as other subject communications must also be approved by an IRB that continues to oversee that trial. In the case of gene therapy studies, an IBC at the local level may also review and maintain oversight over the particular study, in addition to the IRB. The FDA, an IRB, and IBC, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk or that research requirements are not being met.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor that regularly reviews accumulated data and advises the study sponsor regarding the continuing safety of the trial. This group may also review interim data to assess the continuing validity and scientific merit of the clinical trial. This group receives special access to unblinded data during the clinical trial and may advise the sponsor to halt, pause, or otherwise modify the clinical trial.

Information about certain clinical trials, including results, must be submitted within specific timeframes for listing on the ClinicalTrials.gov website. Sponsors or distributors of investigational products for the diagnosis, monitoring, or treatment of one or more serious diseases or conditions must also have a publicly available policy on evaluating and responding to requests for expanded access. Investigators must also provide certain information to the clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA.

Subsequent clinical protocols and amendments must also be submitted to an active IND but are not subject to the 30-day review period imposed on an original IND. Progress reports detailing the results of the clinical trials must also be submitted at least annually to the FDA and the IRB and more frequently if serious adverse events or other significant safety information is found. There is a risk that once a new protocol or amendment is submitted to an active IND there may be an extended period before the FDA may comment or provide feedback. This may result in a need to modify an ongoing clinical trial to incorporate this feedback or even a clinical hold of the trial. There is also risk that FDA may not provide comments or feedback but may ultimately disagree with the design of the study once a BLA is submitted.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase I: The biological product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early understanding of its effectiveness.
- Phase II: The biological product is administered to a limited patient population to further identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase III: The biological product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the potency and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labelling of the product. Typically, two Phase III trials are required by the FDA for product approval. Under some limited circumstances, however, the FDA may approve a BLA based upon a single Phase III clinical study plus confirmatory evidence or a single large multicenter trial without confirmatory evidence.

Recent legislation further established a new program that may be used to facilitate future marketing applications and development programs following a first product approval. Specifically, the Consolidated Appropriations Act, 2023 established a program whereby a platform technology that is incorporated within or utilized by an approved drug or biologic product may be designated as a platform technology, provided that certain conditions are met, in which case development and approval of subsequent products using such technology may be expedited.

In addition, under the Pediatric Research Equity Act (the "PREA"), a BLA or BLA supplement for a new active ingredient, indication, dosage form, dosage regimen, or route of administration, must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Orphan products are also exempt from the PREA requirements.

The manufacture of investigational drugs and biologics for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and biologics and active ingredients and therapeutic substances imported into the U.S. are also subject to regulation by the FDA. Further, the export of investigational products outside of the U.S. is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA.

Concurrent with clinical trials, companies usually complete additional nonclinical animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, manufacturers must develop methods for testing the identity, strength, quality, potency, and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Regulation and FDA Guidance Governing Gene Therapy Products

The FDA has and continues to issue various guidance documents with respect to the development and commercialization of gene therapies. These include guidance on, among other things, the proper preclinical and nonclinical assessment of gene therapies; the chemistry, manufacturing, and controls; the design and conduct of clinical trials and product development; the design and analysis of shedding studies for virus or bacteria based gene therapies; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects and patients who have been exposed to gene therapies via long-term follow-up with associated regulatory reporting. The FDA has also issued guidance on the development of gene therapies for the treatment of neurodegenerative diseases, rare diseases, and hemophilia, as such products may face special challenges.

Certain gene therapy studies are also subject to the National Institutes of Health's Guidelines for Research Involving Recombinant DNA Molecules, ("NIH Guidelines"). The NIH Guidelines include the review of the study by an IBC. The IBC assesses the compliance of the research with the NIH Guidelines, assesses the safety of the research and identifies any potential risk to public health or the environment.

Compliance with cGMP Requirements

Manufacturers of biologics must comply with applicable cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Manufacturers and others involved in the manufacture and distribution of such products must also register their establishments with the FDA and certain state agencies and provide the FDA a list of products manufactured at the facilities. Recently, the information that must be submitted to the FDA regarding manufactured products was expanded through the Coronavirus Aid, Relief, and Economic Security (CARES) Act to include the volume of drugs produced during the prior year. Establishments may be subject to periodic unannounced inspections and remote regulatory assessments by government authorities to ensure compliance with cGMPs and other laws. Discovery of non-compliance may result in the FDA placing restrictions on a product, manufacturer, or holder of an approved BLA, and may extend to requiring withdrawal of the product from the market, recall, shutdown, enforcement letters, among other consequences. Noncompliance with the applicable manufacturing requirements may also require costly corrective and preventative actions. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are following cGMP requirements and adequate to assure consistent production of the product within required specifications.

FDA Programs to Expedite Product Development

The FDA has several programs to expedite product development, including fast track designation and breakthrough therapy designation. These are outlined in specific FDA guidance. Under the fast track program, the sponsor of a biologic candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the product candidate. To be eligible for a fast track designation, the FDA must determine that a product candidate is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. This may be demonstrated by clinical or nonclinical data. If granted, the benefits include greater interactions with the FDA and potentially rolling review of sections of the BLA. In some cases, a fast track product may be eligible for accelerated approval or priority review.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, enacted in 2012, a sponsor can request designation of a product candidate as a breakthrough therapy. A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Products designated as breakthrough therapies are potentially eligible for rolling review, as well as intensive guidance on an efficient development program beginning as early as Phase I trials, and a commitment from the FDA to involve senior managers and experienced review staff in a proactive collaborative, cross disciplinary review.

Biologics studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means the FDA may approve the product based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. A biologic candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. By the date of approval of an accelerated approval product, FDA must specify the conditions for the required post approval studies, including enrollment targets, the study protocol, milestones, and target completion dates. FDA may also require, and frequently does require, that the confirmatory Phase 4 studies be commenced prior to FDA granting a product accelerated approval. Reports on the progress of the required Phase 4 confirmatory studies must be submitted to FDA every 180 days after approval. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug or biologic from the market on an expedited basis using a statutorily defined streamlined process. Failure to conduct the required Phase 4 confirmatory studies or to conduct such studies with due diligence, as well as failure to submit the required update reports can subject a sponsor to penalties. All promotional materials for drug or biologic candidates approved under accelerated regulations are subject to prior review by the FDA. In recent years, the accelerated approval pathway has come under significant FDA and public scrutiny. Accordingly, the FDA may be more conservative in granting accelerated approval or, if granted, may be more apt to withdrawal approval if clinical benefit is not confirmed.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Submission of a BLA

The results of the nonclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls, and proposed labeling, among other things, are submitted to the FDA as part of a BLA requesting a license to market the product for one or more indications. The submission of a BLA is subject to an application user fee, though products with orphan designation are exempt from the BLA filing fee. The sponsor of an approved BLA is also subject to annual program user fees. Orphan products may also be exempt from program fees provided that certain criteria are met. These fees are typically increased annually. Under the Prescription Drug User Fee Act ("PDUFA") the FDA has agreed to specified performance goals in the review of BLAs.

Most such applications are meant to be reviewed within ten months from the filing acceptance date (typically 60 days after date of filing), and most applications for priority review products are meant to be reviewed within six months of the filing acceptance date (typically 60 days after date of filing). Priority review designation may be assigned to product candidates that are intended to treat serious conditions and, if approved, would provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of the serious condition.

The FDA may refuse to file an application and request additional information. In this event, the application must be refiled with the additional information. The refiled application is also subject to assessment of content before the FDA accepts it for review. Once the submission is accepted, the FDA begins an in-depth substantive review. The FDA will assign a date for its final decision for the product (the "PDUFA action date") but can extend this date to complete review of a product application or to consider additional information submitted during the application review period. The PDUFA action date is only a goal, thus, the FDA does not always meet its PDUFA dates.

The FDA may also refer certain applications to an advisory committee. Before approving a product candidate for which no active ingredient (including any ester or salt of active ingredients) has previously been approved by the FDA, the FDA must either refer that product candidate to an external advisory committee or provide in an action letter, a summary of the reasons why the FDA did not refer the product candidate to an advisory committee. The FDA may also refer other product candidates to an advisory committee if the FDA believes that the advisory committee's expertise would be beneficial. An advisory committee is typically a panel that includes clinicians and other experts, which review, evaluate, and make a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA reviews applications to determine, among other things, whether a product candidate meets the agency's approval standards and whether the manufacturing methods and controls are adequate to assure and preserve the product's identity, strength, quality, potency, and purity. Before approving a marketing application, the FDA typically will inspect or conduct remote regulatory assessments of the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities, including contract manufacturers and subcontractors, are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a marketing application the FDA will inspect or conduct remote regulatory assessments of one or more clinical trial sites to assure compliance with good clinical practices ("GCPs").

After evaluating the marketing application and all related information, including the advisory committee recommendation, if any, and inspection and remote regulatory inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the biological product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. Many drug applications receive complete response letters from the FDA during their first cycle of FDA review.

If the FDA approves a product, it may limit the approved indications for use of the product; require that contraindications, warnings, or precautions be included in the product labeling, including boxed warnings; require that post-approval studies, including Phase 4 clinical trials and trials to ensure that population representative data is collected, be conducted to further assess a biologic's efficacy and safety after approval; or require testing and surveillance programs to monitor the product after commercialization. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. The FDA may also not approve label statements that are necessary for successful commercialization and marketing.

In addition to the above conditions of approval, the FDA also may require submission of a REMS to ensure that the benefits of the product candidate outweigh the risks. The REMS plan could include medication guides, physician communication plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools. An assessment of the REMS must also be conducted at set intervals. Following product approval, a REMS may also be required by the FDA if new safety information is discovered, and the FDA determines that a REMS is necessary to ensure that the benefits of the product outweigh the risks. In guidance, FDA stated that during the review of a BLA for a gene therapy, it will assess whether a REMS is necessary. Several gene therapy products that have been approved by FDA have required substantial REMS, which included requirements for dispensing hospital and clinic certification, training, adverse event reporting, documentation, and regulatory audits and monitoring conducted by the sponsor, among other conditions. REMS, such as these, can be expensive and burdensome to implement, and burdensome for hospitals, clinics, and healthcare providers to comply with.

Biosimilars and Exclusivity

The Biologics Price Competition and Innovation Act of 2009 ("BPCIA") which amended the PHSA authorized the FDA to approve biosimilars under Section 351(k) of the PHSA. Under the BPCIA, a manufacturer may apply for licensure of a biologic product that is biosimilar to or interchangeable with a previously approved biological product or reference product. For the FDA to approve a biosimilar product, it must find that it is highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there are no clinically meaningful differences between the reference product and proposed biosimilar product in safety, purity or potency. A finding of interchangeability requires that a product is determined to be biosimilar to the reference product, and that the product can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

An application for a biosimilar product may not be submitted to the FDA until four years following approval of the reference product, and it may not be approved until 12 years following approval of the reference product. These exclusivity provisions only apply to biosimilar companies and not companies that rely on their own data and file a full BLA. Moreover, this exclusivity is not without limitation. Certain changes and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the twelve-year exclusivity period. Further, the twelve-year exclusivity period in the U.S. for biologics has been controversial and may be shortened in the future.

The PHSA also includes provisions to protect reference products that have patent protection. The biosimilar product sponsor and reference product sponsor may exchange certain patent and product information for the purpose of determining whether there should be a legal patent challenge. Based on the outcome of negotiations surrounding the exchanged information, the reference product sponsor may bring a patent infringement suit and injunction proceedings against the biosimilar product sponsor. The biosimilar applicant may also be able to bring an action for declaratory judgment concerning the patent.

The FDA maintains a list of approved biological products, which is commonly referred to as the Purple Book. This list includes product names, the date of licensure, and any periods of regulatory exclusivity. Following the exchange of patent information between the biosimilar and reference product sponsor, the reference product sponsor must also provide the exchanged patent information and patent expiry dates to the FDA. The FDA then publishes this information in the Purple Book.

To increase competition in the drug and biologic product marketplace, Congress, the executive branch, and the FDA have taken certain legislative and regulatory steps. By example, the FDA finalized a guidance to facilitate biologic product importation. Moreover, the 2020 Further Consolidated Appropriations Act included provisions requiring that sponsors of approved biologic products, including those subject to REMS, provide samples of the approved products to persons developing biosimilar products within specified timeframes, in sufficient quantities, and on commercially reasonable market-based terms. Failure to do so can subject the approved product sponsor to civil actions, penalties, and responsibility for attorney's fees and costs of the civil action. This same bill also includes provisions with respect to shared and separate REMS programs.

Orphan Drug Exclusivity

Under the Orphan Drug Act of 1983, the FDA may designate a biological product as an orphan drug if it is intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., or more in cases in which there is no reasonable expectation that the cost of developing and making a biological product available in the U.S. for treatment of the disease or condition will be recovered from sales of the product. Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain orphan drug designation if there is a product already approved by the FDA that is considered by the FDA to be the same as the already approved product and is intended for the same indication. This hypothesis must be demonstrated to obtain orphan exclusivity. With respect to gene therapies, the FDA has issued a specific guidance on how the agency interprets its sameness regulations. Specifically, whether two products are deemed to be the same by the FDA will depend on the products' transgene expression, viral vectors groups and variants, and additional product features that may contribute to therapeutic effect. Minor product differences will not, generally, result in a finding that two products are different and there are some factors that FDA will consider on a case-by-case basis. Any of the FDA sameness determinations could impact our ability to receive approval for our product candidates and to obtain or retain orphan drug exclusivity.

If a product with orphan designation receives the first FDA approval, it may be granted seven years of marketing exclusivity, which means that the FDA may not approve any other applications for the same product for the same indication for seven years, unless clinical superiority is demonstrated. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. Notably, a 2021 judicial decision, *Catalyst Pharms., Inc. v. Becerra*, 14 F. 4th 1299 (11th Cir 2021), challenged and reversed an FDA decision on the scope of orphan product exclusivity for the drug, Firdapse. Under this decision, orphan drug exclusivity for Firdapse blocked approval of another company's application for the same drug for the entire disease or condition for which orphan drug designation was granted, not just the disease or condition for which approval was received. In a January 2023 Federal Register notice, however, FDA stated that it intends to continue to apply its regulations tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved. The exact scope of orphan drug exclusivity will likely be an evolving area.

Orphan drug designation does not change the FDA's standard for product approval. The FDA's regulations, however, provide flexibility in meeting such approval standards such that the FDA may exercise scientific judgment in determining the kind and quantity of data required for approval and during development programs. Per guidance issued by the FDA in 2023, "[t]his flexibility extends from the early stages of development to the design of adequate and well-controlled clinical investigations required to demonstrate effectiveness to support marketing approval and to establish safety data needed for the intended use." The FDA states that it "is committed to helping sponsors create successful drug development programs that address the particular challenges posed by each disease."

Pediatric Exclusivity

Under the Pediatric Research Equity Act of 2003, pediatric exclusivity provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity in the US, including orphan exclusivity and reference biologic exclusivity. This six-month exclusivity may be granted if the FDA issues a written request to the sponsor for the pediatric study, the sponsor submits a final study report after receipt of the written request and meets the terms and timelines in the FDA's written request.

Regenerative Advanced Therapy Designation

The 21st Century Cures Act became law in December 2016 and created a new program under Section 3033 in which the FDA has authority to designate a product as a regenerative medicine advanced therapy ("RMAT"). A drug is eligible for a RMAT designation if: 1) it is a regenerative medicine therapy which is a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except those products already regulated under Section 361 of the PHSA; 2) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and 3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. A RMAT designation request must be made with the submission of an IND or as an amendment to an existing IND. FDA will determine if a product is eligible for RMAT designation within 60 days of submission. Advantages of the RMAT designation include all the benefits of the fast track and breakthrough therapy designation programs, including early interactions with the FDA. These early interactions may be used to discuss potential surrogate or intermediate endpoints to support accelerated approval. In 2019 the FDA stated in guidance that human gene therapies, including genetically modified cells, that lead to a sustained effect on cells or tissues, may meet the definition of a regenerative therapy.

FDA Regulation of Companion Diagnostics and Other Combination Products

We may seek to develop companion diagnostics for use in identifying patients that we believe will respond to our gene therapies. Similarly, our product candidates may require delivery devices. A biologic product may be regulated as a combination product if it is intended for use in conjunction with a medical device, such as a drug delivery device or an in vitro diagnostic device. For combination products, the biologic and device components must, when used together, be safe and effective and the product labeling must reflect their combined use. In some cases, the medical device component may require a separate premarket submission. Moreover, clinical trial sponsors using investigational devices in their studies must comply with FDA's investigational device exemption regulations. If the device component (e.g., in vitro diagnostic device) is not packaged with the drug component and authorized by the FDA as a combination product, or approved or cleared as a medical device, the device component must comply with the FDA general controls applicable to a medical device, including establishment registration, device listing, device labeling, unique device identifier, quality system regulation, medical device reporting, and reporting of corrections and removals requirements. If the device component is packaged with the drug component (e.g., drug delivery device), then only certain FDA general controls applicable to a medical device will apply (assuming the manufacturer's quality system complies with the cGMPs).

If the safety or effectiveness of a biologic product is dependent on the results of a diagnostic, the FDA may require that the in vitro companion diagnostic device and biologic product be contemporaneously authorized by the FDA, with labeling that describes the use of the two products together. The type of premarket submission required for a companion diagnostic device will depend on the FDA device classification. A premarket approval ("PMA"), application is required for high-risk devices classified as Class III; a 510(k) premarket notification is generally required for moderate risk devices classified as Class II. Low risk devices classified as Class I generally do not require any FDA premarket authorization, with limited exceptions. A de novo request may be used for novel devices not previously classified by the FDA (and hence are automatically Class III) but are low or moderate risk (due to the application of special controls) and thus can be re-classified as Class II or Class I. Except in some limited circumstances, the FDA generally will not approve a biologic that is dependent upon the use of a companion diagnostic device if the device is not contemporaneously FDA-approved or -cleared. It's also possible that an in vitro diagnostic device could be subject to FDA enforcement discretion from compliance with the FDCA if it meets the definition of a Laboratory Developed Test ("LDT"). However, FDA issued a final rule in April 2024 to end enforcement discretion for LDTs and actively regulate such products as medical devices. Under this final rule, LDTs are required to come into compliance with FDA's medical device regulatory requirements in a staged approach over the course of four years. The implementation of this LDT final rule could potentially be affected by the Executive Order, Regulatory Freeze Pending Review, issued by President Trump on January 20, 2025 and/or the anticipated change in leadership at FDA under the new administration.

Post-approval Requirements

Any products manufactured or distributed pursuant to the FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements related to manufacturing, recordkeeping, and reporting, including adverse experience reporting, deviation reporting, shortage reporting, and periodic reporting, product sampling and distribution, advertising, marketing, promotion, certain electronic records and signatures, and post-approval obligations imposed as a condition of approval, such as Phase 4 clinical trials, REMS, and surveillance to assess safety and effectiveness after commercialization.

After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing annual program user fee requirements for approved products, excluding orphan products provided that certain criteria are met. Regulatory authorities may withdraw product approvals, require label modifications, or request product recalls, among other 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.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval or notification before being implemented. In fact, in 2023, the FDA issued a guidance specifically on demonstrating product comparability, and the management and reporting of manufacturing changes for investigational and licensed cellular and gene therapy products. FDA regulations also require investigation and correction of any deviations from cGMP and specifications and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in production and quality control to maintain cGMP compliance.

The FDA also strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. A company can make only those advertising and promotional claims relating to a product that are consistent with the label approved by the FDA. Physicians, in their independent professional medical judgment, may prescribe legally available products for unapproved indications that are not described in the product's labeling and that differ from those tested and that have been approved by the FDA. Biopharmaceutical companies, however, are required to promote their products only for the approved indications and in a manner that is consistent with the provisions of the approved label. Companies must also provide adequate balancing information on a product's risks in its advertising and promotional pieces. In 2023, the FDA took a few actions in the advertising and promotional spaces, including issuing a final rule and a guidance on risk and efficacy disclosures in direct-to-consumer advertising. At the beginning of 2025, FDA also finalized guidance on communication of off-label scientific information about approved products. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including, but not limited to, criminal fines and civil penalties under the FDCA and False Claims Act, exclusion from participation in federal healthcare programs, mandatory compliance programs under corporate integrity agreements, suspension and debarment from government procurement and non-procurement programs, and refusal of orders under existing government contracts.

Moreover, the enacted Drug Quality and Security Act ("DQSA"), imposes obligations on sponsors of biopharmaceutical products related to product tracking and tracing. Among the requirements of this legislation, sponsors are required to provide certain information regarding the products to individuals and entities to which product ownership is transferred, are required to label products with a product identifier, and are required to keep certain records regarding the product. The transfer of information to subsequent product owners by sponsors is also required to be done electronically and will be required to allow interoperable electronic product tracing at the package level. Sponsors must also verify that purchasers of the sponsors' products are appropriately licensed. Further, under this legislation, manufactures have product verification responsibilities, as well as investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products that would result in serious adverse health consequences or death to humans, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death. Similar requirements additionally are also imposed through this legislation on other companies within the biopharmaceutical product supply chain, such as distributors and dispensers, as well as certain sponsor licensees and affiliates.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements before or after approval, may result in significant regulatory actions. Such actions may include refusal to approve pending applications, license or approval suspension or revocation, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, cyber letters, modification of promotional materials or labeling, provision of corrective information, imposition of post-market requirements including the need for additional testing, imposition of distribution or other restrictions under a REMS, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, FDA debarment, injunctions, consent decrees, corporate integrity agreements, suspension and debarment from government procurement and non-procurement programs, refusal of orders under existing government contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement, civil penalties, criminal prosecution, including fines and imprisonment, and adverse publicity, among other adverse consequences.

Additional Controls for Biologics

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the U.S. and between states.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing the results of all the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer.

In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

Patent Term Restoration

If approved, biologic products may also be eligible for periods of U.S. patent term restoration. If an application for patent term restoration is timely filed with the U.S. Patent and Trademark Office and granted, patent term restoration extends the patent life of a single unexpired patent, that has not previously been extended, for a maximum of five years. The total patent life of the product with the extension also cannot exceed fourteen years from the product's approval date. Subject to the prior limitations, the period of the extension is calculated by adding half of the time from the effective date of an IND to the initial submission of a complete marketing application, and all the time between the submission of the marketing application and its approval. This period may also be reduced by any time that the applicant did not act with due diligence.

Anti-Kickback Provisions and other Fraud and Abuse Requirements

The federal Anti-Kickback Statute ("AKS") is a criminal statute that prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs, in whole or in part. The term "remuneration" has been interpreted broadly to include anything of value. The AKS has been interpreted to apply to arrangements between biopharmaceutical industry members on the one hand and prescribers, purchasers, and formulary managers on the other. The Beneficiary Inducement Civil Monetary Penalties Law imposes similar restrictions on interactions between the biopharmaceutical industry and federal healthcare program beneficiaries. There are certain statutory exceptions and regulatory safe harbors to the AKS protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly, and practices that involve remuneration that may be alleged to be intended to induce or reward prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the AKS. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances.

Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce or reward referrals of federal healthcare program business, including purchases of products paid by federal healthcare programs, the statute has been violated. The Patient Protection and Affordable Care Act, of 2010, as amended, (the "ACA") modified the intent requirement under the AKS to a stricter standard, such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it to have committed a violation. In addition, the ACA also provided that a violation of the AKS is grounds for the government or a whistleblower to assert that a claim for reimbursement submitted to a federal healthcare program for payment of items or services resulting from such violation constitutes a per se false or fraudulent claim for purposes of the federal civil False Claims Act. The Department of Health and Human Services ("HHS") promulgated a regulation in November 2020 with respect to the safe harbors that is effective in two phases. First, the regulation excludes from the definition of "remuneration" limited categories of (a) Pharmacy Benefit Manager ("PBM") rebates or other reductions in price to a plan sponsor under Medicare Part D or a Medicaid Managed Care Organization plan reflected in point-of-sale reductions in price and (b) PBM service fees. Second, the regulation expressly provides that rebates to plan sponsors under Medicare Part D, either directly to the plan sponsor under Medicare Part D or indirectly through a PBM, will not be protected under the AKS discounts safe harbor. The Inflation Reduction Act of 2022 extended a moratorium on the implementation, administration or enforcement of this final rule until January 1, 2032.

The federal civil False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or avoiding, decreasing, or concealing an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. The civil False Claims Act has been used to assert liability on the basis of kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare provider or supplier numbers when detailing a provider of services, improper promotion of off-label uses not expressly approved by the FDA in a product's label, and allegations as to misrepresentations with respect to products, contract requirements, and services rendered. In addition, private payers have been filing follow-on lawsuits alleging fraudulent misrepresentation, although establishing liability and damages in these cases is more difficult than under the FCA. Intent to deceive is not required to establish liability under the civil False Claims Act. Rather, a claim may be false for deliberate ignorance of the truth or falsity of the information provided or for acts in reckless disregard of the truth or falsity of that information. Civil False Claims Act actions may be brought by the government or may be brought by private individuals on behalf of the government, called "qui tam" actions. If the government decides to intervene in a qui tam action and prevails in the lawsuit, the individual will share in the proceeds from any damages, penalties or settlement funds. If the government declines to intervene, the individual may pursue the case alone. The civil FCA provides for treble damages and a civil penalty for each false claim, such as an invoice or pharmacy claim for reimbursement, which can aggregate into tens and even hundreds of millions of dollars. For these reasons, since 2004, False Claims Act lawsuits against biopharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements, as much as $3.0 billion, regarding certain sales practices and promoting off label uses. Civil False Claims Act liability may further be imposed for known Medicare or Medicaid overpayments, for example, overpayments caused by understated rebate amounts, that are not refunded within 60 days of the identification of the overpayment, even if the overpayment was not caused by a false or fraudulent act. In addition, civil judgment for violating the FCA may result in exclusion from federal healthcare programs, suspension and debarment from government procurement and non-procurement programs, and refusal of orders under existing government contracts. The majority of states also have statutes similar to the AKS and civil False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer.

The government may further prosecute conduct constituting a false claim under the criminal False Claims Act. The criminal False Claims Act prohibits the making or presenting of a claim to the government knowing such claim to be false, fictitious, or fraudulent and, unlike the civil False Claims Act, requires proof of intent to submit a false claim.

The Civil Monetary Penalties Law is another potential statute under which biopharmaceutical companies may be subject to enforcement. Among other things, the civil monetary penalties statue imposes fines against any person who is determined to have knowingly presented, or caused to be presented, claims to a federal healthcare program that the person knows, or should know, is for an item or service that was not provided as claimed or is false or fraudulent.

Payment or reimbursement of prescription therapeutics by Medicaid or Medicare requires sponsors to submit certified pricing information to the Centers for Medicare and Medicaid Services ("CMS"). The Medicaid Drug Rebate statute requires sponsors to calculate and report price points, which are used to determine Medicaid manufacturer rebate payments shared between the states and the federal government and Medicaid payment rates for certain therapeutics. For therapeutics paid under Medicare Part B, sponsors must also calculate and report their Average Sales Price, which is used to determine the Medicare Part B payment rate. In addition, therapeutics covered by Medicaid are subject to an additional inflation penalty which can substantially increase rebate payments. For certain products, including those approved under a BLA (including biosimilars), the Veterans Health Care Act (the "VHCA") requires sponsors to calculate and report to the Department of Veterans Affairs ("VA") a different price called the Non-Federal Average Manufacturer Price, which is used to determine the maximum price that can be charged to certain federal agencies, referred to as the Federal Ceiling Price ("FCP"). Like the Medicaid rebate amount, the FCP includes an inflation penalty. A Department of Defense regulation requires sponsors to provide this discount on therapeutics dispensed by retail pharmacies when paid by the TRICARE Program. All these price reporting requirements create risk of submitting false information to the government, potential FCA liability and exclusion from certain of these programs.

The VHCA also requires sponsors of covered therapeutics participating in the Medicaid program to enter into Federal Supply Schedule contracts with the VA through which their covered therapeutics must be sold to certain federal agencies at FCP. This necessitates compliance with applicable federal procurement laws and regulations, including submission of commercial sales and pricing information, and subjects companies to contractual remedies as well as administrative, civil, and criminal sanctions. In addition, the VHCA requires sponsors participating in Medicaid to agree to provide different mandatory discounts to certain Public Health Service grantees and other safety net hospitals and clinics under the 340B program based on the sponsor's reported Medicaid pricing information. The 340B program has its own regulatory authority to impose sanctions for non-compliance, adjudicate overcharge claims against sponsors by the purchasing entities, and impose civil monetary penalties for instances of overcharging.

The federal Health Insurance Portability and Accountability Act of 1996, ("HIPAA"), also created federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, a healthcare benefit program, regardless of whether the payor is public or private, in connection with the delivery of or payment for healthcare benefits, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. Additionally, the ACA amended the intent requirement of certain of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

In addition, as part of the ACA, the federal government enacted the Physician Payment Sunshine Act. Manufacturers of drugs, biologics and devices for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) are required to annually report to CMS certain payments and other transfers of value made to or at the request of covered recipients, which are physicians (as defined under the Social Security Act), physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and certified nurse midwifes licensed in the U.S. and U.S. teaching hospitals, as well as ownership and investment interests held by physicians and members of their immediate family. Payments made to principal investigators and research institutions for clinical trials are also included within this law. Reported information is made publicly available by CMS. Failure to submit required information may result in civil monetary penalties. If not preempted by this federal law, several states currently also require reporting of marketing and promotion expenses, as well as gifts and payments to healthcare professionals and organizations. State legislation may also prohibit gifts and various other marketing related activities or require the public posting of information. Certain states also require companies to implement compliance programs.

Further, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, ("HITECH Act"), and their respective implementing regulations impose certain requirements on covered entities relating to the privacy, security, and transmission of certain individually identifiable health information known as protected health information. Among other things, the HITECH Act, and its implementing regulations, made HIPAA's security standards and certain privacy standards directly applicable to business associates, defined as persons or organizations, other than members of a covered entity's workforce, that create, receive, maintain, or transmit protected health information on behalf of a covered entity for a function or activity regulated by HIPAA. The HITECH Act also strengthened the civil and criminal sanctions that may be imposed against covered entities, business associates, and individuals, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. HIPAA privacy rules governing disclosures of protected health information by covered entities for research purposes may apply to gene therapy studies. In addition, other federal and state laws, such as the California Consumer Privacy Act and state security breach notification laws and state consumer healthcare privacy laws, may govern the privacy and security of health and other information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Many states have also adopted laws similar to each of the above federal laws, which may be broader in scope and apply to items or services reimbursed by any third-party payor, including commercial insurers. Certain state laws also regulate sponsors' use of prescriber-identifiable data. Certain states also require implementation of commercial compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance program guidance promulgated by the federal government, or otherwise restrict payments or the provision of other items of value that may be made to healthcare providers and other potential referral sources; impose restrictions on marketing practices; or require sponsors to track and report information related to payments, gifts, and other items of value to physicians and other healthcare providers and entities. Recently, states have enacted or are considering legislation intended to make drug prices more transparent and deter significant price increases that impose reporting requirements on biopharmaceutical companies. These laws may affect our future sales, marketing, and other promotional activities by imposing administrative and compliance burdens. Such laws also typically impose significant civil monetary penalties for each instance of reporting noncompliance that can quickly aggregate into the tens of millions of dollars.

If our operations are found to be in violation of any of the laws or regulations described above or any other laws that apply to us, we may be subject to penalties or other enforcement actions, including significant civil monetary penalties, damages, criminal fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, corporate integrity agreements, suspension and debarment from government procurement and non-procurement programs, refusal of orders under existing government contracts, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our business.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, to which we are subject, imposes certain recordkeeping requirements and prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity.

Coverage, Pricing and Reimbursement

The containment of healthcare costs has become a priority of federal, state, and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payers and independent non-profit healthcare research organizations such as the Institute for Clinical and Economic Review are also increasingly challenging the prices charged for medical products and services and examining the medical necessity, budget-impact, and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payers do not consider a product to be cost-effective compared to other available therapies and/or the standard of care, they may not cover the product after approval as a benefit under their plans or, if they do, measures including prior authorization and step-throughs could be required, manufacturer rebates may be negotiated or required and/or the level of payment may not be sufficient to allow a company to sell its products at a profit. The U.S. federal and state governments and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products for branded prescription drugs. In this regard, for example, on November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation payment model under which reimbursement for certain Medicare Part B drugs and biologicals will be based on a price that reflects the lowest per capital Gross Domestic Product-adjusted ("GDP-adjusted") price of any non-U.S. member country of the Organization for Economic Co-operation and Development ("OECD") with a GDP per capita that is at least sixty percent of the U.S. GDP per capita. While this rule now has been rescinded, government negotiation of certain Medicare drug pricing continues to be the focus of recent proposed legislation. The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. Failure of the Joint Select Committee on Deficit Reduction to reach required deficit reduction goals triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year. While President Biden previously signed legislation 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. The Inflation Reduction Act of 2022 requires manufacturers of selected drugs to negotiate discounted prices with the Secretary of the Department of Health and Human Services. Failure to reach an agreement can subject manufacturers to an excise tax or withdrawal of all drug products from coverage under Medicare and Medicaid. Adoption of additional healthcare reform controls and measures and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

As a result, the marketability of any product which receives regulatory approval for commercial sale may suffer if the government and third-party payers choose to provide low coverage and reimbursement. In addition, an increasing emphasis on managed care in the U.S. has increased and will continue to increase the pressure on drug pricing. Decisions regarding whether to cover any of our products, the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Further, no uniform policy for coverage and reimbursement exists in the U.S., and coverage and reimbursement can differ significantly from payor to payor. Coverage policies, third party reimbursement rates and drug pricing regulation may change at any time. In particular, the ACA contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. Multiple other current and proposed legislative and regulatory efforts require and likely will in the future require payment of increased manufacturer rebates and implement mechanisms to reduce drug prices. Even if favorable coverage and reimbursement status is attained for one or more products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Regulation in the European Union

Product development, the regulatory approval process and safety monitoring of medicinal products and their manufacturers in the European Union proceed broadly in the same way as they do in the U.S. Therefore, many of the issues discussed above apply similarly in the context of the European Union. In addition, drugs are subject to the extensive price and reimbursement regulations of the various EU member states. The Clinical Trial Regulation EU 536/2014 ("CTR"), which replaced the Clinical Trials Directive 2001/20/EC, as amended ("CTD"), on January 31, 2022, provides a system for the approval of clinical trials in the European Union. The CTR is directly applicable in all member states without the need for national implementation. Whilst, for trials conducted in only one country, approval has to be obtained from the competent national authority of an EU member state in which the clinical trial is to be conducted before cross-border trials within the EU, it is possible to make a single harmonized electronic submission and have a single assessment process for clinical trials conducted in multiple member states. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the Clinical Trial Application ("CTA"), which must be supported by an investigational medicinal product dossier with supporting information prescribed by the CTR and corresponding national laws of the member states and further detailed in applicable guidance documents. In the case of Advanced Therapy Investigational Medical Products ("ATIMPs") consisting of or containing Genetically Modified Organisms ("GMOs"), as is the case for our products, an additional approval for the environmental and biosafety aspects of the use and release of the GMO is required by the GMO competent authorities. Unlike EU Regulations, EU Directives require national implementation and GMO Directives have been implemented in different ways by Member States; either following the Directive for "Contained use" (Directive 2009/41/EC) or "deliberate release" (Directive 2001/18/EC). As a consequence, in some EU member states the GMO application must be approved before the CTA is submitted, in some after approval of the CTA, and in some, in parallel.

The sponsor of a clinical trial, or its legal representative, must be based in the European Economic Area ("EEA"). European regulators and ethics committees also require the submission of adverse event reports during a study and a copy of the final study report. Under the CTR, member states may dispense with the requirement for a legal representative for a non-EU resident sponsor provided there is a contact person based in the EEA.

Under the CTR, the introduction of a new databased called the Clinical Trial Information System ("CTIS"), requires sponsors to upload and submit all data, including initial clinical trial application data and documentation, to the CTIS, with such data being publicly available, with few exceptions. This means data transparency throughout the development process with the onus on sponsors to protect patient and commercial confidentiality at the point of submission.

Marketing approval

Marketing approvals under the European Union regulatory system may be obtained through a centralized or decentralized procedure. The centralized procedure results in the grant of a single marketing authorization that is valid for all 27 EU member states. Pursuant to Regulation (EC) No 726/2004, as amended, the centralized procedure is mandatory for drugs developed by means of specified biotechnological processes, and advanced therapy medicinal products as defined in Regulation (EC) No 1394/2007, as amended. Drugs for human use containing a new active substance for which the therapeutic indication is the treatment of specified diseases, including but not limited to acquired immune deficiency syndrome, neurodegenerative disorders, auto-immune diseases and other immune dysfunctions, as well as drugs designated as orphan drugs pursuant to Regulation (EC) No 141/2000, as amended, also fall within the mandatory scope of the centralized procedure. Because of our focus on gene therapies, which fall within the category of advanced therapy medicinal products ("ATMPs") and orphan indications, our products and product candidates will need to go through the centralized procedure.

In the marketing authorization application ("MAA") the applicant must properly and sufficiently demonstrate the quality, safety, and efficacy of the drug. The Committee for Medicinal Products for Human Use ("CHMP") is the European Medicines Agency's ("EMA") committee responsible for human medicines. Guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs have been issued and include, among other things, the nonclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a MAA; and post-approval measures required to monitor patients and evaluate the long-term efficacy and potential adverse reactions of ATMPs. Although these guidelines are not legally binding, we believe that our compliance will effectively be necessary to gain and maintain approval for any of our product candidates. The maximum timeframe for the evaluation of an MAA under the centralized procedure is 210 days after receipt of a valid application subject to clock stops during which the applicant deals with CHMP questions.

Market access can be expedited through the grant of conditional authorization for a medicine that may fulfil unmet needs which may be granted provided that the benefit-risk balance of the product is positive. The benefit-risk balance is likely to be positive if the applicant can provide comprehensive data and the benefit to public health of the medicinal product's immediate availability on the market outweighs the risks due to need for further data. Such authorizations are valid for one year and can be renewed annually. The holder will be required to complete specific obligations (ongoing or new studies, and in some cases additional activities) with a view to providing comprehensive data confirming that the benefit-risk balance is positive. Once comprehensive data on the product have been obtained, the conditional authorization may be converted into a standard marketing authorization ("MA") (not subject to specific obligations). Initially, this is valid for 5 years, but can be renewed for unlimited validity. Applicants for conditional authorizations can benefit from early dialogue with CHMP through scientific advice or protocol assistance and discuss their development plan well in advance of the submission of a MAA. Other stakeholders (e.g., health technology assessment bodies) can be included.

In addition, the priority medicines ("PRIME") scheme for medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options based on early clinical data, is intended to support the development of medicines that target an unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation so these medicines can reach patients earlier. Early dialogue and scientific advice also ensure that patients only participate in trials designed to provide the data necessary for an application, making the best use of limited resources.

The European Union also provides for a system of regulatory data and market exclusivity. According to Article 14(11) of Regulation (EC) No 726/2004, as amended, and Article 10 of Directive 2001/83/EC, as amended, upon receiving marketing authorization, new chemical entities approved on the basis of complete independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application during the eight-year period from when the first placement of the product on the EEA market. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator can gain the period of data exclusivity, another company nevertheless could also market another version of the drug if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical test, preclinical tests, and clinical trials. The EMA has also issued guidelines for a comprehensive comparability exercise for biosimilars, and for specific classes of biological products. Under European Commission proposals for revisions to the EU's pharmaceutical legislation, the standard period of data protection may be reduced from eight to six years, but this may be extended by up to four years if particular criteria are fulfilled: i.e., two additional years if the new product is available in all EU Member States; an additional six months if the product addresses an unmet medical need; an additional six months for new chemical entities where the supporting clinical trials use an evidence-based comparator based on EMA scientific advice; and an additional year if, during the data protection period following authorization, the MA holder receives an authorization for an additional therapeutic indication for which there is a significant clinical benefit in comparison with existing therapies (replacing the additional year of marketing protection available under the current regime). The additional period of marketing exclusivity protection (described above) will remain as two years following the expiry of the data protection period. These proposals will be subject to continuing discussion so it is not certain when and in what form the new legislation will be adopted.

Under Regulation (EC) No 141/2000 article 3 as amended (Orphan Drug Regulation, ("ODR")) a product can benefit from orphan drug status if it is intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European Community (EC) when the application is made. The principal benefit of such status is 10 years' market exclusivity once the MA is granted the subsequent approval of similar medicines with similar indications although this may be reduced to six years under certain circumstances including if the product is sufficiently profitable not to justify maintenance of market exclusivity. Under the above-mentioned proposed new legislation, other than for orphan drugs addressing a high unmet medical need, the current 10-year period would be reduced to nine years. These periods may be extended by one year if either: the new product is available in all EU member states; or at least two years before the expiry of the orphan exclusivity period, the orphan MA holder obtains an MA for one or more further therapeutic indications for a different orphan condition.

Additional rules apply to medicinal products for pediatric use under Regulation (EC) No 1901/2006, as amended. Potential incentives include a six-month extension of any supplementary protection certificate granted pursuant to Regulation (EC) No 469/2009, however not in cases in which the relevant product is designated as an orphan medicinal product pursuant to the ODR. Instead, medicinal products designated as orphan medicinal product may enjoy an extension of the ten-year market exclusivity period granted under Regulation (EC) No 141/2000, as amended, to twelve years subject to the conditions applicable to orphan drugs. The proposed new legislation will retain the 6-month SPC extension but there would be an explicit obligation to place an authorized product with a pediatric indication on the market in every member state where the adult presentation is marketed. Additionally, the current separate reward of two years market exclusivity for pediatric indications of orphan products would no longer apply under the proposed legislation.

Manufacturing and promotion

Pursuant to European Commission Directive 2003/94/EC as transposed into the national laws of the member states, the manufacturing of investigational medicinal products and approved drugs is subject to a separate manufacturer's license and must be conducted in strict compliance with cGMP requirements, which mandate the methods, facilities, and controls used in manufacturing, processing, and packing of drugs to assure their safety and identity. Manufacturers must have at least one qualified person permanently and continuously at their disposal. The qualified person is ultimately responsible for certifying that each batch of finished product released onto the market has been manufactured in accordance with cGMP and the specifications set out in the marketing authorization or investigational medicinal product dossier. cGMP requirements are enforced through mandatory registration of facilities and inspections of those facilities. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs, and lost revenues, and subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action, or possible civil and criminal penalties.

Advertising

In the European Union, the promotion of prescription medicines is subject to intense regulation and control, including a prohibition on direct-to-consumer advertising. All medicines advertising must be consistent with the product's approved summary of products characteristics, factual, accurate, balanced and not misleading. Advertising of medicines pre-approval or off-label is prohibited. Some jurisdictions require that all promotional materials for prescription medicines be subjected to either prior internal or regulatory review & approval.

Other Regulatory Requirements

A holder of a MA for a medicinal product is legally obliged to fulfill several obligations by virtue of its status as a marketing authorization holder ("MAH"). The MAH can delegate the performance of related tasks to third parties, such as distributors or marketing collaborators, provided that this delegation is appropriately documented and the MAH maintains legal responsibility and liability.

The obligations of an MAH include:

- *Manufacturing and Batch Release.* MAHs should guarantee that all manufacturing operations comply with relevant laws and regulations, applicable GMP, with the product specifications and manufacturing conditions set out in the marketing authorization and that each batch of product is subject to appropriate release formalities.

- *Pharmacovigilance.* MAHs are obliged to establish and maintain a pharmacovigilance system, including a qualified person responsible for oversight, to submit safety reports to the regulators and comply with the good pharmacovigilance practice guidelines adopted by the EMA.
- *Advertising and Promotion.* MAHs remain responsible for all advertising and promotion of their products, including promotional activities by other companies or individuals on their behalf and in some cases, must conduct internal or regulatory pre-approval of promotional materials.
- *Medical Affairs/Scientific Service.* MAHs are required to disseminate scientific and medical information on their medicinal products to healthcare professionals, regulators, and patients.
- *Legal Representation and Distributor Issues.* MAHs are responsible for regulatory actions or inactions of their distributors and agents.
- *Preparation, Filing and Maintenance of the Application and Subsequent Marketing Authorization.* MAHs must maintain appropriate records, comply with the MA's terms and conditions, fulfill reporting obligations to regulators, submit renewal applications and pay all appropriate fees to the authorities.

We may hold any future marketing authorizations granted for our product candidates in our own name or appoint an affiliate or a collaborator to hold MAs on our behalf. Any failure by an MAH to comply with these obligations may result in regulatory action against an MAH and ultimately threaten our ability to commercialize our products.

Reimbursement

In the European Union, the pricing and reimbursement mechanisms by private and public health insurers vary largely by country and even within countries. In respect of the public systems, reimbursement for standard drugs is determined by guidelines established by the legislature or responsible national authority. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. Other member states allow companies to determine the prices for their medicines but monitor and control company profits and may limit or restrict reimbursement and can include retrospective rebates to the government. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products and some of EU countries require the completion of studies that compare the cost-effectiveness of a particular product candidate to currently available therapies to obtain reimbursement or pricing approval. Special pricing and reimbursement rules may apply to orphan drugs.

Inclusion of orphan drugs in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any drug. Acceptance of any medicinal product for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. In addition, results-based rules or agreements on reimbursement may apply. Recently, a process has been formalized that allows sponsors to receive parallel advice from EMA and relevant national health technology assessment ("HTA") bodies for pivotal clinical studies designed to support marketing approval. This process was followed for etranacogene dezaparvovec.

Orphan Drug Regulation

We have been granted orphan drug exclusivity for AMT-130 for the treatment of Huntington's disease subject to the conditions applicable to orphan drug exclusivity in the European Union. The ODR states that a drug will be designated as an orphan drug if its sponsor can establish:

- that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the community when the application is made, or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment; and
- that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, that the drug will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a drug as an orphan drug. An application for the designation of a drug as an orphan drug must be submitted at any stage of development of the drug before filing of a MAA.

If an EU-wide community marketing authorization in respect of an orphan drug is granted pursuant to Regulation (EC) No 726/2004, as amended, the European Union and the member states will not, for a period of 10 years, accept another MAA, or grant a MA or accept an application to extend an existing MA, for the same therapeutic indication, in respect of a similar drug.

This period may however be reduced to six years if, at the end of the fifth year, it is established, in respect of the drug concerned, that the criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity. Notwithstanding the foregoing, a MA may be granted, for the same therapeutic indication, to a similar drug if:

- the holder of the MA for the original orphan drug has given its consent to the second applicant;
- the holder of the MA for the original orphan drug is unable to supply sufficient quantities of the drug; or
- the second applicant can establish in the application that the second drug, although similar to the orphan drug already authorized, is safer, more effective, or otherwise clinically superior.

Regulation (EC) No 847/2000 lays down definitions of the concepts similar drug and clinical superiority, which concepts have been expanded upon in subsequent European Commission guidance. Other incentives available to orphan drugs in the European Union include financial incentives such as a reduction of fees or fee waivers and protocol assistance. Orphan drug designation does not shorten the duration of the regulatory review and approval process. As described above, the above proposed legislation would, if implemented, impact orphan protection in the future.

Human Capital Resources

As of December 31, 2024, we had a total of 209 employees, 147 of whom are based in The Netherlands, 44 in the U.S. and 15 in other European countries. The split of employees between operations, clinical development, pre-clinical and technology and general and administrative functions are included below:

	December 31, 2024	December 31, 2023
Operations	66	258
Clinical development	44	60
Pre-clinical development and technology	38	64
General and administrative	61	98
Total	**209**	**480**

As of December 31, 2024, 73 of our employees had an M.D. or Ph.D. degree, or the foreign equivalent. During 2017, we established a works council in the Netherlands. None of our employees are subject to collective bargaining agreements or other labor organizations. We believe that we have good relations with all our employees and with the works council in the Netherlands.

Our values are to:

- Be passionate about the patient;
- Act with integrity and respect;
- Take ownership and act with urgency;
- Collaborate for success;
- Innovate every day; and
- Focus relentlessly on quality.

Our people are a critical component in our continued success. We strive to maximize the potential of our human capital resources by creating a respectful, rewarding and inclusive work environment that enables our employees to further our values. Development of our culture is reflected as part of our annual corporate goals. We invest in numerous learning opportunities focused on individual, management and team development and other initiatives to support our employees and build our culture.

Additional Information

uniQure B.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. We are a leader in the field of gene therapy and seek to deliver to patients suffering from rare and other devastating diseases single treatments with potentially curative results. Our business was founded in 1998 and was initially operated through our 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 the initial public offering, we converted into a public company with limited liability (naamloze vennootschap) and changed its legal name from uniQure B.V. to uniQure N.V.

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

Our website address is www.uniqure.com. We make available free of charge through our investor website our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, proxy statements for our meetings of shareholders, and any amendments to these reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding uniQure and other issuers that file electronically with the SEC.

We currently announce material information to our investors and others using filings with the SEC, press releases, public conference calls, webcasts, or our investor relations website (uniqure.com/investors-media). Also available through our website's "Investors & Newsroom: Corporate Governance" page are charters for the Audit, Compensation and Nominating and Corporate Governance committees of our board of directors (the "Board"), along with a copy of our Code of Business Conduct and Ethics, available at uniqure.com/investors-media/corporate-governance. The information on our website is not part of, nor shall it be deemed to be incorporated by reference into, this Annual Report on Form 10-K or any other filings with the SEC.

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 Annual Report on Form 10-K, including our financial statements and related notes thereto, 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.

Risks Related to Our Business and the Development of Our Product Candidates

We are dependent on the success of our lead product candidate, AMT-130, for the treatment of Huntington's disease. A failure of AMT-130 in clinical development, including inability to demonstrate sufficient safety or efficacy, or challenges associated with its regulatory approval, manufacturing or commercialization 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 for the treatment of Huntington's disease. In July 2024, we announced updated interim data from our ongoing Phase I/II clinical trials of AMT-130, as summarized under "*Business— Our Development of AMT-130 for Huntington's Disease*" in this Annual Report on Form 10-K. These interim data follow notification from FDA in May 2024 that the agency 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. In addition, in December 2024, following our initial Type B meeting, we announced that we had reached agreement with FDA on key elements of an Accelerated Approval pathway for AMT-130. In correspondence leading up to and following the Type B meeting, FDA agreed that data from the ongoing Phase I/II studies of AMT-130, compared to a natural history external control, may serve as the primary basis for a BLA submission under FDA's Accelerated Approval pathway. FDA also agreed that cUHDRS may be used as an intermediate clinical endpoint and that reductions in NfL measured in CSF may serve as supportive evidence of therapeutic benefit in the application for accelerated approval.

There are numerous factors that could impede or otherwise negatively impact our further development of AMT-130, including, but not limited to, potential patient safety issues; our failure to demonstrate sufficient clinical efficacy or durability of response data to warrant further development or accelerated approval by FDA, EMA or any other regulatory authority; our ability to achieve alignment with FDA and other regulatory authorities on the primary statistical analysis plan and CMC requirements to support registration and the timing of such regulatory alignment; the results from future interim data readouts from our Phase I/II trial, including the three-year follow-up data from treated patients and safety and tolerability data from the third cohort; any requirement for a Phase III confirmatory study; the timing and resources associated with our planned marketing applications; our ability to successfully commercialize AMT-130 should we choose to do so without a partner; challenges with potential development or commercial partners, should we choose to pursue further development or commercialization of AMT-130 with a partner; and our ability to fund the further development and commercialization of the AMT-130 program.

Any one or combination of these factors could force us to halt or discontinue the ongoing clinical trials of AMT-130 or related commercialization efforts. 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.

Notwithstanding alignment with FDA on key elements of the accelerated approval pathway, 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. In June 2024, we announced that the 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. Following our initial Type B meeting with the FDA, we announced in December 2024 that we had reached agreement with FDA on key elements of an accelerated approval pathway for AMT-130 and have initiated BLA readiness activities based on this regulatory alignment. We are also advancing three other product candidates through Phase I/II clinical development – AMT-260 for the treatment of mTLE, 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 identifying and recruiting patients in our clinical studies;
- 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 measurements of clinical efficacy, our interpretation and statistical analyses of data collected from preclinical studies and clinical trials;
- 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 development programs;
- interruptions in manufacturing clinical supply of our product candidates or issues with product candidates failing to 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 manufacturers or their 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 our product candidates in humans. Such trials, regulatory review and approval take many years. Our clinical trials may never yield results that demonstrate that our 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 reputational damage.

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 that we may not have sufficient resources to conduct or 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. 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 our clinical trials, which may delay or impede our planned trials and development timelines. In addition, we or any of our collaborators may not be able to identify and enroll sufficient eligible patients to participate in these trials as required by the FDA, the EMA or other regulatory authorities. 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 several of 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 age range required for trial eligibility for certain 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. Patients may also be reluctant to enroll in clinical trials for gene therapy candidates where other therapeutic alternatives are available due uncertainty about the safety or effectiveness gene therapies and the possibility that treatment with one gene therapy could preclude future gene therapy treatments due to the formation of antibodies following and in response to the treatment, or other unknown factors associated with novel therapeutics.

Our inability to successfully initiate or complete preclinical and clinical studies could result in additional costs to us or impair our ability to receive marketing approval, to generate revenues from product sales or from reaching certain development milestones, or obtain regulatory approval. 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 or how the results from our clinical trials are analyzed, whether as a result of regulatory feedback or changes in clinical trial procedures and protocols, may also impact the results of subsequent analyses or 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, or may have conditional approvals revoked. Data obtained from preclinical and clinical activities may be subject to varying interpretations and analyses, which may delay, limit, or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections due to shifting political priorities, resulting changes in regulatory agencies or other 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 crossed over to treatment with AMT-130 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. Early evidence of slowing of disease progression in our AMT-130 clinical trial may not be predictive of continued evidence of potential efficacy as we continue to collect follow-up data from patients enrolled in the trial.

Interim or preliminary results from our clinical trials may change as more data become available, as such data are subject to regulatory audit and verification procedures, and regulatory review, which could result in material changes in the final results and conclusions.

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 such 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 regulatory 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 July 2024, 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. As part of the July 2024 update, we announced a statistically significant, dose-dependent, slowing in disease progression for high-dose patients dosed with AMT-130, as measured by cUHDRS, as well as a statistically significant reduction of NfL in CSF. Such measures of statistical significance were based on a post-hoc analysis of data from patients treated with AMT-130 compared to a propensity score-weighted external control cohort. Interim data from our clinical trials, including the AMT-130 trial, and our analyses of that data are subject to the risk that one or more of our interim conclusions may materially change as more patient data become available and as regulatory interactions focused on statistical analysis of the clinical data progress, among other factors. Significant differences between interim data and subsequent data could change the nature of our conclusions with respect to the safety and efficacy of our product candidates, which could adversely impact our business.

We have and may in the future disclose interim results based on post-hoc analyses, the pooling of data from multiple studies, or using statistical assessments or comparisons, including comparisons to historical controls, which regulatory authorities may not agree with. The FDA may find that calculations of statistical significance using nominal p-values are not sufficiently reliable or subject to certain statistical limitations and, as a result, determine that our preliminary results are insufficient evidence of clinical efficacy.

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 negatively impact the value of the particular program, its prospects for approval and our business. In December 2024, following our initial Type B meeting, we announced that we had reached agreement with FDA on key elements of an accelerated approval pathway for AMT-130, including that data from the ongoing Phase I/II studies of AMT-130, compared to a natural history external control, may serve as the primary basis for a BLA submission under FDA's Accelerated Approval pathway. FDA also agreed that cUHDRS may be used as an intermediate clinical endpoint and that reductions in NfL measured in CSF may serve as supportive evidence of therapeutic benefit in the application for accelerated approval. Notwithstanding alignment with the agency on these elements, we may fail to continue to demonstrate clinical efficacy or durability of response data to warrant further development or accelerated approval by FDA, EMA or any other regulatory authority.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial may be top-line results based on what is typically extensive information, and others may not agree with what we determine is the material or otherwise appropriate information to include in our public disclosures. Any information we determine not to disclose may ultimately be deemed significant by 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 cUHDRS 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. As such, we anticipate proposing to the FDA a pre-specified statistical analysis to support a potential BLA submission. An unfavorable view of our proposed statistical analyses by regulatory authorities could negatively impact our ability to obtain, or the timing of, regulatory approval, which would have a material adverse effect on our revenue and adversely impact our business and financial results.

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.

We seek 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 for which commercialization has been exclusively out-licensed to CSL Behring, we may not be successful in identifying or developing additional products that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential new product candidates that we identify may not be suitable for or may fail in 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. 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 other value-driving opportunities. 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.

We may not be successful in obtaining rights from external parties to new product candidates and key technologies, or in securing partnerships to support the development or commercialization of our product candidates.

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. 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 our existing product candidates, including the costs associated with submitting a BLA for AMT-130 and related commercial planning and readiness activities, we may seek to out-license some of our product candidates or technologies to other pharmaceutical or biotechnology companies or other third parties to 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 or superior 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 the 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 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.

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 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, PTC Therapeutics, Roche, Wave Life Sciences, Alnylum Pharmaceuticals, Regeneron and Skyhawk Therapeutics (for Huntington's disease), Neurona and Combigene (for TLE), Biogen, Ionis, Neurimmune, Regeneron, Alnylum Pharmaceuticals and Voyager Therapeutics (for ALS) and Amicus Therapeutics, Sanofi, Takeda, Chiesi, Idorsia, Sangamo Therapeutics, 4D Molecular Therapeutics, Skyline Pharmaceuticals and CANbridge (for Fabry disease).

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

Many of the companies with which we are competing or may compete in the future have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products. 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.

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 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, reductions in staffing or other personnel limitations within a regulatory agency, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Due to the recent change in presidential administration in the U.S., we face substantial uncertainty regarding potential regulatory developments that may adversely affect our business, including those related to potential decreases in spending in the federal government, potential staffing reductions, or any other potential constraints on the FDA's ability to engage in routine oversight and product review activities or its ability to exercise regulatory authority. 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. Under proposed EU legislation, there is also a suggested amendment in relation to advanced therapy medicinal products to the effect that hospital pharmacies would be afforded greater flexibility to prepare product for dispensing on the basis of the estimated prescriptions within that hospital for the following 7 days rather than, as at present, in response to individual prescriptions.

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 leverage certain specialized regulatory pathways and designations, such as the FDA's accelerated approval pathway and RMAT designation, to develop our product candidates or to seek licensure. Even if one or more of our product candidates receives such a designation or is permitted to pursue such a pathway, we may be unable to obtain and maintain the benefits associated with such designations and pathways.

In May 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 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 December 2024, following our initial Type B meeting which was scheduled on the basis of our RMAT designation for AMT-130, we announced that we had reached agreement with FDA on key elements of an accelerated approval pathway for AMT-130, as described under "Business—Recent Product Candidate Developments" in this Annual Report on Form 10-K. 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 (other than AMT-130) 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. As part of our alignment with FDA in December 2024 on the accelerated approval pathway for AMT-130, the agency agreed that cUHDRS may be used as an intermediate clinical endpoint and that reductions in NfL measured in CSF may serve as supportive evidence of therapeutic benefit in the application for accelerated approval.

There is no guarantee that we would be able to obtain accelerated approval as FDA may disagree with our interim endpoint or may find that such endpoint is not met following subsequent clinical data. These designations and accelerated approval 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. Even though we have aligned with the FDA on elements of the accelerated approval pathway for AMT-130, we may not ultimately be successful in obtaining marketing approval for AMT-130, 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 and it is unclear how the incoming Trump Administration in the U.S. will address regulations related to accelerated approval pathways, if at all. 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, AMT-191 and AMT-162 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 for a number of reasons, including, but not limited to 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. 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. It is also possible that periods of regulatory exclusivity may change. By example, the EU has proposed exclusivity changes, in the form of draft legislation, that would effectively shorten the periods of EU orphan market exclusivity and data exclusivity.

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.

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, if approved, 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 access treatment with our products and our potential 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 the future. Currently, if a drug product is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 as well as the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 ("OBRA"), the Veterans Health Care Act of 1992, Deficit Reduction Act of 2005, and the Patient Protection and Affordable Care Act, each as amended. 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 ("IRA"), was signed into law. Among other things, the IRA requires manufacturers of certain high-Medicare spend 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 coverage and/or 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.

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, and frequently does, require that this confirmatory trial be commenced prior to FDA granting a product accelerated approval. If FDA requires that a confirmatory study be underway prior to BLA approval, this could delay any planned BLA submissions and FDA marketing approvals. Moreover, 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 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, whether we choose to pursue further development or commercialization our product candidates alone or with a partner. If we are successful in obtaining marketing approval from applicable regulatory authorities for AMT-130 or any of our other product candidates, our ability to generate revenues from our product candidates will depend on our success in:

- actual receipt and maintenance of marketing approvals from applicable regulatory authorities;
- launch of commercial sales of our products, if approved, whether alone or in collaboration with others;
- maintaining regulatory approvals, including manufacturing approvals for our third-party manufacturing sites;
- complying with any applicable post-approval commitments and requirements, and maintaining a continued acceptable overall safety profile;
- 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;
- obtaining adequate reimbursement for the total patient population and each subgroup to sustain a viable commercial business model in U.S. and EU markets; and
- obtaining and maintaining patent and trade secret protection and non-patent, exclusivities for our product candidates.

Even if our product candidates are approved, they may be subject to limitations that make commercialization difficult, and we may experience these difficulties regardless of whether we choose to commercialize our product candidates alone or with a partner. 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.

Any approved gene therapy we seek to commercialize 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.

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.

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 development on product candidates designed to treat 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 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.

Risks Related to Manufacturing and Our Dependence on Third Parties

The Lexington Transaction may not yield the benefits that we expect and may result in additional risks to our business, including those related to Genezen's ability to manufacture HEMGENIX in accordance with regulatory requirements and to meet CSL Behring's supply requirements for commercial product.

In connection with the closing of the Lexington Transaction in July 2024, we and Genezen entered into certain additional agreements, including a commercial supply agreement pursuant to which Genezen will manufacture and supply our requirements of HEMGENIX® pursuant to our manufacturing and supply obligations to CSL Behring, and 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 discretionary services related to the manufacture of HEMGEMIX®, 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 as we expect. In addition, we may be exposed to additional costs and risks related to or as a result of the Lexington Transaction, including, without limitation 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, supply-related risks related Genezen's ability and capacity to satisfy our continued obligations to CSL Behring and the supply requirements of our other product candidates, including the CMC and supply-related requirements for our BLA submission for AMT-130, contractual default under our agreements with Genezen or with CSL Behring, and other third-party risks relative to our partnership with Genezen. 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. 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 are highly complex and 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 and regulatory timelines, 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. 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 our development and commercial supply agreement with CSL Behring. While uniQure has 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 related to HEMGENIX® to a third-party contract manufacturer designated by CSL Behring. Until CSL Behring completes the transfer of manufacturing technology to this new manufacturer, and until such manufacturer is able to demonstrate that it is capable of supporting the commercial requirements of HEMGENIX® sufficient for regulatory approval, we will continue to incur significant costs associated with the manufacturing and supply of HEMGENIX® through our contractual relationship with Genezen. 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 capacity and resource constraints, or its inability to adapt to new manufacturing 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.

The manufacturing of our products and product candidates is subject to significant government regulations and approvals. We currently rely and expect to continue to rely on third parties to manufacture our product candidates, and these third parties may not perform satisfactorily or may fail to comply with these regulations or maintain these approvals.

The manufacturing of our products and product candidates is subject to significant government regulation. 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. 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 are subject to FDA inspections, including after we submit a BLA. We are completely dependent on Genezen and our other contract manufacturers to execute on our manufacturing processes for HEMGENIX® and other product candidates and for compliance with cGMP requirements. 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.

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 our proprietary manufacturing processes. 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 no 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 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 timely 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.

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 business development strategy or existing development programs. Any collaboration we enter into may pose 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 research, 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 from 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 different forms of intellectual property, including in-licensed and fully or co-owned patents and patent applications 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 or regions, 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, may not prevent competitors from competing with us or otherwise provide us with any competitive advantage. At least some of the patents we own are or may become subject to 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 desirable patent applications. For example, our defense of certain patent cases in the Netherlands, the EU 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 jurisdictions 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 jurisdictions 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. 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, share 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 confidential or 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 protections, 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 Our Financial Position and Need for Additional Capital

We had net losses in the years ended December 31, 2024 and 2023, have incurred significant losses in previous years and expect to incur losses in the future, and may never achieve or maintain profitability.

We had a net loss of $239.6 million in the year ended December 31, 2024 and $308.5 million in the year ended December 31, 2023. Other than a gain in the year ended December 31, 2021, which was primarily attributable to one-time license revenue from CSL Behring we have incurred significant losses throughout our operating history. As of December 31, 2024, we had an accumulated deficit of $1,130.0 million. We have financed our operations to date 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 2025 primarily from our existing cash resources. We have devoted substantially all our financial resources and efforts to date to research and development of our products and product candidates, including the conduct of preclinical studies and clinical trials and related manufacturing requirements. Even if we succeed in receiving marketing approval for and commercialize AMT-130 or other of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional potential products 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:

- incur costs associated with late-stage development of AMT-130 as well as the preparation of commercialization of AMT-130;
- continue to fund the clinical development of our other product candidates;
- 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 approval for AMT-130 and for any other product candidates;
- hire and retain personnel to support our business;
- enhance our operational, financial and management information systems and personnel;
- maintain, expand and protect our intellectual property portfolio; and
- incur legal, accounting and other expenses operating as a public company.

We 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. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business or otherwise increase the size of our future net losses. 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 and support the commercial launch of AMT-130, 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 to support the development of our product pipeline and continuing operations. On January 7, 2025, we entered into an underwriting agreement Leerink Partners LLC, Stifel, Nicolaus & Company, Incorporated and Guggenheim Securities, LLC., as representatives of the several underwriters named therein, in connection with the issuance and sale of 4,411,764 or our ordinary shares at a public offering price of $17.00 per share, less underwriting discounts and commissions, pursuant to a shelf registration statement on Form S-3 and accompanying prospectus (Registration No. 333-284168), which became effective upon filing on January 7, 2025, and a prospectus supplement thereunder. The offering closed on January 10, 2025, and we net proceeds of approximately $70.1 million, after deducting underwriting discounts and fees. We received an additional $10.6 million in net proceeds upon the underwriters' exercise of their option to purchase additional ordinary shares at the public offering price in February 2025. Based on our current operating plan, research and development plans and our timing expectations related to the progress of our programs, and following the January 2025 public offering, we believe that our existing cash and cash equivalents and investment securities will be sufficient to fund our operations through the second half of 2027. We have based our current estimates of our financing requirements on assumptions that may prove to be wrong, and we could use our capital resources sooner than we 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 business development and strategic initiatives, including divestitures such as the Lexington Transaction, acquisitions, partnerships, collaborations or other transactions, may not achieve their intended benefits or goals and may result in additional risks to our business.

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 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.

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 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 streamline operations and reduce 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 regulatory or 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.

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

As of December 31, 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. 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.

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, have in the past been 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.

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. 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 sales of approved products. 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;
- product recalls, withdrawals, revocation of approvals, or labeling, marketing, or promotional restrictions;
- diversion of resources of our management from pursuing 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 5,000,000 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 (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. 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.

There may be future changes in legal and regulatory requirements that may materially impact our results of operations.

Future changes in legal and regulatory requirements may introduce new risks into our operations and future prospects, which we are not able to currently anticipate. By example, changes taking place in the United States associated with a new federal administration, as well as changes in legal and regulatory standards, including the reduced level of deference due to administrative agencies following a 2024 Supreme Court decision, may introduce uncertainties with respect to our current and future operations and our future likelihood of success. It is possible that new federal or state laws or regulations may be passed, or laws and regulations may be enforced differently than they were before, which may expose us to additional legal and regulatory risk or uncertainty and require the expenditure of additional resources to ensure that we are able to comply. Such actions could also adversely restrict our business and operations. There could also be changes in FDA's approval standards that could impact our ability to obtain BLA approval and market our product candidates within the currently anticipated timeframes or otherwise impact the competitive market for our product candidates. Such changes may necessitate the conduct of additional development work, including preclinical and clinical trials, and manufacturing development. By example, for products intended for rare and serious diseases with unmet medical needs, FDA is authorized to exercise regulatory flexibility when making a medical risk-benefit judgment. It is possible that whether and how FDA exercises any such regulatory flexibility, including with respect to specialized pathways, such as accelerated approval, may change, which could impact our ability to obtain approval for AMT-130 or any of our product candidates. Further, legal and regulatory changes may impact how we may market and sell our products in the future, if they are approved, as well as how they are reimbursed. Moreover, there could be changes in the federal workforce and agency policies that may result in regulatory delays, including with respect to FDA's review of marketing applications and other submissions, and that may impact the ability to communicate with and obtain guidance from the agencies. At this time, it is too early to predict the exact nature of any changes that may take place or whether and how they may impact our business and results of operations.

Risks Related to Our Ordinary Shares

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

Our ordinary 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 February 24, 2025 the sale price of our ordinary shares ranged from a high of $82.49 to a low of $3.73. The closing price on February 24, 2025 was $11.48 per ordinary share.

In recent years, the stock market in general and the market for shares of biotechnology and 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 competing products or technologies;
- results of our clinical trials or those of our competitors;
- public perception and market reaction to our interim data from our clinical trials;
- public perception of gene therapies and companies developing gene therapies;
- interactions with the FDA and other regulatory authorities on the design of our clinical trials, regulatory endpoints and accelerated approval pathways available to us;
- regulatory delays and greater government regulation of potential products due to adverse events;
- regulatory, legal and political 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;
- pipeline reprioritizations, strategic transactions and restructurings;
- future issuances, sales, resales or repurchases or anticipated issuances, sales, resales or repurchases, of our ordinary shares, including due to the expiration of contractual lock-up agreements;
- 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 technologies;
- actual or anticipated changes in estimates as to financial results, development timelines;
- failure to meet expectations of investors or 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 realization of any of the 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 25.2% of our issued share capital. As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to influence 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 influence 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.

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 limited liability 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. Under Dutch law, our board members are required to act in the long-term interest of the company, considering the interests of shareholders, employees, and other stakeholders. This governance approach differs from that of some U.S. jurisdictions, where directors may focus primarily on maximizing shareholder value. As a result, decisions made by our board may 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, such as the public offering of our ordinary shares completed in January 2025. Our shareholders' reluctance to approve further issuances of ordinary shares could adversely affect our ability to raise capital and fund development programs and continued operations. Dutch corporate governance laws evolve over time, and future changes may impact the governance structure and shareholder rights applicable to Dutch public limited companies whose securities are traded in the United States or otherwise adversely affect the rights of investors.

For more information on relevant provisions of Dutch corporate law and of our articles of association, see the description of our capital stock included in Exhibit 4.1 and our articles of association filed as Exhibit 3.1 to this Annual Report on Form 10-K.

Provisions of our articles of association or Dutch corporate law might deter acquisition bids for us that might otherwise be considered favorable and could make it more difficult to replace our board, ensuring continuity and stability in corporate governance in line with Dutch law and case law requirements. t.

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 suspended 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.

Furthermore, in accordance with Dutch corporate law, shareholders with the right to propose agenda items for the general meeting or request the convening of a general meeting must first engage in consultation with the board. If exercising such rights may result in a change in our strategy (for example, through the dismissal of one or more directors), the board must be given the opportunity to invoke a reasonable period to respond to the shareholders' intentions. If invoked, the board must use such response period for further deliberation and constructive consultation with the concerned shareholder(s) and thereafter report on this consultation and the exploration of alternatives to the general meeting. The response period may be invoked only once for any given general meeting and shall not apply in respect of a matter for which a response period or a statutory cooling-off period (as discussed below) has been previously invoked.

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. Shareholders representing at least 3% of our issued share capital may request the Enterprise Chamber (*Ondernemingskamer*) for early termination of the cooling-off period. The Enterprise Chamber must rule in favor of the request if the shareholders can demonstrate that (i) our board of directors, in light of the circumstances at hand when the cooling-off period was invoked, could not reasonably have concluded that the relevant proposal or hostile offer constituted a material conflict with the interests of our company and its business, or

(ii) our board of directors cannot reasonably believe that a continuation of the cooling-off period would contribute to careful policy-making; or (iii) other defensive measures, having the same purpose, nature, and scope as the cooling-off period, have been activated during the cooling-off period.

We do not expect to pay dividends in the foreseeable future. Accordingly, any returns on an investment in our ordinary shares will likely depend entirely upon any future appreciation in the price of our ordinary shares, which is uncertain.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently expect 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 paying dividends. In addition, payment of future cash dividends may be made only if our shareholders' (deficit) / equity exceeds the sum of our paid-in and called-up share capital plus the reserves required to be maintained by Dutch law or by our articles of association. 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.

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.

We believe that we were a passive foreign investment company ("PFIC") for the 2024 taxable year. A corporation organized outside the U.S. generally will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which at least 75% of its gross income is passive income or on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held to produce passive income. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions. Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will continue to qualify as a PFIC in future taxable years. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate, and may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were considered a PFIC for the current taxable year or any future taxable year during which a U.S. holder holds ordinary shares, certain adverse U.S. federal income tax consequences may apply to such U.S. holders and a such 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. A U.S. holder may be able to make certain tax elections that would lessen the adverse impact of PFIC status; however, in order to make certain of 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 ordinary shares, the possible implications to them of our being treated as a PFIC (including the availability of applicable elections, and whether making any such election would be advisable in their particular circumstances) as well as the U.S. federal, state, local and foreign tax considerations applicable to such holders in connection with the purchase, ownership and disposition of our ordinary 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. Accordingly, under Dutch private international law, the rights and obligations of our shareholders vis-à-vis the company originating from Dutch corporate law and our articles of association, as well as the civil liability of our officers (*functionarissen*), including our directors and executive officers, are governed in certain respects by Dutch law.

Certain of our executive officers reside outside the United States. Depending on the subject matter of the action brought against us and/or our officers, United States courts may lack jurisdiction over such persons. If a Dutch court has jurisdiction, that court will apply Dutch procedural law and Dutch private international law to determine applicable substantive law. Depending on the subject matter of the claim, a competent Dutch court may apply Dutch law rather than U.S. securities law. 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. Dutch courts typically do not apply U.S. securities laws directly, but they may consider them if a claim is refiled under Dutch legal principles (such as under general tort law (*onrechtmatige daad*).

The U.S. and the Netherlands currently do not have a treaty providing for the automatic recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. In addition, both the Hague Convention on Choice of Court Agreements (2005) and the Hague Judgments Convention (2019) have entered into force for the Netherlands but have not entered into force for the United States. As a result, 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 enforced 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 Dutch public policy (*ordre public*). Dutch courts may deny the recognition and enforcement of punitive damages or damages that exceed actual compensation. Recognition and enforcement of foreign judgments are solely governed by the Dutch Civil Procedure Code (*Wetboek van Burgerlijke Rechtsvordering*).

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.

We are not obligated to, and do not, comply with all best practice provisions of the Dutch Corporate Governance Code.

We are subject to the Dutch Corporate Governance Code (the "DCGC"). The DCGC contains principles and best practice provisions on corporate governance that regulate relations between the board and the general meeting and matters in respect of financial reporting, auditors, disclosure, compliance and enforcement standards. The DCGC follows the principle of "comply or explain". Accordingly, companies must disclose in their statutory annual reports whether they comply with the provisions of the DCGC. If a company, subject to the DCGC, does not comply with certain provisions, it must provide an explanation for such non-compliance. While we are subject to the DCGC, we do not comply with all of its best practice provisions. This may affect your rights as a shareholder and you may not have the same level of protection as a shareholder in a Dutch company that fully complies with the DCGC.

General Risks

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 subject to the notice provisions in such agreements. 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.

We may be adversely affected by unstable market and economic conditions and potential macroeconomic effects, such as inflation, new or increased tariffs and higher interest rates, which may negatively impact our business, financial condition and share price.

Macroeconomic conditions beyond our control such as economic instability, changes in tax laws and regulations, including based on the recent U.S. presidential election, trade restrictions, additional tariffs, export controls, inflation, high interest rates, volatile energy costs, geopolitical issues, armed hostilities, such as the ongoing conflicts between Russia and Ukraine and in the Middle East, 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 investments outside of the biotechnology sector with more predictable investment 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 share price or could require us to delay or abandon development or commercialization plans.

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

Our management is responsible for establishing and maintaining adequate internal control over financial reporting and disclosure controls. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with applicable accounting principles. 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 or disclosure controls, we could experience material misstatements in our financial statements and fail to meet our reporting obligations under the Exchange Act, which would likely cause investors to lose confidence in our reported financial information or disclosures. This could in turn limit our access to capital markets and our ability to fund our business, harm our results of operations, and could 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.

Our internal computer systems, or those of our collaborators, third-party vendors, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our business and 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 and hackers, malicious code, employee theft or misuse, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures, among other potential risks. The size and complexity of our information technology systems, and those of our collaborators, third-party vendors, contractors and consultants, and the large amounts of proprietary and confidential information stored on these 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 patients involved in our clinical trials or our 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 and expose us to claims for damages, regulatory fines, penalties or litigation. 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 designed 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 this Annual Report on Form 10-K for more information regarding our cybersecurity risk management, strategy and governance.

If securities or industry analysts do not publish, 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 ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not control these analysts, or the content and opinions included in their reports. If one or more of the analysts who cover us downgrades our ordinary shares or publishes inaccurate or unfavorable research about our business, our ordinary share price could 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 share 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, along with expected regulatory approval timelines for our product candidates. 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 share price may decline.

Environmental sustainability and social initiatives that we undertake may impose additional costs on our business and expose us to new risks.

Concern over the impact of climate change may result in new or additional legislative and regulatory requirements to reduce or mitigate its effects on the environment, which could result in increased expenses and expenditure of company resources as we seek to comply with such requirements. More broadly, there has been increasing public focus by shareholders, patients, activists, the media, governmental and non-governmental organizations and other constituencies on a variety of environmental, social and other sustainability matters, resulting in new and pending international agreements and national, regional, and local legislation, regulatory measures, public reporting obligations and potential policy changes across jurisdictions.

We may experience pressure in some of the countries in which we operate to make commitments with respect to our greenhouse gas emissions as well as other sustainability-focused matters. 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, including new reporting requirements for businesses operating in the European Union, which may require the that we dedicate additional capital and personnel resources toward compliance with these measures. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be harmed. Furthermore, increasing attention on environmental and sustainability 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. We cannot guarantee that any initiatives we adopt to respond to stakeholder expectations will have the desired effect. Moreover, initiatives that we adopt in some countries in which we operate may be viewed differently in other countries in which we operate. Any failure to meet the expectations of our investors, regulators, stock exchanges or other stakeholders with respect to sustainability matters could materially adversely affect our business, financial condition, and results of operations.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We recognize the importance of assessing, identifying, and managing material risks associated with cybersecurity threats, as such term is defined in Item 106(a) of Regulation S-K. These risks include, among other things, operational risks, the risk of intellectual property theft, fraud, harm to employees or third parties with which we conduct business and violation of data privacy or security laws.

Identifying and assessing cybersecurity risk is integrated into our overall risk management systems and processes. Cybersecurity risks related to our business are identified and addressed through a multi-faceted approach that consists of third-party assessments, testing of our information systems and information technology security. To defend against, detect and respond to cybersecurity incidents, we, among other things: have enabled regular monitoring of our environment by a combination of external partners and internal security tools, conduct regular employee trainings, monitor emerging laws and regulations related to data protection and information security and implement appropriate changes.

Consistent with our cybersecurity risk management policies and controls, we have prepared and implemented an incident response plan with several components, including: (i) engagement of a third party security operations center for regular vulnerability scanning and technical monitoring of our systems, (ii) detection and analysis of cybersecurity incidents that present risk of unauthorized access to company assets, including the escalation and triaging of incidents that present acute risks to our business, (iii) containment, eradication and data recovery, and (iv) post-incident analysis. Such incident responses are overseen by leaders from our information technology, finance, legal and compliance teams.

Cybersecurity events and data incidents are evaluated, assessed based on severity and prioritized for response and remediation. Under our incident response plan and related policies, incidents are evaluated to determine materiality as well as operational and business impact and reviewed for privacy impact. Our team of cybersecurity professionals then collaborate with technical and business stakeholders to further analyze the risk to the company, and form detection, mitigation and remediation strategies. As part of the above processes, we regularly engage external consultants to assess our internal cybersecurity programs and compliance with applicable practices and standards.

Cybersecurity Governance

Cybersecurity is an important part of our risk management processes and an area of focus for our board of directors and management team. Our board of directors has delegated responsibility to the Audit Committee for the oversight of risks from cybersecurity threats. Members of the Audit Committee receive regular updates from senior management, including leaders from our information technology, legal and compliance teams regarding matters of cybersecurity. This includes existing and new cybersecurity risks, information on how management is addressing and/or mitigating those risks, cybersecurity incidents (if any) and status on key information security initiatives.

Despite our cybersecurity efforts, we may not be successful in preventing or mitigating a cybersecurity incident that could have a material adverse effect on our business. For a discussion of cybersecurity risks applicable to us, see Part I, Item 1A, *Risk Factors*, under the heading “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” in this Annual Report on Form 10-K.

Item 2. Properties.

We operate approximately 12,000 square feet of multi-use office space in Lexington, Massachusetts, which is subject to a lease that expires in 2030 and may be renewed for one subsequent five-year term.

We operate approximately 111,000 square feet (seven floors) of multi-use space in Amsterdam, The Netherlands, which is subject to a lease that, as amended to date, terminates in 2032 with an option to extend the lease in five-year increments. To date we have entered into subleases with respect to two of the seven floors in the Amsterdam facility. We lease an additional approximately 12,000 square feet of space in the Amsterdam facility, which is subject to a lease that expires in December 2027.

We operate approximately 7,400 square feet of multi-use office space in Basel, Switzerland, which is subject to a lease that expires in 2026 and may be renewed for two subsequent terms of three years.

We believe that our facilities are adequate to meet current needs and that suitable alternative spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Part II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our ordinary shares are listed on the Nasdaq Global Select Market under the symbol "QURE". We have never paid any cash dividends on our ordinary shares, and we do not anticipate paying cash dividends in the foreseeable future. We anticipate that we will retain all earnings, if any, to support operations and to finance the growth and development of our business for the foreseeable future.

Unregistered Sales of Equity Securities

During the period covered by this Annual Report on Form 10-K, we have not issued any securities that were not registered under the Securities Act of 1933, as amended (the "Securities Act").

Issuer Purchases of Equity Securities

We did not make any purchases of our ordinary shares during the period covered by this Annual Report on Form 10-K.

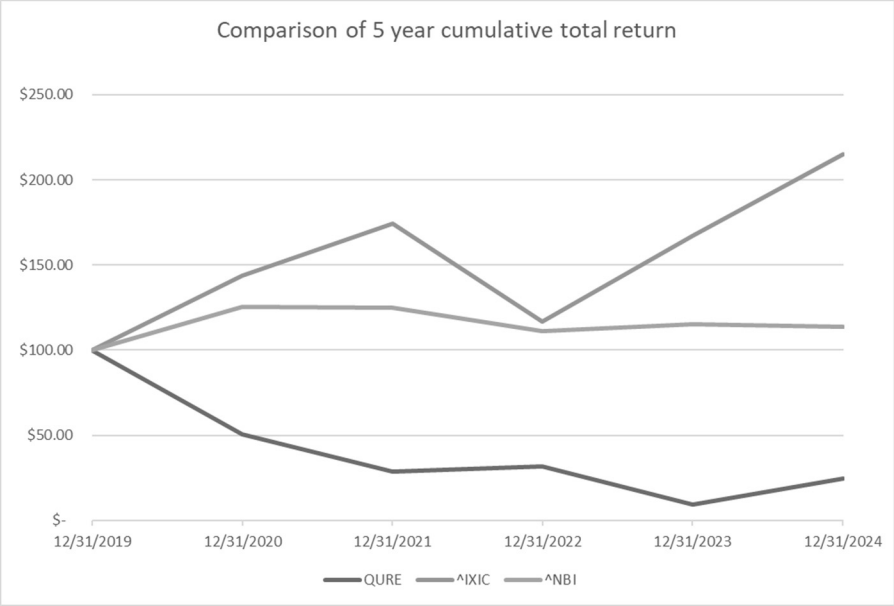
Holders

As of February 24, 2025, there were approximately three holders of record of our ordinary shares. The actual number of shareholders is greater than this number of record holders, and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include shareholders whose shares may be held in trust by other entities.

Share Performance Graph

The following graph compares the performance of our ordinary shares ("QURE") for the periods indicated with the performance of the NASDAQ Composite Index ("^IXIC") and the Nasdaq biotechnology index ("^NBI"). This graph assumes an investment of $100 after market close on December 31, 2019 in each of our ordinary shares, the NASDAQ Composite Index, and the NASDAQ Biotechnology Index. Pursuant to the applicable SEC rules, all values assume reinvestment of the full amount of all dividends; however, no dividends have been declared on our ordinary shares to date. The performance of our ordinary shares shown on the graph below is not necessarily indicative of the future performance of our ordinary shares.

This graph and related information are not "soliciting material," is not deemed "filed" with the SEC and, except to the extent incorporated by reference, is not to be incorporated by reference into any of our filings under the Securities Act, or the U.S. Securities Exchange Act of 1934, as amended (the "Exchange Act"), whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following Management's Discussion and Analysis of Financial Condition and Results of Operations ("MD&A") is intended to help the reader understand our results of operations and financial condition. This MD&A is provided as a supplement to, and should be read in conjunction with, our audited consolidated financial statements and the accompanying notes thereto and other disclosures included in this Annual Report on Form 10-K, including the disclosures under "Risk Factors." Our 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.

Except for the historical information contained herein, the matters discussed in this MD&A may be deemed to be forward-looking statements. Forward-looking statement 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. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Words such as "may," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements.

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, refractory mesial temporal lobe epilepsy ("mTLE"), and Fabry disease.

Huntington's disease program (AMT-130)

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 the U.S. and European studies. 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. As of February 2025, we have enrolled 12 patients into a third cohort to further investigate both doses of AMT-130 together with perioperative immunosuppression using the current, established stereotactic administration procedure.

RMAT Designation

In June 2024, we announced that the FDA granted us RMAT designation for AMT-130.

Updated Interim Data

In July 2024, we announced updated interim clinical data, including up to 24 months of follow-up data from 29 patients enrolled in the U.S. study and the European study as of a March 31, 2024 cut-off date.

Regulatory Alignment

In December 2024, following our initial Type B meeting, we announced that we had reached agreement with FDA on key elements of an accelerated approval pathway for AMT-130.

Other clinical candidates

In November 2024, we announced that the that the first patient was dosed in the GenTLE Phase I/IIa clinical trial of AMT-260 for the treatment of refractory mTLE. In addition, the FDA recently approved a protocol amendment expanding the inclusion criteria for certain patients in the first cohort to include patients with non-lesional mesial temporal lobe epilepsy in the non-dominant hemisphere.

In August 2024, we announced that the first patient was dosed in a Phase I/IIa clinical trial of AMT-191 for the treatment of Fabry disease. In February 2025, we announced that we completed the enrollment of the first cohort of the clinical trial and that we would proceed enrolling the second cohort of the clinical trial.

In October 2024, we announced the first patient was dosed in a Phase I/IIa clinical trial of AMT-162 for the treatment of SOD1-ALS. In January 2025, we announced that we completed the enrollment of the first cohort of the clinical trial and that we would proceed enrolling the second cohort of the clinical trial.

Sale of commercial manufacturing activities

In June 2024, we and Genezen entered into the Lexington Transaction, which closed in July 2024. Genezen acquired manufacturing facility including equipment and related manufacturing operations with a carrying value of $15.2 million, inventory with a carrying value of $8.8 million and certain other assets (including allocated goodwill) with a carrying value of $2.8 million associated with the Lexington Facility on Closing.

As consideration for the Lexington Transaction, we received from Genezen (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 valued at $13.3 million and (iii) a right to purchase HEMGENIX® at terms considered favorable to market terms (the "Consideration") valued at $16.7 million. We also included a firm purchase commitment liability, valued at $8.8 million for our customer contract with CSL Behring inherently related to the right to purchase HEMGENIX® in the consideration received.

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

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 CSA, Genezen manufactures and supplies CSL Behring's commercial demand for HEMGENIX® on our behalf. 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.

Organizational restructuring

In August 2024, we announced the Restructuring to conserve capital and streamline the organization. As a result of the Restructuring and Lexington Transaction, we eliminated approximately 300 positions or 65% of our workforce.

We substantially completed the Restructuring at the end of 2024. We have incurred $5.2 million of employee severance costs in the year ended December 31, 2024 and estimate that we will incur additional costs in the range of $0.5 million to $1.0 million in 2025.

Financing

Royalty financing agreement

In May 2023, we 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, we received an upfront payment of $375.0 million in exchange for the Purchaser's rights to the lowest royalty tier on CSL Behring's worldwide net sales of HEMGENIX® for certain current and future royalties due to us. We will be obligated to pay $25.0 million of the first worldwide sales milestone payment from CSL Behring, if received, to the Purchaser. The Purchaser will receive 1.85 times the upfront payment (or $693.8 million) 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 payment through December 31, 2038 ("Second Hard Cap Date"). If, on or prior to the defined dates for each cap amount, the total amount of royalty payments received by the Purchaser equals or exceeds the cap amount applicable to such date, the Royalty Financing Agreement will automatically terminate and all rights to the HEMGENIX® royalty payments will revert back to us. We have no obligation to repay any amounts received from the Purchaser in the event that the applicable cap amount is not reached during the term of the Royalty Financing Agreement.

As of December 31, 2024 we expect to satisfy our commitment to the Purchaser prior to the Second Hard Cap Date. Until December 2024, we assumed that we would satisfy the commitments to the Purchaser prior to the First Hard Cap Date.

We 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.

Hercules loan repayment and amendment

Upon entering into the Royalty Financing Agreement in May 2023, we and Hercules amended our existing term loan facility. Through the May 2023 amendment we extended the maturity date and interest-only period from December 1, 2025 to January 5, 2027 (the "Maturity Date").

In connection with the Closing we once more amended the facility. As a condition to Hercules' consent to the Lexington Transaction we prepaid $50.0 million of the total $100.0 million principal outstanding in July 2024. The remaining $50.0 million principal outstanding will need to be repaid at the Maturity Date.

Financing

In January 2025, we raised $70.1 million of net proceeds, after deducting underwriting discounts and commissions and other offering expenses payable by us, through a follow-on public offering of 4.4 million ordinary shares at a price to the public of $17.00 per ordinary share. In February 2025, we raised an additional $10.6 million in net proceeds upon the underwriters' exercise of their option to purchase an additional 0.7 million ordinary shares at the public offering price.

Financial Highlights

Key components of our results of operations include the following:

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Total revenues	$ 27,119	$ 15,843	$ 106,483
Cost of license revenues	(1,267)	(65)	(1,254)
Cost of contract manufacturing revenues	(17,060)	(13,563)	(2,089)
Research and development expenses	(143,782)	(214,864)	(197,591)
Selling, general and administrative expenses	(52,657)	(74,591)	(55,059)
Net loss	(239,556)	(308,478)	(126,789)

As of December 31, 2024, we had $367.5 million in cash and cash equivalents and investment securities (December 31, 2023: $617.9 million cash and cash equivalents and investment securities). We had a net loss of $239.6 million in 2024 and a net loss of $308.5 million and $126.8 million in 2023 and 2022, respectively. As of December 31, 2024, we had an accumulated deficit of $1,130.0 million (December 31, 2023: $890.4 million).

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

Critical Accounting Policies and Estimates

In preparing our consolidated financial statements in accordance with U.S. GAAP and pursuant to the rules and regulations promulgated by the SEC we make assumptions, judgments and estimates that can have a significant impact on our net loss/income and affect the reported amounts of certain assets, liabilities, revenue and expenses, and related disclosures. On an ongoing basis, we evaluate our assumptions, estimates and judgments, including those related to what we believe to be our critical accounting policies. Refer to Note 2 *"Summary of significant accounting policies"* for a summary of our significant accounting policies.

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, judgments or estimates. We also discuss our critical accounting estimates with the Audit Committee of our Board of Directors.

We consider the following to be our critical accounting estimates in the year ended December 31, 2024:

- Contingent consideration recorded in relation to the uniQure France SAS business combination;
- Valuation of the intangible asset with favorable terms recorded as part of the Lexington Transaction;
- Date at which we expect to satisfy the commitment under the Royalty Financing Agreement.

Contingent consideration

In July 2021 ("Acquisition Date"), we acquired uniQure France SAS ("Acquisition Date") and we recorded contingent consideration related to amounts potentially payable to uniQure France SAS's former shareholders. The amounts payable in accordance with the share and purchase agreement ("SPA") are contingent upon realization of certain milestones associated with AMT-260. Contingent consideration was measured at fair value at the Acquisition Date with changes in fair value recognized in the consolidated statements of operations in research and development expenses.

Changes in contingent consideration can result from changes in the assumed achievement and timing of estimated milestones and the discount rate used to estimate the fair value of the liability:

- We had used discount rates ranging from 15.3% to 15.6% to calculate the contingent consideration as of December 31, 2023. As of December 31, 2024 we used discount rates ranging from 15.3% to 16.2% to reflect increases in market interest rates. An increase in the discount rate reduces the fair value of the contingent consideration liability whereas a decrease in the discount rate increases the fair market value of the contingent consideration liability.

- We need to regularly update our estimate of when a milestone is expected to be achieved. An achievement of a milestone at a later than currently expected date reduces the fair value of the contingent consideration liability whereas an achievement at an earlier than currently expected date increases the fair value of the contingent consideration liability.

- We initially recorded the contingent consideration liability on the Acquisition Date assuming a 40% probability of advancing the TLE research program into clinical development. We developed this estimate using data from an external study regarding the average likelihood of advancing into clinical development at a certain stage or preclinical development. For the year ended December 31, 2022, we had increased the probability to 66.0% following the commencement of toxicology studies for the TLE program. During the year ended December 31, 2023 we increased the probability to 100.0% following the clearance of the IND application for AMT-260 in August 2023. We did not change the probabilities of any further milestones following the dosing of the first patient in a Phase I/II clinical trial in November 2024. The increase in probabilities resulted in a $14.2 million expense in the year ended December 31, 2023 and a $4.4 million expense in the year ended December 31, 2022. This also resulted in an increase of the probability that AMT-260 may advance to late-stage development and commercialization.

The fair value of the contingent consideration liability as of December 31, 2024 was EUR 10.5 million ($10.9 million) and as of December 31, 2023 was EUR 39.0 million ($43.0 million). The reduction was primarily driven by a EUR 26.8 million ($28.2 million) milestone payment we made in December 2024 related to the first patient dosed in the AMT-260 clinical trial. If as of December 31, 2024, we 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 EUR 33.7 million ($35.0 million). If as of December 31, 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.

Intangible asset

Part of the consideration received in the Lexington Transaction included 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 value required us to estimate the current and future commercial supply prices of HEMGENIX® to compare these to the contractually agreed terms at Closing. 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, relevant market data, current and historical commercial supply agreements, as well as historical production cost information 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.

Date at which we expect to satisfy the commitment under the Royalty Financing Agreement

On May 12, 2023, we entered into the Royalty Financing Agreement with the Purchaser. Under the terms of the Royalty Financing Agreement we 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 us (refer to Note 13 "Royalty Financing Agreement" for further details). Pursuant to the agreement, the total amount of royalties to be received by the Purchaser is subject to an increasing cap equal to (i) $693.8 million up to the First Hard Cap Date if such thresholds are met or, if such cap is not met by the First Hard Cap Date (ii) $843.8 million through the Second Hard Cap Date. If, on or prior to the defined dates for each cap amount, the total amount of royalty payments received by the Purchaser equals or exceeds the cap amount applicable to such date, the Royalty Financing Agreement will automatically terminate and all rights to the HEMGENIX® royalty payments will revert back to us. We have no obligation to repay any amounts received from the Purchaser in the event that the applicable cap amount is not reached during the term of the Royalty Financing Agreement.

As of December 31, 2024, we expect to satisfy our commitment to the Purchaser prior to the Second Hard Cap Date. Until December 2024, we assumed that we would satisfy the commitments to the Purchaser prior to the First Hard Cap Date. As a result of this change in estimate we expect that our total payments of interest expense will increase from $318.8 million by $150.0 million to $468.8 million over a term that was extended from 9 years to 15.5 years.

Revenue recognition related to CSL Behring variable milestone payments

We sold the exclusive global rights HEMGENIX™ to CSL Behring in 2021. The consideration received included variable milestone payments which we recorded as revenue once probable. We recorded $100.0 million of variable milestone revenue related to a first sale of HEMGENIX™ as license revenue in the year ended December 31, 2022 following the November 2022 BLA approval. We collected the payment in July 2023. We do not consider this to be a critical accounting estimate for the years ended December 31, 2024 and 2023 because we currently do not expect to recognize any regulatory milestone payments within the next 12 months.

Recently Adopted Accounting Pronouncements

In the year ended December 31, 2024, we adopted Accounting Standards Update (ASU) 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07"). This update requires us to disclose segment expenses that are significant and regularly provided to our chief operating decision maker ("CODM"). In addition, ASU 2023-07 requires us to disclose the title and position of its CODM and how the CODM uses segment profit or loss information in assessing segment performance and deciding how to allocate resources. The adoption of this update did not have a material impact on our financial position or results of operations but resulted in expanded disclosures in the segment reporting section of the financial statements. We adopted ASU 2023-07 using a retrospective transition method.

Results of Operations

The following table presents a comparison of the years ended December 31, 2024, 2023 and 2022.

	Year ended December 31,				
	2024	2023	2022	2024 vs 2023	2023 vs 2022
			(in thousands)		
Total revenues	$ 27,119	$ 15,843	$ 106,483	$ 11,276	$ (90,640)
Operating expenses:					
Cost of license revenues	(1,267)	(65)	—	(1,202)	(65)
Cost of contract manufacturing	(17,060)	(13,563)	(3,343)	(3,497)	(10,220)
Research and development expenses	(143,782)	(214,864)	(197,591)	71,082	(17,273)
Selling, general and administrative expenses	(52,657)	(74,591)	(55,059)	21,934	(19,532)
Total operating expenses	**(214,766)**	**(303,083)**	**(255,993)**	**88,317**	**(47,090)**
Other income	7,926	6,059	7,171	1,867	(1,112)
Other expense	(4,573)	(1,690)	(820)	(2,883)	(870)
Loss from operations	**(184,294)**	**(282,871)**	**(143,159)**	**98,577**	**(139,712)**
Non-operating expense, net	(52,833)	(23,686)	14,900	(29,147)	(38,586)
Loss before income tax benefit	**$ (237,127)**	**$ (306,557)**	**$ (128,259)**	**69,430**	**(178,298)**
Income tax (expense) / benefit	(2,429)	(1,921)	1,470	(508)	(3,391)
Net loss	**$ (239,556)**	**$ (308,478)**	**$ (126,789)**	**$ 68,922**	**$ (181,689)**

Revenues and cost of revenues

Our revenues and associated costs for the years ended December 31, 2024, 2023 and 2022 were as follows:

	Year ended December 31,				
	2024	2023	2022	2024 vs 2023	2023 vs 2022
			(in thousands)		
License revenues	$ 10,133	$ 2,758	$ 100,000	$ 7,375	$ (97,242)
Contract manufacturing revenues	6,114	10,835	1,717	(4,721)	9,118
Collaboration revenues	10,872	2,250	4,766	8,622	(2,516)
Total revenues	**$ 27,119**	**$ 15,843**	**$ 106,483**	**$ 11,276**	**$ (90,640)**
Cost of license revenues	(1,267)	(65)	(1,254)	(1,202)	1,189
Cost of contract manufacturing revenues	(17,060)	(13,563)	(2,089)	(3,497)	(11,474)
Total cost	**$ (18,327)**	**$ (13,628)**	**$ (3,343)**	**$ (4,699)**	**$ (10,285)**

CSL Behring

We sold the exclusive global rights to HEMGENIX® to CSL Behring in 2021 ("License Sale"). We recognize license revenue in relation to the License Sale when it becomes probable that regulatory and sales milestone events will be achieved as well as when royalties on sales of HEMGENIX® have been earned. We recognized $10.1 million, $2.8 million and $100.0 million of license revenue for the years ended December 31, 2024, 2023 and 2022, respectively. We recognized $10.1 million and $2.8 million of license revenue in 2024 and 2023 related to royalty payments owed on HEMGENIX® sales, when earned. We recognized $100.0 million of license revenue in 2022 related to a milestone payment owed on the first sale of HEMGENIX® in the U.S. in 2023.

In 2008, we entered into a license agreement with St. Jude Children's Research Hospital ("St. Jude"), which we amended in 2012. Under this license agreement, St. Jude has granted us an exclusive license, with a right to sublicense, to patent rights relating to expression of hFIX in gene therapy vectors, to make, import, distribute, use, and commercialize products containing hFIX covered by a valid patent claim in the field of gene therapy for treatment or prophylaxis of hemophilia B. The majority of the U.S. patent rights will expire in 2028 and the European patent rights (along with one U.S. patent) will expire in 2025.

With respect to our collaboration with CSL Behring, we have agreed with St. Jude on an apportionment of certain amounts we receive from CSL Behring as sublicensing revenue that is equivalent to a low-single digit percentage of such amounts. The agreement will remain in effect until no further payment is due relating to any licensed product under this agreement or either we or St. Jude exercise our rights to terminate it. St. Jude may terminate the agreement in specified circumstances relating to our insolvency. We may terminate the agreement for convenience at any time subject to a specified notice period.

We treat license payments to St. Jude as contract fulfillment costs associated with license revenue we receive from CSL Behring and recognize these as costs of license revenues. We incurred $1.3 million, $0.1 million and $1.3 million of such cost in the years ended December 31, 2024, 2023 and 2022, respectively.

We recognize collaboration revenues associated with services we provide to CSL Behring. Collaboration revenue is recognized when the performance obligations are satisfied. We recognized $10.9 million, $2.3 million and $3.0 million of collaboration revenue for the years ended December 31, 2024, 2023 and 2022, respectively. The increase in collaboration revenue in 2024 of $8.6 million compared to 2023 was primarily related to additional development and other services provided in relation to the transfer of manufacturing responsibility to CSL Behring. The decrease in collaboration revenue in 2023 of $0.7 million compared to 2022 was primarily related to a reduction in services requested by CSL Behring following the submissions of the BLA and MAA for HEMGENIX® in 2022.

We provided contract manufacturing service to CSL Behring between April 2022 and July 2024. We transferred these activities to Genezen as part of the Lexington Transaction. Following the Closing of the Lexington Transaction, title to HEMGENIX® supply directly passes from the contract manufacturer, Genezen, to CSL Behring. We do not control HEMGENIX® before it is transferred to CSL Behring. We arrange for HEMGENIX® to be provided by Genezen to CSL Behring. We determined that we are an agent in the sale of HEMGENIX® to CSL Behring.

As a result of being an agent, we recognize 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. We recognized contract manufacturing revenues related to contract manufacturing HEMGENIX® for CSL Behring when earned upon sales of HEMGENIX® to CSL Behring. We recognized $6.1 million, $10.8 million and $1.7 million contract manufacturing revenues in the years ended December 31, 2024, 2023 and 2022, respectively.

We incurred $17.1 million of cost of contract manufacturing revenues related to the manufacture of HEMGENIX® in the year ended December 31, 2024 and $13.6 million and $2.1 million of cost of contract manufacturing revenues, in the years ended December 31, 2023 and 2022 respectively. Costs of contract manufacturing revenues increased in the year ended December 31, 2024 compared to the year ended December 31, 2023 primarily due to expensing costs that could not be recovered from selling HEMGENIX® under the terms of our development and commercial supply agreement with CSL Behring. Costs of contract manufacturing revenues increased in the year ended December 31, 2023 compared to the year ended December 31, 2022 due to the increase in sales of HEMGENIX® and a write-down of inventory that had a cost basis in excess of its expected net realizable value.

BMS

Following the termination of the collaboration, research and license agreements and the amended agreements with Bristol-Myers Squibb ("BMS") in February 2023, we did not recognize any further revenue for services rendered. We recognized nil collaboration revenue for the years ended December 31, 2024 and 2023 and $1.8 million for the year ended December 31, 2022.

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 research and development expenses primarily consist of costs incurred for the research and development of our product candidates, which include:

- *AMT-130 (Huntington's disease).* We have been incurring costs related to our U.S. study since February 2019. Since 2021, we have also incurred costs related to our European study;
- AMT-260 *(Temporal lobe epilepsy)*. We have incurred costs related to the development of AMT-260. We acquired this program in July 2021;
- AMT-191 *(Fabry disease)*. We have incurred costs related to the development of AMT-191 for the treatment of Fabry disease;
- AMT-162 (*Amyotrophic Lateral Sclerosis caused by mutations in SOD1*) We have incurred costs related to the acquisition in addition to costs incurred to initiate and conduct a Phase I/II clinical trial;
- *AMT-061 (Hemophilia B)*. 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 periods ended December 31, 2023 and 2024 are presented net of reimbursements due from CSL Behring and include settlement amounts from the transition.
- *Preclinical research programs*. We incurred costs related to the research of multiple preclinical gene therapy product candidates with the potential to treat certain rare and other serious medical conditions; and
- *Technology platform development and other related research*. We incurred significant research and development costs related to manufacturing prior to the Closing of the Lexington Transaction and other enabling technologies that are applicable across all our programs.

Our R&D expenses may vary substantially from period to period based on the timing of our research and development activities, including 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.

Research and development expenses for the year ended December 31, 2024 were $143.8 million, compared to $214.9 million and $197.6 million for the years ended December 31, 2023 and 2022, respectively. Other research and development expenses are separately classified in the table below. These are not allocated as they are deployed across multiple projects under development.

	Year ended December 31,				
	2024	2023	2022	2024 vs 2023	2023 vs 2022
			(in thousands)		
Huntington's disease (AMT-130)	$ 17,989	$ 12,991	$ 19,846	$ 4,998	$ (6,855)
Temporal lobe epilepsy (AMT-260)	12,053	13,037	16,199	(984)	(3,162)
Amyotrophic lateral sclerosis (AMT-162)	7,306	16,039	—	(8,733)	16,039
Fabry disease (AMT-191)	4,814	2,659	2,862	2,155	(203)
Programs in preclinical development and platform related expenses	3,927	11,005	7,157	(7,078)	3,848
Hemophilia B (AMT-061)	—	(1,336)	2,474	1,336	(3,810)
Total direct research and development expenses	**$ 46,089**	**$ 54,395**	**$ 48,538**	**$ (8,306)**	**$ 5,857**
Employee and contractor-related expenses	49,818	74,514	64,935	(24,696)	9,579
Facility expenses	21,627	29,490	23,582	(7,863)	5,908
Share-based compensation expense	9,295	16,881	18,402	(7,586)	(1,521)
Disposables	5,084	13,232	17,830	(8,148)	(4,598)
Severance costs	3,967	2,188	—	1,779	2,188
Impairment charge	—	1,438	—	(1,438)	1,438
Fair value changes related to contingent consideration	(1,817)	15,895	7,081	(17,712)	8,814
Other expenses	9,719	6,831	17,223	2,888	(10,392)
Total other research and development expenses	**$ 97,693**	**$ 160,469**	**$ 149,053**	**$ (62,776)**	**$ 11,416**
Total research and development expenses	**$ 143,782**	**$ 214,864**	**$ 197,591**	**$ (71,082)**	**$ 17,273**

Direct research and development expenses

Huntington disease (AMT-130)

In the years ended December 31, 2024, 2023 and 2022, we incurred $18.0 million, $13.0 million and $19.8 million expenses respectively. Our external costs for the development of AMT-130 were primarily related to the execution of our U.S. and European studies. The increase of $5.0 million in external cost in 2024 compared to 2023 is a result of enrolling patients into a third cohort between November 2023 and December 2024 as well as expenses we incurred associated with the RMAT application and in preparation of the Type B meeting with the FDA in November 2024. The decrease of $6.8 million in external cost in 2023 compared to 2022 is a result of the completion of U.S. patient enrollment in March 2022.

Temporal lobe epilepsy (AMT-260)

In the years ended December 31, 2024, 2023 and 2022 we incurred $12.1 million, $13.0 million and $16.2 million expenses respectively. In August 2023, the FDA cleared our IND application, and we started incurring costs for the preparation of a Phase I clinical trial.

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

In January 2023, we entered into a global licensing agreement with Apic Bio for AMT-162. In the years ended December 31, 2024 and 2023, we incurred $7.3 million and $6.0 million of expenses, respectively, to initiate a Phase I/II clinical trial in which enrolled the first patient in October 2024. During the year ended December 31, 2023, we incurred expenses of $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 years ended December 31, 2024, 2023 and 2022 we incurred $4.8 million, $2.7 million and $2.9 million expenses, respectively, related to our development of AMT-191. In November 2023, the FDA cleared the IND application, and we started incurring additional costs for Phase I/II clinical trial preparation. Costs incurred in the year ended December 31, 2022 primarily related to our preclinical activities.

Preclinical programs & platform development

In the years ended December 31, 2024, 2023 and 2022 we incurred $3.9 million, $11.0 million and $7.2 million expenses, respectively, related to our preclinical activities associated with product candidates for various other research programs and technology innovation projects.

Hemophilia B (AMT-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 years ended December 31, 2023 and 2022 are presented net of reimbursements due from CSL Behring and include settlement amounts from the transition.

Other research & development expenses

- We incurred $49.8 million in employee and contractor expenses in the year ended December 31, 2024 compared to $74.6 million in 2023 and $64.9 million in 2022. Our cost decreased in 2024 by $24.7 million compared to 2023 primarily as a result of the July 2024 Lexington Transaction as well as the October 2023 and August 2024 reorganizations. The increase in 2023 of $9.6 million, compared to 2022, primarily related to the hiring of new personnel and contractors in 2022 through mid-2023 to support our clinical-stage programs and manufacturing operations;
- We incurred $21.6 million in operating expenses and depreciation expenses related to our rented facilities in Amsterdam and Lexington, Massachusetts in the year ended December 31, 2024 compared to $29.4 million in 2023 and $23.6 million in 2022. The decrease in 2024 compared to 2023 of $7.9 million is primarily a result of the July 2024 Lexington Transaction. Our costs increased by $5.9 million in 2023 compared to 2022 as a result of incurring additional operating and depreciation expenses in both our Lexington and Amsterdam facilities;
- We incurred $9.3 million in share-based compensation expenses in the year ended December 31, 2024 compared to $16.9 million in 2023 and $18.4 million in 2022. The decrease in 2024 of $7.6 million, compared to 2023, is primarily a result of the July 2024 Lexington Transaction, the reorganizations in October 2023 and August 2024 and a decrease in the fair value of the long-term incentive awards granted. The decrease in 2023 of $1.5 million, compared to 2022, is primarily due to the October 2023 reorganization and a decrease in the fair value of long-term incentive awards granted. This was partially offset by cost related to performance share units granted in 2021, for which achievement of related performance conditions was deemed probable in 2023 and 2024;
- We incurred $5.1 million in disposables costs in the year ended December 31, 2024 compared to $13.2 million in 2023 and $17.8 million in 2022. The decrease in 2024 primarily related to the July 2024 Lexington Transaction as well as the reorganizations in October 2023 and August 2024. The decrease in 2023 compared to 2022 was related to the October 2023 reorganization;
- We incurred $4.0 million of severance costs in the year ended December 31, 2024 related to the July 2024 Lexington Transaction and the August 2024 reorganization, compared to $2.1 million of severance cost in 2023 related to the October 2023 reorganization. No such costs were incurred in 2022;
- We incurred nil and $1.4 million of costs in the years ended December 31, 2024 and 2023, respectively, related to the impairment of the Lexington, MA facility right-of-use asset and related leasehold improvements, compared to nil in 2022;
- We recognized a $1.8 million gain in the year ended December 31, 2024 related to a decrease in the fair value of contingent consideration associated with the acquisition of uniQure France SAS, compared to losses of $15.9 million in 2023 and $7.1 million in 2022. The increase in the 2023 loss was primarily due to an increase in the probability of making future milestone payments due upon dosing of the first patient in Phase I/II clinical trial of AMT-260 after receiving IND acceptance in August 2023; and

- We incurred $9.7 million in other expenses in the year ended December 31, 2024 compared to $6.8 million in 2023 and $17.2 million in 2022. The increase in costs in 2024 of $2.9 million, compared to 2023, is primarily a result of an increase in information technology expenses partially offset by decreases in contractual license expenses and consultant-related expenses. The decrease in costs in 2023 of $10.4 million, compared to 2022, is due to decreases in contractual license expenses and consultant-related expenses.

Selling, general and administrative expenses

Our general and administrative expenses consist principally of employee, office, consulting, legal and other professional and administrative expenses. We incurred expenses associated with operating as a public company, including expenses for personnel, legal, accounting and audit fees, board of directors' costs, directors' and officers' liability insurance premiums, Nasdaq listing fees, expenses related to investor relations and fees related to business development and maintaining our patent and license portfolio. Our selling costs included employee expenses as well as advisory fees related to obtaining the commercialization and license agreement ("CSL Behring Agreement") between us and CSL Behring LLC ("CSL Behring").

Selling, general and administrative expenses for the year ended December 31, 2024 were $52.7 million, compared to $74.6 million and $55.1 million for the years ended December 31, 2023 and 2022, respectively.

	Year ended December 31,				
	2024	2023	2022	2024 vs 2023	2023 vs 2022
	(in thousands)				
Employee and contractor-related expenses	$ 21,343	$ 24,399	$ 21,065	$ (3,056)	$ 3,334
Share-based compensation expense	11,928	17,386	15,479	(5,458)	1,907
Professional fees	7,261	11,673	7,133	(4,412)	4,540
Depreciation and facility costs	2,110	2,051	1,181	59	870
Intellectual property fees	1,744	3,819	1,480	(2,075)	2,339
Severance costs	1,223	361	—	862	361
Information technology costs	1,101	6,526	3,190	(5,425)	3,336
Financial advisory fees	—	3,800	1,000	(3,800)	2,800
Other expenses	5,947	4,576	4,531	1,371	45
Total selling, general and administrative expenses	**$ 52,657**	**$ 74,591**	**$ 55,059**	**$ (21,934)**	**$ 19,532**

- We incurred $21.3 million in personnel and contractor expenses in the year ended December 31, 2024 compared to $24.4 million in 2023 and $21.4 million in 2022. The decrease in 2024 of $3.1 million, compared to 2023, 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. The increase in 2023 of $3.3 million, compared to 2022, was primarily related to the hiring of personnel and contractors to support our business operations;
- We incurred $11.9 million of share-based compensation expenses in the year ended December 31, 2024 compared to $17.4 million in 2023 and $15.5 million in 2022. The decrease in 2024 of $5.5 million, compared to 2023, was primarily related to the Lexington Transaction, the October 2023 and August 2024 reorganizations, and a decrease in the fair value of long-term incentive awards granted, partially offset by an increase in long-term incentive awards granted and costs associated with performance share units, granted in December 2021, for which achievement of performance criteria was deemed probable in 2024. The increase in 2023 of $1.9 million, compared to 2022, was primarily related to an increase in long-term incentive awards granted and costs associated with performance share units, granted in December 2021, for which achievement of performance criteria was deemed probable in 2023. These increases were partially offset by a decrease in expense related to a reduction in the fair value of long-term incentive awards granted;
- We incurred $7.3 million in professional fees in the year ended December 31, 2024 compared to $11.7 million in 2023 and $7.1 million in 2022. We regularly incur accounting, audit and legal fees associated with operating as a public company. In 2024, we incurred additional professional fees related to the Lexington Transaction. In 2023, we incurred additional professional fees related to our global licensing agreement with Apic Bio, the Royalty Purchase Agreement and other corporate initiatives;

- We incurred $1.7 million in intellectual property fees including registration and professional fees in the year ended December 31, 2024 compared to $3.8 million in 2023 and $1.5 million in 2022. The decrease of $2.1 million in 2024, compared to 2023, is primarily due to a decrease in professional fees. The increase of $2.3 million in 2023, compared to 2022, is mainly related to an increase in professional fees;
- We incurred $1.2 million of severance costs in the year ended December 31, 2024 related to the Lexington Transaction and the August 2024 reorganization and $0.4 million of severance costs in 2023 related to the October 2023 reorganization. No such costs were incurred in 2022; and
- We incurred nil, $3.8 million and $1.0 million in financial advisory fees pertaining to our licensing transaction with CSL Behring in the years ended December 31, 2024, 2023 and 2022, respectively.

Other items, net

In year ended December 31, 2024, we recognized a $1.2 million net gain related to the Lexington Transaction, with no such amounts recognized in 2023 and 2022.

We recognized $3.2 million in net other expenses during the year ended December 31, 2024 (nil in 2023 and 2022) 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 nil income related to our equity stake in VectorY B.V. in the year ended December 31, 2024. In 2023, we recognized $0.8 million in other expense related to a reduction in the fair market value of our equity stake in VectorY B.V. following an October 2023 financing round. We recognized other income of $0.3 million related to the equity stake in 2022.

In 2024, we recognized $5.6 million in income related to payments received from European authorities to subsidize our research and development efforts in the Netherlands and France compared to $5.3 million in 2023 and $6.1 million in 2022.

Other income for the years ended December 31, 2024, 2023, and 2022 also includes income from the subleasing of a portion of our Amsterdam facility and Lexington research and development facility. We present expenses related to such income as other expense.

Other non-operating items, net

Our non-operating items, net, for the years ended December 31, 2024, 2023 and 2022 were as follows:

	Year ended December 31,				
	2024	2023	2022	2024 vs 2023	2023 vs 2022
			(in thousands)		
Interest income	$ 21,415	$ 19,562	$ 609	$ 1,853	$ 18,953
Interest expense - Royalty Financing Agreement	(50,865)	(26,933)	—	(23,932)	(26,933)
Interest expense - Hercules debt facility	(12,876)	(14,624)	(11,704)	1,748	(2,920)
Foreign currency (losses) / gains, net	(10,507)	(1,691)	23,235	(8,816)	(24,926)
Other non-operating gains	—	—	2,760	—	(2,760)
Total non-operating (expense) / income, net	**$ (52,833)**	**$ (23,686)**	**$ 14,900**	**$ (29,147)**	**$ (38,586)**

We recognize interest income associated with our cash and cash equivalents and investment securities. We recognized interest income of $21.4 million in 2024, $19.6 million in 2023 and $0.6 million in 2022. Our interest income increased in 2024 by $1.9 million compared to 2023 primarily due to the interest income earned on investment securities and cash on hand. Interest income increased by $19.0 million in 2023, compared to 2022, as a result of receiving $370.1 million of net proceeds from the May 2023 royalty financing agreement and a $100.0 million milestone payment from CSL Behring in July 2023.

We recognized non-cash interest expenses related to the May 2023 royalty financing agreement of $50.9 million in 2024, $26.9 million in 2023 and nil in 2022.

We recognized interest expense of $12.9 million in 2024, $14.6 million in 2023 and $11.7 million in 2022 related to the Hercules debt facility. Interest expense decreased by $1.7 million in 2024, compared to 2023, primarily due to the $50.0 million repayment of Hercules debt in July 2024, as well as a decrease in market interest rates. Interest expense increased by $2.9 million in 2023 compared to 2022 due to an increase in market interest rates related to the Hercules debt.

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. In 2024, we recognized a net foreign currency loss of $10.5 million related to our borrowings from Hercules, the May 2023 royalty financing agreement and our cash and cash equivalents and investment securities as well as loans between entities within the uniQure group. We recognized a net loss of $1.7 million in 2023 and a net gain of $23.2 million in 2022.

In 2024 and 2023, we recognized no Other non-operating gains. In 2022, we recognized a $2.8 million net gain related to a decrease in the fair value market value of a derivative financial liability

Income tax

We recognized $2.3 million of deferred tax expense in 2024 compared to $1.9 million of deferred tax expense in 2023 and $1.5 million of deferred tax income in 2022. In 2024 and 2023 deferred tax expense recorded in the U.S., related to the consumption of net operating losses.

From 2022 up to mid-2023 we recognized deferred tax income in France as a result of the buildup of net operating losses by the French entity. The deferred tax income in France in 2024 is almost fully offset with an increase in valuation allowance.

Financial Position, Liquidity and Capital Resources

As of December 31, 2024, we had cash and cash equivalents, restricted cash and investment securities of $368.9 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 second half 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. The amount and timing of our actual expenditures may vary significantly depending on numerous factors, including the timing of a potential BLA submission, approval and commercialization of AMT-130. We expect that we will require additional funding if we decide to advance any of our other clinical product candidates into late-stage clinical development. Our material cash requirements include the following contractual and other obligations:

Debt

As of December 31, 2024, we had an outstanding loan amount owed to Hercules Capital, Inc. ("Hercules") for an aggregate principal amount of $50.0 million. In July 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 $16.0 million, with $8.6 million payable within 12 months. We are contractually required to repay the $50.0 million principal outstanding in full in January 2027.

Leases

We entered into lease arrangements for facilities, including corporate, laboratory and office space. As of December 31, 2024, we had fixed lease payment obligations of $23.0 million, with $4.1 million payable within 12 months. Following the Closing of the Lexington Transaction, we assigned our lease for the Lexington facility to Genezen. This reduced our fixed lease payment obligations by $20.7 million. We continue to guarantee such payments until the end of the lease term in May 2029.

Commitments related to acquisition of uniQure France SAS (nominal amounts)

In relation to our acquisition of uniQure France SAS, 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. In December 2024, we made a payment of EUR 30.0 million ($31.5 million) to the former shareholders of uniQure France SAS following the dosing of the first patient in Phase I/II clinical trial for AMT-260. As of December 31, 2024, our remaining commitment amounts include a EUR 160.0 million ($166.2 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 milestone will be achieved at all, is generally uncertain. These payments are owed in euro and have been translated at the foreign exchange rate as of December 31, 2024, of $1.04/€1.00. As of December 31, 2024, we expect these obligations will become payable between 2029 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 License Sale 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 2027. As of December 31, 2024, our remaining minimum purchase commitments to Genezen amount to $36.5 million, with $15.8 million to be paid within the next 12 months. CSL Behring's minimum purchase commitments to us over the next 12 months are $13.6 million.

Our DMSA with Genezen requires us to take or pay contract development services during a three-year period ending July 2027. As of December 31, 2024 our remaining minimum purchase commitments amount to $12.5 million with $4.0 million to be paid within the next 12 months.

The table below summarizes our consolidated cash flow data for the years ended December 31:

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Cash, cash equivalents and restricted cash at the beginning of the period	$ 244,544	$ 231,173	$ 559,353
Net cash used in operating activities	(182,728)	(145,929)	(145,060)
Net cash generated from / (used in) investing activities	162,968	(205,686)	(182,734)
Net cash (used in) / generated from financing activities	(59,486)	362,721	1,445
Foreign exchange impact	(4,969)	2,265	(1,831)
Cash, cash equivalents and restricted cash at the end of period	**$ 160,329**	**$ 244,544**	**$ 231,173**

We had previously incurred losses and cumulative negative cash flows from operations since our business was founded by our predecessor entity AMT Holding N.V. in 1998, with the exception of generating income in 2021 after receiving the upfront payment upon Closing of the CSL Behring Agreement. We continued to incur losses in the current period. We recorded a net loss of $239.6 million for the year ended December 31, 2024, and net loss of $308.5 million in 2023, and a net loss of $126.8 million in 2022. As of December 31, 2024, we had an accumulated deficit of $1,130.0 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 $370.1 million from selling a portion of royalties due from our collaboration partner CSL Behring in 2023. Between July 2021 and July 2023, we have collected $617.4 million from CSL Behring as a result of the sale of HEMGENIX® to CSL and other milestones collected from CSL, and we are eligible to receive additional milestone payments, as well as royalties (to the extent not owed to settle the liability from the Royalty Financing Transaction) on net sales of HEMGENIX®.

In January 2025, we raised $70.1 million of net proceeds, after deducting underwriting discounts and commissions and other offering expenses payable by us, through a follow-on public offering of 4.4 million ordinary shares at a price to the public of $17.00 per ordinary share. In February 2025, we raised an additional $10.6 million in net proceeds upon the underwriters' exercise of their option to purchase an additional 0.7 million ordinary shares at the public offering price.

On May 12, 2023 we and Hercules amended our debt facility. The amendment extends the Maturity Date and interest-only period from December 2025 to January 2027. In connection with the Closing of the Lexington Transaction in July 2024 we amended the debt facility again and repaid $50.0 million of the principal balance outstanding. 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. 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 debt 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 debt 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 financings, or is available only on unfavorable terms, we may be unable to meet our cash needs. If we raise additional funds through collaborations, strategic alliances or marketing, distribution, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, which could have a material adverse effect on our business, financial conditions, results of operations and cash flows.

Net Cash used in operating activities

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Cash flows from operating activities			
Net loss	$ (239,556)	$ (308,478)	$ (126,789)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation, amortization and impairment	12,641	11,900	8,537
Amortization of discount on investment securities	(10,901)	(10,917)	—
Share-based compensation expense	22,258	35,093	34,204
Royalty financing agreement interest expense, net of interest paid	44,203	25,616	—
Deferred tax expense / (income)	2,429	1,921	(1,470)
Change in fair value of contingent consideration and derivative financial instrument, net	(1,817)	15,895	4,320
Unrealized foreign exchange losses / (gains), net	15,415	(2,206)	(22,083)
Other items, net	(3,848)	4,721	1,605
Changes in operating assets and liabilities:			
Accounts receivable, prepaid expenses, and other current assets and receivables	(2,243)	(1,323)	(4,083)
Contract asset related to CSL Behring milestone payments	-	100,000	(45,000)
Inventories	2,421	(6,740)	(6,924)
Accounts payable	1,520	(4,169)	9,238
Accrued expenses, other liabilities, and operating leases	(5,642)	(5,328)	3,385
Contingent consideration milestone payment	(19,608)	(1,914)	—
Net cash used in operating activities	**$ (182,728)**	**$ (145,929)**	**$ (145,060)**

Net cash used in operating activities was $182.7 million for the year ended December 31, 2024, and consisted of a net loss of $239.6 million adjusted for non-cash items, including depreciation, amortization and impairment expense of $12.6 million, amortization of the discount on investment securities of $10.9 million, share-based compensation expense of $22.3 million, $44.2 million of interest expense net of interest paid related to the May 2023 royalty financing agreement, a change in deferred taxes of $2.4 million, $1.8 million change in the fair value of contingent consideration and unrealized foreign exchange losses of $15.4 million. Net cash generated from operating activities also included unfavorable changes in operating assets and liabilities of $3.9 million. There was a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $2.2 million. There was an decrease in inventory balances of $2.4 million. There was a net decrease in accounts payable, accrued expenses, other liabilities, and operating leases of $4.1 million, primarily related to a increase of $1.5 million in accounts payable and a decrease of $5.6 million related to various accruals. Net cash used in operating activities also includes a payment for a contingent consideration milestone of $19.6 million.

Net cash used in operating activities was $145.9 million for the year ended December 31, 2023, and consisted of a net loss of $308.5 million adjusted for non-cash items, including depreciation, amortization and impairment expense of $11.9 million, amortization of the discount on investment securities of $10.9 million, share-based compensation expense of $35.1 million, $25.6 million of interest expense net of interest paid related to the May 2023 royalty financing agreement, a change in deferred taxes of $1.9 million, $15.9 million change in the fair value of contingent consideration and unrealized foreign exchange gains of $2.2 million. Net cash generated from operating activities also included favorable changes in operating assets and liabilities of $80.5 million. There was a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $1.3 million. There was a net decrease in contract assets of $100.0 million 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 $6.7 million. There was a net decrease in accounts payable, accrued expenses, other liabilities, and operating leases of $9.5 million, primarily related to a decrease of $4.2 million in accounts payable and a decrease of $5.3 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 used in operating activities was $145.1 million for the year ended December 31, 2022, and consisted of a net loss of $126.8 million adjusted for non-cash items, including depreciation and amortization expense of $8.5 million, share-based compensation expense of $34.2 million, changes in the fair value of contingent consideration and the derivative financial liability of $4.3 million, unrealized foreign exchange gains of $22.1 million and a change in deferred taxes of $1.5 million. Net cash generated from operating activities also included unfavorable changes in operating assets and liabilities of $43.4 million. There was a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $4.1 million. There was a net increase in contract assets related to CSL Behring milestone payments of $45.0 million. The net increase related to $100.0 million recognized as a contract asset in the current period and collection of $55.0 million of the contract asset related to the CSL milestones of $55.0 million in March 2022 and April 2022. There was an increase in inventories of $6.9 million related to the production of HEMGENIX® under the CSL Behring Agreement. These changes also relate to a net increase in accounts payable, accrued expenses, other liabilities, and operating leases of $12.6 million, primarily related to an increase in accounts payable.

Net cash generated from / (used in) investing activities

In 2024, we generated $163.0 million from our investing activities compared to using $205.7 million in 2023 and $182.7 million in 2022.

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Proceeds from maturity of debt securities	$ 534,498	$ 167,907	—
Investment in debt securities	(359,841)	(366,439)	$ (163,146)
Divestment of commercial manufacturing facility	(8,321)	—	—
Capital expenditures - European sites	(1,783)	(3,389)	(11,904)
Capital expenditures - Lexington site	(1,585)	(3,765)	(5,784)
Acquisition of uniQure France SAS, net of cash acquired	—	—	(1,900)
Net cash generated from / (used in) investing activities	**$ 162,968**	**$ (205,686)**	**$ (182,734)**

Net cash (used in) / generated from financing activities

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Cash flows from financing activities			
Proceeds from Royalty Financing Agreement, net of debt issuance costs	$ -	$ 370,062	$ -
Proceeds from issuance of shares related to employee stock option and purchase plans	2,123	308	1,445
Repayment of long-term debt	(53,050)	-	-
Contingent consideration milestone payment	(8,559)	(7,649)	-
Net cash (used in) / generated from financing activities	**$ (59,486)**	**$ 362,721**	**$ 1,445**

In December 2024, following the dosing of the first patient in Phase I/II clinical trial for AMT-260, we made a payment of EUR 30.0 million ($31.5 million) to the former shareholders of uniQure France SAS based on contractually defined milestones. EUR 26.8 million ($28.2 million) of this payment related to a contingent consideration of which EUR 8.2 million ($8.6 million) was classified as cash flows from financing activities and EUR 18.7 million ($19.6 million) was classified as a net cash flow used in operating activities.

In September 2023, following the FDA's clearance of the IND application for AMT-260, we made a payment of EUR 10.0 million ($10.7 million) to the former shareholders of uniQure France SAS based on contractually defined milestones. EUR 8.9 million ($9.6 million) of this payment related to a contingent consideration of which EUR 7.2 million ($7.6 million) was classified as cash flows from financing activities and EUR 1.8 million ($1.9 million) was classified as a net cash flow used in operating activities.

Funding requirements

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

- activities related to submission of a BLA for AMT-130 in Huntington's disease;
- activities to prepare for the commercialization of AMT-130 in Huntington's disease in the United States;
- investments to launch AMT-130 in Huntington's disease in the United States including the amounts of revenue we generate following the launch;
- earnout payments we might owe the former shareholders of uniQure France SAS, which are subject to the achievement of specific development and regulatory milestones;
- contractual milestone payments and royalties we might be owed in accordance with the CSL Behring Agreement;
- the scope, timing, results, and costs of our current and planned clinical trials;
- 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 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 7A. Quantitative and Qualitative Disclosures About Market Risk.

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

Market Risk

Currency risk

We are exposed to foreign exchange risk arising from various currencies, primarily with respect to the U.S. dollar and euro and to a lesser extent to the British pound and the Swiss Franc. As our U.S. operating entity primarily conducts its operations in U.S. dollars, its exposure to changes in foreign currency is insignificant. Similarly, the exposure to changes in foreign currencies of our Swiss and French entities are insignificant as well.

Our Dutch entities hold significant amounts of U.S. dollars in cash and cash equivalents and investment securities, have debt and interest obligations to Hercules denominated in U.S. dollars, generate collaboration revenue denominated in U.S. dollars, receive services from vendors denominated in U.S. dollars and occasionally British Pounds and fund the operations of our U.S. operating entity in U.S. dollars. Foreign currency denominated account receivables and account payables are short-term in nature (generally 30 to 45 days).

Variations in exchange rates will impact earnings and other comprehensive income or loss. On December 31, 2024, if the euro had weakened 10% against the U.S. dollar with all other variables held constant, pre-tax loss for the year would have been $25.0 million higher (December 31, 2023: pre-tax loss $6.0 million higher), and other comprehensive income would have been $11.0 million higher (December 31, 2023: other comprehensive loss $0.3 million higher). Conversely, if the euro had strengthened 10% against the U.S. dollar with all other variables held constant, pre-tax loss for the year would have been $25.0 million lower (December 31, 2023: pre-tax loss $6.0 million lower), and other comprehensive income would have been $12.1 million lower (December 31, 2023: other comprehensive loss $2.6 million lower).

We strive to mitigate foreign exchange risk through holding sufficient funds in euro and dollars to finance budgeted cash flows for generally 18 months.

The sensitivity in other comprehensive income to fluctuations in exchange rates primarily relates to the translation of the net assets of our Dutch entities from their functional currency euro into our reporting currency U.S. dollar.

Price risk

The market prices for the provision of preclinical and clinical materials and services, as well as external contracted research, may vary over time.

The commercial prices of any of our products or product candidates are currently uncertain.

We are not exposed to commodity price risk.

We do not hold investments classified as available-for-sale or at fair value through profit or loss; therefore, we are not exposed to equity securities price risk.

Interest rate risk

Our interest rate risk arises from short- and long-term debt and investment securities.

In June 2013, we entered into the Hercules Agreement, which was last amended in July 2024, under which our borrowings bear interest at a variable rate with a fixed floor. Long-term debt issued at fixed rates expose us to fair value interest rate risk. As of December 31, 2024, the loan bore an interest rate of 12.2%.

As of December 31, 2024, if interest rates on borrowings had been 1.0% higher with all other variables held constant, pre-tax earnings for the year would have been $0.8 million lower (2023: $1.0 million lower; 2022: $1.0 million lower.)

We invest in government debt in accordance with our investment policy. We are exposed to interest rate risk as market interest rates could differ from the interest rates that we fix at the time of acquiring these investment securities. As we intend to hold these to maturity, we do not recognize changes in the fair value of our investment which are caused by changes in market interest rates.

This means that a change in prevailing interest rates may cause the fair value of the investment to fluctuate. For example, if we hold a security that was issued at a fixed interest rate at the then-prevailing rate and the prevailing interest rate later rises, the fair value of our investment will probably decline.

The duration of all of our investment securities held as of December 31, 2024, was between two to five months. Due to the relatively short-term nature of these financial instruments and our ability and intention to hold these investments to maturity, we believe there is no material exposure to interest rate risk.

Credit Risk

Credit risk is managed on a consolidated basis. Credit risk arises from cash and cash equivalents and deposits with banks and financial institutions, outstanding receivables and committed transactions with collaboration partners and security deposits paid to landlords. We currently have no debtors other than CSL Behring.

We deposited funds as security to our landlord related to our facility in Amsterdam. We also deposited funds to the provider of our U.S. corporate credit cards. The deposits are neither impaired nor past due.

Our cash and cash equivalents include bank balances, demand deposits and other short-term highly liquid investments (with maturities of less than three months at the time of purchase) that are readily convertible into a known amount of cash and are subject to an insignificant risk of fluctuation in value. Restricted cash includes deposits made in relation to facility leases. We also have short-term investment securities in U.S. and European government bonds maturing within two to five months. Our investment policy requires us to invest in U.S. and European government bonds with the highest investment credit rating. Due to the high credit quality of our counterparties, we believe there is no material exposure to credit risk in our portfolio of investment securities.

Liquidity Risk

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 second half 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. The amount and timing of our actual expenditures may vary significantly depending on numerous factors, including the timing of a potential BLA submission, approval and commercialization of AMT-130. We expect that we will require additional funding if we decide to advance any of our other clinical product candidates into late-stage clinical development.

The table below analyzes our financial liabilities in relevant maturity groupings based on the length of time until the contractual maturity date, as of the balance sheet date. Disclosed in the table below are the contractual undiscounted cash flows. Balances due within 12 months equal their carrying value as the impact of discounting is not significant.

	Undefined	Less than 1 year	Between 1 - 3 years	Between 3 - 5 years	Over 5 years
			(in thousands)		
At December 31, 2024					
Long-term debt	$ —	$ 8,616	$ 57,403	$ —	$ —
Accounts payable, accrued expenses and other current liabilities	—	36,452	—	—	—
Commitments related to acquisition of uniQure France SAS (maximum nominal amounts)[1]	166,195	—	—	—	—
Total	**$ 166,195**	**$ 45,068**	**$ 57,403**	**$ —**	**$ —**
At December 31, 2023					
Long-term debt	$ —	$ 13,420	$ 134,150		
Accounts payable, accrued expenses and other current liabilities	—	37,120	—		
Commitments related to acquisition of uniQure France SAS (maximum nominal amounts)[2]	209,707	—	—		
Total	**$ 209,707**	**$ 50,540**	**$ 134,150**	**$ —**	**$ —**

(1) Payments are due in EUR and have been translated at the foreign exchange rate as of December 31, 2024, of $1.04 / €1.00
(2) Payments are due in EUR and have been translated at the foreign exchange rate as of December 31, 2023, of $1.10 / €1.00

In relation to our acquisition of uniQure France SAS, 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. The timing of achieving these milestones, as well as whether the milestone will be achieved at all, and consequently the timing of payments is generally uncertain. We expect these obligations will become payable between 2029 and 2033. If and when due, up to 25% of the milestone payments can be settled with our ordinary shares.

Item 8. Financial Statements and Supplementary Data.

The information required by this Item 8 is included in Part IV, Item 15, and is incorporated by reference.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer ("CEO", our principal executive officer) and chief financial officer ("CFO", our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2024. Based on such evaluation, our CEO and CFO have concluded that as of December 31, 2024, our disclosure controls and procedures were effective.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. This rule defines internal control over financial reporting as a process designed by, or under the supervision of, a company's chief executive officer and chief financial officer and effected by our board of directors, management and other personnel, 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 and includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the financial statements.

We assessed the effectiveness of our internal control over financial reporting as of December 31, 2024. This assessment was performed under the direction and supervision of our CEO and CFO and based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). Our management's assessment of the effectiveness of our internal control over financial reporting included testing and evaluating the design and operating effectiveness of our internal controls. In our management's opinion, we have maintained effective internal control over financial reporting as of December 31, 2024, based on criteria established in the COSO 2013 framework.

Our independent registered public accounting firm, which has audited the consolidated financial statements included in this Annual Report on Form 10-K, has also issued an audit report on the effectiveness of our internal control over financial reporting as of December 31, 2024. Their report is filed within this Annual Report on Form 10-K.

Inherent Limitations of Internal Controls

Our management, including our CEO and CFO, does not expect that our disclosure controls and procedures or our internal controls will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements due to error or fraud.

Changes in internal control over financial reporting

During the fourth quarter of 2024, 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.

Item 9B. Other Information

Trading Arrangements

During the three months ended December 31, 2024, none of our directors or officers informed us of the adoption, modification or termination of a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(a) of Regulation S-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

None.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

We maintain an insider trading policy governing the purchase, sale and/or other dispositions of our securities by our directors, officers, employees, consultants and contractors, as well as the Company itself. We believe that the insider trading policy is reasonably designed to promote compliance with insider trading laws, rules and regulations, as well as the applicable laws and regulations of the Nasdaq listing standards. A copy of our insider trading policy is filed as Exhibit 19.1 to this Annual Report on Form 10-K.

The remaining information required by Item 10 is incorporated by reference from our Proxy Statement for our 2025 annual meeting of shareholders, which we will file within 120 days of December 31, 2024, or will be included in an amendment to this Annual Report on Form 10-K.

Item 11. Executive Compensation

The information required by this item is incorporated by reference from our Proxy Statement for our 2025 annual meeting of shareholders, which we will file within 120 days of December 31, 2024, or will be included in an amendment to this Annual Report on Form 10-K.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item is incorporated by reference from our Proxy Statement for our 2025 annual meeting of shareholders, which we will file within 120 days of December 31, 2024, or will be included in an amendment to this Annual Report on Form 10-K.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item is incorporated by reference from our Proxy Statement for our 2025 annual meeting of shareholders, which we will file within 120 days of December 31, 2024, or will be included in an amendment to this Annual Report on Form 10-K.

Item 14. Principal Accounting Fees and Services

The information required by this item is incorporated by reference from our Proxy Statement for our 2025 annual meeting of shareholders, which we will file within 120 days of December 31, 2024, or will be included in an amendment to this Annual Report on Form 10-K.

Part IV

Item 15. Exhibits, Financial Statements Schedules

Exhibits, Financial Statements Schedules

(a) *Financial Statements*. The following consolidated financial statements of uniQure N.V. are filed as part of this report:

(b) *Financial Statements Schedules*. Financial Statement Schedules have been omitted because of the absence of conditions under which they are required or because the required information, where material, is shown in the financial statements or notes.

(c) *Other Exhibits*. The Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K is incorporated herein by reference.

Item 16. Form 10-K Summary

Not applicable.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS
FOR THE YEARS ENDED DECEMBER 31, 2024, 2023 AND 2022

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
uniQure N.V.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of uniQure N.V. and subsidiaries ('the Company') as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, shareholders' (deficit) / equity, and cash flows for each of the years in the three-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ('PCAOB') and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Valuation of intangible asset at initial recognition arising from favorable terms in the Commercial Supply Agreement

As described in Notes 3 and 6 to the consolidated financial statements, the Company recorded an intangible asset valued at $16.7 million derived from the consideration received following the sale of the Lexington facility and based on the Commercial Supply Agreement entered into with Genezen. This intangible asset represents the rights to purchase HEMGENIX® at terms considered favorable to market terms. The valuation at initial recognition is based on the difference between the contractually agreed price under the Commercial Supply Agreement and the estimated commercial supply price for purchases to be made under the agreement.

We identified the valuation of the intangible asset at initial recognition arising from favorable terms in the Commercial Supply Agreement as a critical audit matter. We performed a sensitivity analysis to identify the significant assumptions used to value the intangible asset, individually and in the aggregate, and determined this assumption to be the commercial supply price. Minor changes in this assumption could have a significant impact on the valuation of the intangible asset at initial recognition A high degree of subjective auditor judgement was required to evaluate the commercial supply price assumption for the goods supplied under the agreement, due to the lack of direct observable commercial supply prices.

The following are the primary procedures we performed to address this critical audit matter:

- We evaluated the design and tested the operating effectiveness of certain internal controls related to the valuation of the intangible asset.
- We evaluated management's methodology for determining the commercial supply price in the absence of comparable agreements, by comparing management's estimate of commercial supply price to contracts in place with other suppliers and to the Company's historical production costs to assess the reasonableness of management's commercial supply price assumption.

/s/ KPMG Accountants N.V.

We have served as the Company's auditor since 2019.

Amstelveen, the Netherlands
February 27, 2025

uniQure N.V.

CONSOLIDATED BALANCE SHEETS

	December 31, 2024	December 31, 2023
	(in thousands, except share and per share amounts)	
Current assets		
Cash and cash equivalents	$ 158,930	$ 241,360
Current investment securities	208,591	376,532
Accounts receivable	5,881	4,193
Inventories, net	—	12,024
Prepaid expenses	9,281	15,089
Other current assets and receivables	7,606	2,655
Total current assets	**390,289**	**651,853**
Non-current assets		
Property, plant and equipment, net	20,424	46,548
Other investments	27,464	2,179
Operating lease right-of-use assets	13,647	28,789
Intangible assets, net	71,043	60,481
Goodwill	22,414	26,379
Deferred tax assets, net	9,856	12,276
Other non-current assets	1,399	3,184
Total non-current assets	**166,247**	**179,836**
Total assets	**$ 556,536**	**$ 831,689**
Current liabilities		
Accounts payable	$ 7,227	$ 6,586
Accrued expenses and other current liabilities	29,225	30,534
Current portion of contingent consideration	—	28,211
Current portion of operating lease liabilities	3,601	8,344
Total current liabilities	**40,053**	**73,675**
Non-current liabilities		
Long-term debt	51,324	101,749
Liability from royalty financing agreement	434,930	394,241
Operating lease liabilities, net of current portion	11,136	28,316
Contingent consideration, net of current portion	10,860	14,795
Deferred tax liability, net	7,043	7,543
Other non-current liabilities, net of current portion	7,942	3,700
Total non-current liabilities	**523,235**	**550,344**
Total liabilities	**563,288**	**624,019**
Commitments and contingencies		
Shareholders' (deficit) / equity		
Ordinary shares, €0.05 par value: 80,000,000 shares authorized as of December 31, 2024 and December 31, 2023 and 48,988,087 and 47,833,830 ordinary shares issued and outstanding as of December 31, 2024 and December 31, 2023, respectively	2,945	2,883
Additional paid-in-capital	1,173,068	1,148,749
Accumulated other comprehensive loss	(52,800)	(53,553)
Accumulated deficit	(1,129,965)	(890,409)
Total shareholders' (deficit) / equity	**(6,752)**	**207,670**
Total liabilities and shareholders' (deficit) / equity	**$ 556,536**	**$ 831,689**

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

uniQure N.V.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year ended December 31,		
	2024	2023	2022
	(in thousands, except share and per share amounts)		
License revenues	$ 10,133	$ 2,758	$ 100,000
Contract manufacturing revenues	6,114	10,835	1,717
Collaboration revenues	10,872	2,250	4,766
Total revenues	**27,119**	**15,843**	**106,483**
Operating expenses:			
Cost of license revenues	(1,267)	(65)	(1,254)
Cost of contract manufacturing revenues	(17,060)	(13,563)	(2,089)
Research and development expenses	(143,782)	(214,864)	(197,591)
Selling, general and administrative expenses	(52,657)	(74,591)	(55,059)
Total operating expenses	**(214,766)**	**(303,083)**	**(255,993)**
Other income	7,926	6,059	7,171
Other expense	(4,573)	(1,690)	(820)
Loss from operations	**(184,294)**	**(282,871)**	**(143,159)**
Interest income	21,415	19,562	609
Interest expense	(63,741)	(41,557)	(11,704)
Foreign currency (losses) / gains, net	(10,507)	(1,691)	23,235
Other non-operating gains, net	—	—	2,760
Loss before income tax (expense) / benefit	**$ (237,127)**	**$ (306,557)**	**$ (128,259)**
Income tax (expense) / benefit	(2,429)	(1,921)	1,470
Net loss	**$ (239,556)**	**$ (308,478)**	**$ (126,789)**
Other comprehensive income / (loss):			
Foreign currency translation gain / (losses), net	426	6,874	(29,435)
Defined benefit pension gain / (loss), net of taxes	327	(2,136)	—
Total comprehensive loss	**$ (238,803)**	**$ (303,740)**	**$ (156,224)**
Earnings per ordinary share - basic and diluted			
Basic and diluted net loss per ordinary share	$ (4.92)	$ (6.47)	$ (2.71)
Weighted average shares - basic and diluted	48,649,129	47,670,986	46,735,045

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

uniQure N.V.

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' (DEFICIT) / EQUITY

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total shareholders' (deficit) / equity
	No. of shares	Amount				
	(in thousands, except share and per share amounts)					
Balance at December 31, 2021	**46,298,635**	**$ 2,802**	**$ 1,076,972**	**$ (28,856)**	**$ (455,142)**	**$ 595,776**
Loss for the period	—	—	—	—	(126,789)	(126,789)
Other comprehensive loss	—	—	—	(29,435)	—	(29,435)
Income tax benefit of past share issuance cost	—	—	808			808
Exercises of share options	152,356	8	1,272	—	—	1,280
Restricted and performance share units distributed during the period	505,799	27	(27)	—	—	—
Share-based compensation expense	—	—	34,204	—	—	34,204
Issuance of ordinary shares relating to employee stock purchase plan	11,242	1	164	—	—	165
Balance at December 31, 2022	**46,968,032**	**$ 2,838**	**$ 1,113,393**	**$ (58,291)**	**$ (581,931)**	**$ 476,009**
Loss for the period	—	—	—	—	(308,478)	(308,478)
Other comprehensive income, net	—	—	—	4,738	—	4,738
Exercises of share options	14,070	1	129	—	—	130
Restricted and performance share units distributed during the period	832,530	43	(43)	—	—	—
Share-based compensation expense	—	—	35,093	—	—	35,093
Issuance of ordinary shares relating to employee stock purchase plan	19,198	1	177	—	—	178
Balance at December 31, 2023	**47,833,830**	**$ 2,883**	**$ 1,148,749**	**$ (53,553)**	**$ (890,409)**	**$ 207,670**
Loss for the period	—	—	—	—	(239,556)	(239,556)
Other comprehensive income, net	—	—	—	753	—	753
Exercises of share options	169,898	9	2,065	—	—	2,074
Restricted and performance share units distributed during the period	974,209	52	(52)	—	—	—
Share-based compensation expense	—	—	22,258	—	—	22,258
Issuance of ordinary shares relating to employee stock purchase plan	10,150	1	48	—	—	49
Balance at December 31, 2024	**48,988,087**	**$ 2,945**	**$ 1,173,068**	**$ (52,800)**	**$ (1,129,965)**	**$ (6,752)**

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

uniQure N.V.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Cash flows from operating activities			
Net loss	$ (239,556)	$ (308,478)	$ (126,789)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation, amortization and impairment	12,641	11,900	8,537
Amortization of discount on investment securities	(10,901)	(10,917)	—
Share-based compensation expense	22,258	35,093	34,204
Royalty financing agreement interest expense, net of interest paid	44,203	25,616	—
Deferred tax expense / (income)	2,429	1,921	(1,470)
Changes in fair value of contingent consideration and derivative financial instrument, net	(1,817)	15,895	4,320
Unrealized foreign exchange losses / (gains), net	15,415	(2,206)	(22,083)
Other items, net	(3,848)	4,721	1,605
Changes in operating assets and liabilities:			
Accounts receivable, prepaid expenses, and other current assets and receivables	(2,243)	(1,323)	(4,083)
Contract asset related to CSL Behring milestone payments	-	100,000	(45,000)
Inventories	2,421	(6,740)	(6,924)
Accounts payable	1,520	(4,169)	9,238
Accrued expenses, other liabilities, and operating leases	(5,642)	(5,328)	3,385
Contingent consideration milestone payment	(19,608)	(1,914)	—
Net cash used in operating activities	(182,728)	(145,929)	(145,060)
Cash flows from investing activities			
Proceeds on maturity of debt securities	534,498	167,907	—
Investment in debt securities	(359,841)	(366,439)	(163,146)
Divestment of commercial manufacturing facility	(8,321)	—	—
Purchases of property, plant, and equipment	(3,368)	(7,154)	(17,688)
Acquisition of uniQure France SAS, net of cash acquired	—	—	(1,900)
Net cash generated from / (used in) investing activities	162,968	(205,686)	(182,734)
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	2,123	308	1,445
Repayment of long-term debt	(53,050)	—	—
Contingent consideration milestone payment	(8,559)	(7,649)	—
Net cash (used in) / generated from financing activities	(59,486)	362,721	1,445
Currency effect on cash, cash equivalents and restricted cash	(4,969)	2,265	(1,831)
Net (decrease) / increase in cash, cash equivalents and restricted cash	(84,215)	13,371	(328,180)
Cash, cash equivalents and restricted cash at beginning of period	244,544	231,173	559,353
Cash, cash equivalents and restricted cash at the end of period	**$ 160,329**	**$ 244,544**	**$ 231,173**
Cash and cash equivalents	$ 158,930	$ 241,360	$ 228,012
Restricted cash related to leasehold and other deposits	1,399	3,184	3,161
Total cash, cash equivalents and restricted cash	**$ 160,329**	**$ 244,544**	**$ 231,173**
Supplemental cash flow disclosures:			
Cash paid for interest	$ (20,567)	$ (16,878)	$ (9,247)
Non-cash decrease in accounts payables and accrued expenses and other current liabilities related to purchases of property, plant, and equipment	$ (672)	$ (513)	$ (964)

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

uniQure N.V.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Corporate information

uniQure B.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 25, Amsterdam 1105 BP, the Netherlands and its telephone number is +31 20 240 6000. The Company's website address is www.uniqure.com.

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 its consolidated financial statements in compliance with generally accepted accounting principles in the United States ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

The consolidated financial statements have been prepared under the historical cost convention, except for derivative financial instruments and contingent consideration, which are recorded at fair value through profit or loss.

The 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.

The consolidated financial statements presented have been prepared on a going concern basis based on the Company's cash and cash equivalents as of December 31, 2024 and the Company's budgeted cash flows for the twelve months following the issuance date.

2.2 Use of estimates

The preparation of consolidated financial statements, in conformity with U.S. GAAP and Securities and Exchange Commission ("SEC") rules and regulations, 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 consolidated financial statements and reported amounts of revenues and expenses during the reporting period. Estimates and assumptions are primarily made in relation to contingent consideration related to the acquisition of uniQure France SAS, the valuation of the intangible asset with favorable terms recorded as part of the sale the Company's commercial manufacturing activities located in Lexington, MA ("Lexington Transaction") in July 2024 and the date at which the Company expects to satisfy its commitment under the Royalty Financing Agreement (refer to definition in Note 2.3.27). If actual results differ from the Company's estimates, or to the extent these estimates are adjusted in future periods, the Company's results of operations could either benefit from, or be adversely affected by, any such change in estimate.

2.3 Accounting policies

The principal accounting policies applied in the preparation of these consolidated financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

2.3.1 Consolidation

The consolidated financial statements comprise the financial statements of the Company and its subsidiaries. Subsidiaries are all entities over which the Company has a controlling financial interest either through variable interest or through voting interest. Currently, the Company is not involved with variable interest entities.

Inter-company transactions, balances, income, and expenses on transactions between uniQure entities are eliminated in consolidation. Profits and losses resulting from inter-company transactions that are recognized in assets are also eliminated. Accounting policies of subsidiaries have been changed where necessary to ensure consistency with the policies adopted by the Company.

2.3.2 Current versus non-current classification

The Company presents assets and liabilities in the consolidated balance sheets based on current and non-current classification.

The term current assets is used to designate cash and other assets, or resources commonly identified as those that are reasonably expected to be realized in cash or sold or consumed during the normal operating cycle of the business. The Company's normal operating cycle is twelve months. All other assets are classified as non-current.

The term current liabilities is used principally to designate obligations whose liquidation is reasonably expected to require the use of existing resources properly classifiable as current assets, or the creation of other current liabilities. Current liabilities are expected to be settled in the normal operating cycle. The Company classifies all other liabilities as non-current.

Deferred tax assets and liabilities are classified as non-current assets and liabilities, if any.

2.3.3 Foreign currency translation

The functional currency of the Company and each of its entities (except for uniQure Inc. and Corlieve AG) is the euro (€). This represents the currency of the primary economic environment in which the entities operate. The functional currency of uniQure Inc. is the U.S. dollar ($) and the functional currency of Corlieve AG is the Swiss Franc (CHF). The consolidated financial statements are presented in U.S. dollars.

Foreign currency transactions are measured and recorded in the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the re-measurement of monetary assets and liabilities denominated in foreign currencies at exchange rates prevailing at balance sheet date are recognized in profit and loss.

Upon consolidation, the assets and liabilities of foreign operations are translated into the functional currency of the shareholding entity at the exchange rates prevailing at the balance sheet date; items of income and expense are translated at monthly average exchange rates. The consolidated assets and liabilities are translated from uniQure N.V.'s functional currency, euro, into the reporting currency U.S. dollar at the exchange rates prevailing at the balance sheet date; items of income and expense are translated at monthly average exchange rates. Issued capital and additional paid-in capital are translated at historical rates with differences to the balance sheet date rate recorded as translation adjustments in other comprehensive income / loss. The exchange differences arising on translation for consolidation are recognized in "accumulated other comprehensive income / loss". On disposal of a foreign operation, the component of other comprehensive income / loss relating to that foreign operation is recognized in profit or loss.

2.3.4 Fair value measurement

The Company measures certain 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.

Items measured at fair value on a recurring basis include financial instruments and contingent consideration (Note 7, "*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.

2.3.5 Contingent consideration

Each reporting period, the Company revalues the contingent consideration obligations associated with the acquisition of uniQure France SAS in 2021 to their fair value and records changes in the fair value within research and development expenses. Changes in contingent consideration obligations result from changes in assumptions regarding the probabilities of achieving the relevant milestones, the estimated timing of achieving such milestones, and the interest rate to discount the milestone payments. The probability-adjusted payments are discounted to present value using a discount rate representing the Company's credit risk. This discount rate is determined using the effective interest rate of the Company's existing debt facility adjusted for difference in maturity dates based on market data on effective yields for U.S. bonds with a CCC credit rating.

Payments of portions of contingent consideration initially recorded as of the acquisition date are recorded as cash flows from financing activities, and payments, or the portion of the milestone payments representing changes in the fair value of contingent consideration subsequent to the initial recognition, are recorded as cash flows from operating activities.

Refer to Note 7 "*Fair value measurement*" for further information.

2.3.6 Divestiture of commercial manufacturing activities

On June 29, 2024, affiliates of the Company entered into an Asset Purchase Agreement ("APA") with Genezen Holdings Inc. and its affiliate Genezen MA, Inc. (together "Genezen"). Pursuant to the APA, the Company sold its commercial manufacturing activities located in Lexington, MA (the "Lexington Transaction") to Genezen. The Lexington Transaction closed on July 22, 2024 (the "Closing"). The Lexington Transaction was accounted for as a divestment of the Company's commercial manufacturing activities in accordance with ASC 805, *Business Combinations*.

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, (iii) a right to purchase HEMGENIX® at terms considered favorable to market terms and (iv) a firm purchase commitment liability for its customer contract with CSL Behring inherently related to the right to purchase HEMGENIX®.

Refer to Note 3 "*Divestiture of commercial manufacturing activities"* for further detail.

a. Series C preferred stock

The Company recorded the Series C preferred stock in Genezen Holdings Inc. issued to the Company at its fair value. 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 series C preferred stock is presented within Other investments on the consolidated balance sheets.

b. Convertible promissory note

The convertible promissory note was recognized at its fair value. 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 is presented within Other investments on the consolidated balance sheets.

c. Right to purchase

The Company entered into a Commercial Supply Agreement ("CSA") with Genezen. The CSA provides the Company with rights to purchase HEMGENIX® at terms considered favorable to market terms. In accordance with ASC 805, *Business Combinations,* the Company recorded an intangible asset at its fair value with respect to these favorable terms at Closing. The intangible asset is stated at historical cost less accumulated amortization. The Company amortizes the intangible asset on a straight-line basis over a three-year term. The Company presents the amortization expense within Other expense in the Consolidated Statement of Operations and Comprehensive Loss.

d. Firm purchase commitment liability

The CSA includes a minimum term of three years and minimum purchase commitments of HEMGENIX® over the first three years, unless certain contractual provisions are triggered. The Company expects to resell HEMGENIX® purchased from Genezen via its minimum commitments to CSL Behring at a loss. In accordance with ASC 330, *Inventory,* the Company recognized a liability related to the net losses expected from the purchase of these minimum commitments. The Company presents the current portion of the firm purchase commitment liability within accrued expenses and other current liabilities and the non-current portion within other non-current liabilities on the consolidated balance sheets. The Company subsequently adjusts the liability for any changes to the losses expected to be incurred. The Company presents changes to the liability within other expenses.

2.3.7 Notes to the consolidated statements of cash flows

The consolidated statements of cash flows have been prepared using the indirect method. The cash disclosed in the consolidated statements of cash flows is comprised of cash and cash equivalents and restricted cash. Cash and cash equivalents include bank balances, demand deposits and other short-term highly liquid investments (with maturities of less than three months at the time of purchase) that are readily convertible into a known amount of cash and are subject to an insignificant risk of fluctuation in value.

Cash flows denominated in foreign currencies have been translated at the average exchange rates. Exchange differences, if any, affecting cash and cash equivalents are shown separately in the consolidated statements of cash flows. Interest paid and received, and income taxes are included in net cash (used in) / provided by operating activities.

2.3.8 Segment information

Operating segments are identified as a component of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker ("CODM"), or decision-making group, in making decisions on how to allocate resources and assess performance. The Company views its operations and manages its business as one operating segment, which comprises the discovery and development of innovative gene therapies.

2.3.9 Net loss per ordinary share

The Company follows the provisions of ASC 260*, Earnings Per Share*. In accordance with these provisions, net loss per ordinary share is calculated by dividing net (loss) / income by the weighted average number of ordinary shares outstanding during the period.

Diluted net loss per ordinary share reflects the dilution that would occur if share options or warrants to issue ordinary shares were exercised, performance or restricted share units were distributed, or shares under the employee share purchase plan were issued. However, potential ordinary shares are excluded if their effect is anti-dilutive.

Refer to Note 22 "*Basic and diluted earnings per share*" for further information.

2.3.10 Impairment of long-lived assets

Long-lived assets, which include property, plant, and equipment and finite-lived intangible assets, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying value of an asset or asset group may not be recoverable. Right-of-use assets are also reviewed for impairment in accordance with ASC 360*, Property, Plant, and Equipment*. The recoverability of the carrying value of an asset or asset group depends on the successful execution of the Company's business initiatives and its ability to earn sufficient returns on approved products and product candidates. When events or changes in circumstances occur, the Company assesses recoverability by determining whether the carrying value of such assets will be recovered through the undiscounted expected future cash flows. If the future undiscounted cash flows are less than the carrying amount of these assets, the Company recognizes an impairment loss based on the excess of the carrying value over the fair value of the assets. Fair value is determined through various valuation techniques, including discounted cash flow models, quoted market values, and third-party independent appraisals, as considered necessary.

2.3.11 Goodwill and acquired research and development intangible asset

a. Goodwill

Goodwill represents the excess of the fair value of the consideration transferred over the fair value of the net assets assumed in a business combination. Goodwill is not amortized but is evaluated for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would more likely than not reduce the fair value of the reporting unit below its carrying amount. A reporting unit is an operating segment or one level below an operating segment. In the years ended December 31, 2024, 2023 and 2022, the Company has not recognized any impairment charges related to goodwill.

b. Acquired research and development

As part of the acquisition of uniQure France SAS in 2021 the Company recorded an In-process research and development intangible asset related to the AMT-260 program ("IPR&D Intangible Asset"). The IPR&D Intangible Asset is considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts and is not amortized. If and when development is completed, which would occur when regulatory approval to market a candidate for the treatment of temporal lobe epilepsy is obtained, the associated asset would be deemed finite-lived and would then be amortized based on its respective useful life at that point in time. For the years ended December 31, 2024, 2023 and 2022, the Company has not recognized any impairment charges related to the IPR&D Intangible Asset.

In case of abandonment, the IPR&D Intangible Asset will be written-off. In accordance with ASC 350, *Intangibles – Goodwill and Other*, the Company tests indefinite-lived intangible assets for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate the fair value of the IPR&D Intangible Asset is below its carrying amount.

2.3.12 Investment securities

Investment securities consist of sovereign debt with residual maturities of less than 12 months (presented as current) and beyond (presented as non-current). The Company classifies these securities as held-to-maturity. Held-to-maturity securities are those securities in which the Company has the ability and intent to hold the security until maturity. Held-to-maturity securities are recorded at amortized cost, adjusted for applicable accrued interest and the amortization or accretion of premiums or discounts. Premiums and discounts are amortized or accreted over the term of the related held-to-maturity security as an adjustment to yield using the effective interest rate method.

Investment securities with original maturities of 90 days or less when purchased are presented within cash and cash equivalents (December 31, 2024: $15.3 million, December 31, 2023: nil).

A decline in the market value of any investment security below cost that is deemed to be other than temporary results in a reduction in the carrying amount to fair value. The impairment is charged to operations and a new cost base for the security is established. Other-than-temporary impairment charges are included in interest and other income (expense), net. Interest income is recognized when earned.

Refer to Note 5 "*Investment securities*" for further information.

2.3.13 Accounts receivable

Accounts receivables include amounts due from services provided to CSL Behring as well as unconditional rights to consideration from CSL Behring.

2.3.14 Inventories

The Company started producing commercial materials in April 2022 to supply CSL Behring in accordance with a June 2020 Development and Commercial Supply Agreement between the Company and CSL Behring. From this date until the Closing of the Lexington Transaction in July 2024, the Company presented the costs associated with the aforementioned activities as cost of contract manufacturing.

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

2.3.15 Prepaid expenses

Prepaid expenses are amounts paid in the period, for which the benefit has not been realized, and include payments made for insurance and research and clinical contracts. The related expense will be recognized in the subsequent period as incurred.

2.3.16 Other(non) current assets

Deposits paid are either presented as other current assets or as other non-current assets based on duration of the underlying contractual arrangement. Deposits are classified as restricted cash and primarily relate to facility leases.

Contract assets are presented in current assets or as non-current assets based on the timing of the right to consideration.

2.3.17 Property, plant, and equipment

Property, plant, and equipment is comprised mainly of laboratory equipment, leasehold improvements, construction-in-progress ("CIP") and office equipment. All property, plant and equipment is stated at cost less accumulated depreciation. CIP consists of capitalized expenses associated with construction of assets not yet placed into service. Depreciation commences on CIP once the asset is placed into service based on its useful life determined at that time.

Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed as incurred. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss on the transaction is recognized in the consolidated statements of operations and comprehensive loss.

Depreciation is calculated using the straight-line method over the estimated useful lives of the assets (or in the case of leasehold improvements a shorter lease term), which are as follows:

Leasehold improvements	Between 10 – 15 years
Laboratory equipment	5 years
Office equipment	Between 3 – 5 years

2.3.18 Leases

The Company records leases in accordance with ASC 842*, Leases* and determines if an arrangement is a lease at inception. Operating lease right-of-use assets and lease liabilities are initially recognized based on the present value of future minimum lease payments over the lease term at commencement date calculated using an incremental borrowing rate applicable to the lease asset unless the implicit rate is readily available. Lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Leases with a term of twelve months or less are not recognized on the consolidated balance sheets.

The Company recognizes lease cost on a straight-line basis and presents these costs as operating expenses within the Consolidated statements of operations and comprehensive loss. The Company presents lease payments within cash flows from operations within the Consolidated statements of cash flows.

2.3.19 Accounts payable and accrued expenses

Accounts payables are invoiced amounts related to obligations to pay for goods or services that have been acquired in the ordinary course of business from suppliers. Accounts payables are recognized at the amounts invoiced by suppliers.

Accrued expenses are recognized for goods or services that have been acquired in the ordinary course of business.

Contract liabilities, if any, are presented in accrued expenses.

2.3.20 Long-term debt

Long-term debt is initially recognized at cost and presented net of original issue discount or premium and debt issuance costs on the consolidated balance sheets. Amortization of debt discount and debt issuance costs is recognized as interest expense in profit and loss over the period of the debt, using the effective interest rate method.

2.3.21 Pensions and other post-retirement benefit plans

The Company maintains a defined contribution pension plan for all employees in the Netherlands, which is funded by the Company through payments to an insurance company, with individual accounts for each participants' assets. The Company has no legal or constructive obligation to pay further contributions if the plan does not hold sufficient assets to pay all employees the benefits relating to services rendered in the current and prior periods. The contributions are expensed as incurred. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in the future payments is available.

The Company maintains a qualified 401(k) Plan for all employees located in the United States. The 401(k) Plan offers both a pre-tax and post-tax (Roth) component. Employees may contribute up to the IRS statutory limit each calendar year. The Company matches $0.50 for every $1.00 contributed to the plan by participants up to 6% of base compensation. Employer contributions are recognized as they are contributed, as long as the employee is rendering services in that period. If employer contributions are made in periods after an individual retires or terminates, the estimated cost is accrued during the employee's service period.

Expenses under the defined contribution plans were $2.7 million, $3.6 million and $2.7 million for the years ended December 31, 2024, 2023 and 2022, respectively.

The Company maintains a defined benefit plan for its Swiss employees, including retirement benefit plans required by applicable local law. The Company accounts for pension assets and liabilities in accordance with ASC 715, *Compensation - Retirement Benefits*, which requires the recognition of the funded status of pension plans in the Company's consolidated balance sheet. The liability in respect to defined benefit pension plan is the projected benefit obligation calculated annually by independent actuaries using the projected unit credit method.

The projected benefit obligations as of December 31, 2024 and December 31, 2023 represents the actuarial present value of the estimated future payments required to settle the obligation that is attributable to employee services rendered before that date. Service cost is reported in research and development and general and administrative expenses. All other components of net period costs are reported in interest expense in the consolidated statement of operations and comprehensive loss. Plan assets are recorded at their fair value. Gains or losses arising from plan curtailments or settlements are accounted for at the time they occur. Actuarial gains and losses arising from differences between the actual and the expected return on plan assets are recognized in accumulated other comprehensive income (loss).

2.3.22 Share-based compensation

The Company accounts for its share-based compensation awards in accordance with ASC 718*, Compensation-Stock Compensation.*

All the Company's share-based compensation plans for employees are equity-classified. ASC 718 requires all share-based compensation to employees, including grants of employee options, restricted share units, performance share units and modifications to existing instruments, to be recognized in the consolidated statements of operations and comprehensive loss based on their grant-date fair values, net of an estimated forfeiture rate, over the requisite service period. Forfeitures of employee options are recognized as they occur. Compensation expense related to Performance Share Units is recognized when the Company considers achievement of the milestones to be probable. The requirements of ASC 718 are also applied to nonemployee share-based payment transactions except for specific guidance on certain inputs to an option-pricing model and the attribution of cost.

The Company uses a Hull & White option model to determine the fair value of option awards. The model captures early exercises by assuming that the likelihood of exercises will increase when the share-price reaches defined multiples of the strike price. This analysis is performed over the full contractual term.

2.3.23 Revenue recognition

The Company primarily generates revenue from its commercialization and license agreement with CSL Behring. The Company generated revenue from services provided to Bristol-Myers Squibb ("BMS") until February 21, 2023.

License revenue

In June 2020 the Company entered into a commercialization and license agreement pursuant to which CSL Behring received exclusive global rights to HEMGENIX® which became fully effective in May 2021. The Company concluded that CSL Behring is a customer in accordance with ASC 606*, Revenue from Contracts with Customers.* The Company recognized the revenue related to its performance obligation to sell the exclusive global rights to HEMGENIX® in May 2021. The Company also allocated the following consideration to this performance obligation:

i) Variable milestone payments; and
ii) Sales milestone payments and royalties

The Company recognizes license revenue in relation to the regulatory and sales milestone payments when it becomes probable that these be achieved as well as when royalties on sales of HEMGENIX® have been earned.

Refer to Note 18 "*Collaboration arrangements and concentration of credit risk*" for further detail.

Contract manufacturing revenue

The Company between April 2022 and July 2024 contract manufactured HEMGENIX® for CSL Behring in accordance with a June 2020 Development and Commercial Supply Agreement between the Company and CSL Behring. Following the Closing of the Lexington Transaction in July 2024, title to HEMGENIX® drug product 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 with related accounts receivable presented in other receivables in the consolidated balance sheets.

The Company recognized contract manufacturing revenue when ownership transferred to CSL Behring.

Collaboration revenue

Collaboration revenue related to contracted services is recognized when performance obligations are satisfied.

2.3.24 Other income, other expense

The Company receives certain government and regional grants, which support its research efforts in defined projects, and include contributions towards the cost of research and development. These grants generally provide for reimbursement of approved costs incurred as defined in the respective grants and are deferred and recognized in the statements of operations and comprehensive loss over the period necessary to match them with the costs they are intended to compensate, when it is probable that the Company has complied with any conditions attached to the grant and will receive the reimbursement.

2.3.25 Research and development expenses

Research and development costs are expensed as incurred. Research and development expenses generally consist of laboratory research, clinical trials, statistical analysis, and report writing, regulatory compliance costs incurred with clinical research organizations and other third-party vendors (including post-approval commitments to conduct consistency and comparability studies). In addition, research and development expenses consisted of start-up and validation costs related to the Company's Lexington facility and the development and improvement of the Company's manufacturing processes and methods. Furthermore, research and development costs include costs of materials and costs of intangible assets purchased from others for use in research and development activities. The costs of intangibles that are purchased from others for a particular research and development project and that have no alternative future uses (in other research and development projects or otherwise) are expensed as research and development costs at the time the costs are incurred or at the time when no alternative future use is identified.

2.3.26 Income taxes

Income taxes are recorded in accordance with ASC 740*, Income Taxes*, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amount and the tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more-likely-than-not that some or all the deferred tax assets will not be realized.

The benefits of tax positions are recognized only if those positions are more likely than not, based on the technical merits, to be sustained upon examination. Recognized tax positions are measured at the largest amount of tax benefit that is greater than 50 percent likely of being realized upon settlement. The determination as to whether the tax benefit will more-likely-than-not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2024, and 2023, the Company did not have any significant unrecognized tax benefits.

2.3.27 Royalty Financing Agreement

In May 2023, uniQure biopharma B.V. ("uniQure biopharma"), a wholly-owned subsidiary of the Company entered into an agreement (the "Royalty Financing Agreement") with the HemB SPV, L.P. (the "Purchaser") to sell certain current and future royalties due to uniQure biopharma from CSL Behring under the CSL Behring Agreement by and between uniQure biopharma and CSL Behring from the net sales of HEMGENIX®. Refer to Note 13 *"Royalty Financing Agreement"* for further details of the Royalty Financing Agreement. The Company determined that the Royalty Financing Agreement should be accounted for as debt in accordance with topic ASC 470, *Debt*. The Company initially recognized the debt at fair value. The Company subsequently records the debt at amortized cost and determines the effective interest rate based on its projection of contractual cash flows. Interest expense (presented as "Interest Expense" in the consolidated statements of operations and comprehensive (loss) / income) is recorded over the projected repayment period using the effective interest method. The Company periodically assesses and adjusts the effective interest rate to reflect changes in projected cash flows. The Company prospectively applies the adjusted effective interest rate following the date of change.

In accordance with topic ASC 835, *Interest*, debt issuance costs incurred in relation to the Royalty Financing Agreement are presented as a reduction of carrying amount of the debt. Debt issuance cost is amortized together with the interest expense recorded.

Interest expense, net of interest paid is presented as an adjustment to reconcile net loss to net cash used in operating activities in the consolidated statement of cash flows.

2.3.28 Restructuring expenses

Restructuring charges consist of one-time termination benefits. The Company records one-time termination benefits in accordance with ASC 420, *Exit or Disposal Cost Obligations*. One-time termination benefits are expensed at the date the Company notifies the employee, unless the employee must provide future service, in which case the benefits are expensed ratably over the future service period.

The Company recorded restructuring charges in accordance with ASC 712, *Compensation—Nonretirement Postemployment Benefits* when the terms offered were substantially similar to the terms recently offered. Under this standard, the Company recognizes a liability when the obligation is probable and can be estimated. The Company estimates the cost of these benefits and records a liability for the expected future payments. The liability is adjusted periodically to reflect changes in estimates, and related costs are recognized in the period incurred.

Other costs relate to the impairment of the Company's research and development laboratory in Lexington that was closed as a result of an October 2023 reorganization. The Company recognized an impairment loss of the right-of-use asset and corresponding leasehold improvements in accordance with ASC 360*, Property, Plant and Equipment*.

2.3.29 Recently Adopted Accounting Pronouncements

In the year ended December 31, 2024, the Company adopted Accounting Standards Update (ASU) 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07"). This update requires the Company to disclose segment expenses that are significant and regularly provided to the Company's chief operating decision maker ("CODM"). In addition, ASU 2023-07 requires the Company to disclose the title and position of its CODM and how the CODM uses segment profit or loss information in assessing segment performance and deciding how to allocate resources. The adoption of this update did not have a material impact on the Company's financial position or results of operations but resulted in expanded disclosures in the segment reporting section of the consolidated financial statements. The Company adopted ASU 2023-07 using a retrospective transition method.

There are no other recently issued accounting pronouncements pending adoption that are applicable or expected to have a material impact on the Company.

3. Divestiture of commercial manufacturing activities

Description of transaction

On June 29, 2024, affiliates of the Company agreed with Genezen to sell the Company's commercial manufacturing activities located in Lexington, MA. The Lexington Transaction closed on July 22, 2024.

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 B.V., both wholly owned subsidiaries of the Company, entered into an APA with Genezen on June 29, 2024. Pursuant to the APA, Genezen agreed to acquire the manufacturing facility including equipment and related manufacturing operations with a carrying value of $15.2 million, inventory with a carrying value of $8.8 million and certain other assets (including allocated goodwill) with a carrying value of $2.8 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 also included a firm purchase commitment liability for its customer contract with CSL Behring inherently related to the right to purchase HEMGENIX® in the consideration received.

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 Series C preferred stock had a carrying value of $11.8 million as of December 31, 2024.

The convertible promissory note was recognized at its fair value of $13.3 million at Closing. The convertible promissory note had a balance of $13.7 million as of December 31, 2024. During the year ended December 31, 2024, the Company recognized $0.4 million of interest income. As of December 31, 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 $17.7 million. Following the Closing, $1.7 million of deposits were released and reclassified from restricted cash into cash.

At Closing, uniQure Inc. entered into a 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 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 $2.5 million (presented within Other expense in the Consolidated Statement of Operations and Comprehensive Loss) was recorded during the year ended December 31, 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 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 was accounted for as a reduction of the consideration received. As of December 31, 2024, the Company classified $1.6 million of the liability as Accrued expenses and other current liabilities and $4.8 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 total net 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 in the Consolidated Statement of Operations and Comprehensive Loss.

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

Additionally, uniQure biopharma 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

In 2024, 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 year ended December 31, 2024.

On August 1, 2024, the Company announced a global organizational restructuring. As a result, the Company recorded $3.8 million of severance and other personnel-related expenses during the year ended December 31, 2024.

On October 5, 2023, the Company announced a reorganization plan. As a result, the Company recorded $2.5 million of severance and other personnel related expenses for the impacted employees.

A summary of the restructuring charges for the years ended December 31, 2024 and December 31, 2023 are as follows:

	Year ended December 31, 2024	Year ended December 31, 2023
Severance and other personnel costs	**(in thousands)**	
Research and development	$ 3,967	$ 2,188
Selling, general and administrative	1,223	361
Total	**$ 5,190**	**$ 2,549**

A summary of the changes in the severance and other personnel liabilities, included within accrued expenses and other current liabilities on the consolidated balance sheets, related to the workforce reduction is as follows:

	December 31, 2024	December 31, 2023
	(in thousands)	(in thousands)
Amount of liability at beginning of period	$ **1,027**	$ **—**
Severance and other personnel costs	5,190	2,549
Cash payments during the period	(4,740)	(1,522)
Amount of liability at end of period	**$ 1,477**	**$ 1,027**

5. Investment securities

The following table summarizes the Company's investments into government debt securities as of December 31, 2024 and 2023:

	At December 31, 2024			
	Amortized cost	Gross unrealized holding gains	Gross unrealized holding losses	Estimated fair value
		(in thousands)		
Current investments:				
Government debt securities (held-to-maturity)	$ 208,591	$ 164	$ —	$ 208,755
Total	**$ 208,591**	**$ 164**	**$ —**	**$ 208,755**

	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 debt securities 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 (December 31, 2024: $15.3 million, December 31, 2023: nil).

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

6. Inventories

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

	December 31, 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 $6.3 million and $1.6 million for the years ended December 31, 2024 and December 31, 2023. The costs were recognized as Cost of Contract Manufacturing Revenues. At December 31, 2023, the Company recorded an allowance for inventory of $1.6 million. The Company sold its inventories as part of the Lexington Transaction (refer to Note 3 *"Divestiture of commercial manufacturing activities"* and Note 4 *"Restructuring"*).

7. Fair value measurement

The Company measures certain financial assets and liabilities at fair value, either upon initial recognition or for subsequent accounting or reporting.

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 Company's material financial assets include cash and cash equivalents, restricted cash and investment securities. Cash and cash equivalents and restricted cash are measured at fair value using Level 1 inputs. Restricted cash is included within "Other non-current assets" within the consolidated balance sheets. Investment securities are measured at amortized cost.

The following table sets forth the balances and changes in fair values of liabilities that are measured at fair value using Level 3 inputs:

	Contingent consideration	Derivative financial instruments	Total
		(in thousands)	
Balance at December 31, 2021	**$ 29,542**	**$ 2,805**	**$ 32,347**
Net losses / (gains) recognized in profit or loss	7,080	(2,760)	4,320
Currency translation effects	(1,306)	(45)	(1,351)
Balance at December 31, 2022	**$ 35,316**	**$ —**	**$ 35,316**
Net losses recognized in profit or loss	15,895	—	15,895
Contingent consideration milestone payment	(9,563)	—	(9,563)
Currency translation effects	1,358	—	1,358
Balance at December 31, 2023	**$ 43,006**	**$ —**	**$ 43,006**
Net (gain) recognized in profit or loss	(1,817)	—	(1,817)
Contingent consideration milestone payment	(28,167)	—	(28,167)
Currency translation effects	(2,162)	—	(2,162)
Balance at December 31, 2024	**$ 10,860**	**$ —**	**$ 10,860**

Contingent consideration

The Company is required to pay up to EUR 143.1 million ($148.6 million at the December 31, 2024 foreign exchange rate) to the former shareholders of uniQure France SAS (formerly Corlieve Therapeutics SAS) upon the achievement of the remaining contractually defined milestones in connection with the Company's acquisition of uniQure France in 2021.

The fair value of the contingent consideration liability related to this acquisition as of December 31, 2024 was $10.9 million (December 31, 2023: $43.0 million) using discount rates of approximately 15.3% to 16.2% (December 31, 2023: 15.3% to 15.6%).

Following the clearance of an Investigational New Drug ("IND") application for AMT-260 in August 2023, the Company had increased the probability of achieving a EUR 30.0 million ($33.1 million) milestone payment following the dosing of the first patient in Phase I/II clinical trial from 66.0% to 100.0%. This also resulted in an increase of the probability that AMT-260 may advance to late-stage development and commercialization.

In December 2024, a milestone payment of EUR 30.0 million ($31.5 million) was paid, of which EUR 26.8 million ($28.2 million) related to contingent consideration. In September 2023, a milestone payment of EUR 10.0 million ($10.6 million) was paid, of which EUR 8.9 million ($9.6 million) related to contingent consideration.

If as of December 31, 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 EUR 33.7 million ($35.0 million). If as of December 31, 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.

As of December 31, 2024, the Company classified none of the total contingent consideration of $10.9 million as current liabilities. The balance sheet classification between current and non-current liabilities is based upon the Company's best estimate of the timing of settlement of the remaining relevant milestones.

Derivative financial instruments

Derivative financial instruments BMS

In December 2020, as part of the amended BMS CLA, the Company and BMS had agreed that upon the consummation of a change of control transaction of uniQure occurring prior to December 2026 or BMS' delivery of a cessation notice (as contractually defined) the Company (or its third party acquirer) should have paid to BMS a one-time, non-refundable, non-creditable contractually defined payment ("CoC-payment"). The amended BMS CLA was terminated on February 21, 2023.

The Company had previously determined that the CoC-payment should be recorded as a derivative financial liability upon initial recognition and that subsequent changes in the fair market value of this derivative financial liability should be recorded in profit and loss. As a result of the derecognition of the derivative financial liability in the year ended December 31, 2022, the Company recorded a $2.8 million gain within "Other non-operating (losses) / gains".

Other

As of December 31, 2024, the Company recorded $0.4 million liabilities related to consideration for post-acquisition services, presented within Other non-current liabilities in connection with the Company's acquisition of uniQure France SAS (December 31, 2023: $0.5 million).

Investment securities

Refer to Note 5 "*Investment securities*" for the fair value of the investment securities as of December 31, 2024.

Pension plan assets

Refer to Note 14 "*Retirement benefits*" for the fair value of the plan assets as of December 31, 2024.

8. Property, plant, and equipment, net

The following table presents the Company's property, plant, and equipment as of December 31:

	December 31, 2024	December 31, 2023
	(in thousands)	
Leasehold improvements	$ 24,808	$ 46,512
Laboratory equipment	23,359	43,657
Office equipment	3,913	6,383
Construction-in-progress	—	5,668
Total property, plant, and equipment	52,080	102,220
Less accumulated depreciation	(31,656)	(55,672)
Property, plant and equipment, net	**$ 20,424**	**$ 46,548**

Total depreciation expense was $10.1 million for the year ended December 31, 2024 (December 31, 2023: $10.3 million, December 31, 2022: $8.2 million). Depreciation expense is allocated to research and development expenses and cost of contract manufacturing to the extent it related to the Company's commercial manufacturing facility and equipment and laboratory equipment. All other depreciation expenses are allocated to selling, general and administrative expense.

The Company sold property, plant and equipment with a carrying value of $15.2 million, including leasehold improvements with a carrying value of $6.4 million, laboratory and office equipment with a carrying value of $6.0 million as well as assets under construction with a carrying value of $2.8 million as part of the Lexington Transaction (refer to Note 3 "*Divestment of commercial manufacturing activities"*).

The following table summarizes property, plant, and equipment by geographic region.

	December 31, 2024	December 31, 2023
	(in thousands)	
Dutch sites	$ 19,463	$ 27,095
Lexington, Massachusetts (United States of America)	730	19,437
Other	231	16
Total	**$ 20,424**	**$ 46,548**

9. Right-of-use asset and lease liabilities

The Company's most significant leases relate to office and laboratory space under the following operating lease agreements:

Lexington, Massachusetts / United States

In July 2013, the Company entered into a lease for a facility in Lexington, Massachusetts, United States. In November 2018, the term was expanded by five years to June 2029 and include an additional 30,655 square feet within the same facility and for the same term. The Company in July 2024 assigned the leases to Genezen as part of its divestment of its commercial manufacturing activities and as a result de-recognized its right of use asset and related lease liability. Refer to Note 3 "*Divestment of commercial manufacturing activities".*

In December 2021, the Company entered into a lease for an research and development facility in Lexington, Massachusetts, United States of approximately 13,501 square feet of space. The lease commenced in May 2022 and is set for a non-cancellable period ending March 2029. Following the Company's announcement of a reorganization in 2023, the Company incurred costs amounting to $1.4 million for the year ended December 31, 2023, associated with the impairment of the right-of-use asset and its associated leasehold improvements' carrying value that was determined not be recoverable as of the cease-use date in late 2023. Commencing August 2024 the Company subleased this facility for the residual term.

The fixed lease payments to be received during the remaining term under the agreement to sub-lease amount to $3.2 million as of December 31, 2024.

In February 2022, the Company entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 12,716 square feet. The lease commenced in November 2022 and is set for a non-cancellable period ending March 2030. The lease is renewable for one five-year term.

Amsterdam / The Netherlands

In March 2016, the Company entered into a 16-year lease for a facility in Amsterdam, the Netherlands and amended this agreement in June 2016. The lease for the facility terminates in February 2032, with an option to extend in increments of five-year periods. The lease contract includes variable lease payments related to annual increases in payments based on a consumer price index. In May 2021 the Company leased an additional approximately 1,080 square meters of office space. The lease expires in October 2028.

As of December 31, 2024 the Company is sub-leasing two of the seven floors of its Amsterdam facility for a ten-year term ending on December 31, 2027 with an option for the sub-lessee to extend until December 31, 2031. The sublessee has informed the Company during 2024 of its intention to terminate the sub-lease.

The fixed lease payments to be received during the remaining term under the agreement to sub-lease amount to EUR 2.7 million ($2.8 million) as of December 31, 2024.

Operating lease liabilities

The components of lease cost were as follows:

	Year ended December 31,		
	2024	2023	2022
	(in thousands)		
Operating lease cost	$ 6,486	$ 7,018	$ 5,932
Variable lease cost	1,137	1,238	785
Sublease income	(1,162)	(957)	(849)
Total lease cost	**$ 6,461**	**$ 7,299**	**$ 5,868**

The table below presents the lease-related assets and liabilities recorded on the Consolidated balance sheets.

	December 31, 2024	December 31, 2023
	(in thousands)	
Assets		
Operating lease right-of-use assets	**$ 13,647**	**28,789**
Liabilities		
Current		
Current operating lease liabilities	3,601	8,344
Non-current		
Non-current operating lease liabilities	11,136	28,316
Total lease liabilities	**$ 14,737**	**36,660**

Other information

The weighted-average remaining lease term as of December 31, 2024, is 5.9 years, compared to 6.1 years as of December 31, 2023, and the weighted-average discount rate as of December 31, 2024 is 11.3%, compared to 11.2% as of December 31, 2023. The Company uses an incremental borrowing rate applicable to the lease asset.

The table below presents supplemental cash flow and non-cash information related to leases.

	Year ended December 31,		
	2024	2023	2022
	(in thousands)		
Cash paid for amounts included in the measurement of lease liabilities			
Operating cash flows for operating leases	$ 6,113	$ 7,921	$ 7,532
Right-of-use asset obtained in exchange for lease obligation			
Operating lease	$ —	$ 561	$ 9,824

Undiscounted cash flows

The table below reconciles the undiscounted cash flows as of December 31, 2024, for each of the first five following years and the total of the remaining years to the operating lease liabilities recorded on the Consolidated balance sheet as of December 31, 2024.

	Lexington	Amsterdam[1]	Other[2]	Total
	(in thousands)			
2025	$ 1,394	$ 1,934	$ 274	$ 3,602
2026	1,431	1,934	228	3,593
2027	1,469	1,938	0	3,407
2028	1,508	1,867	—	3,375
2029	763	1,752	—	2,515
Thereafter	130	3,358	—	3,488
Total lease payments	$ 6,695	$ 12,783	$ 502	$ 19,980
Less: amount of lease payments representing interest payments	(1,344)	(3,842)	(57)	(5,243)
Present value of lease payments	5,351	8,941	445	14,737
Less: current operating lease liabilities	(1,394)	(1,934)	(273)	(3,601)
Non-current operating lease liabilities	**$ 3,957**	**$ 7,007**	**$ 172**	**$ 11,136**

(1) Payments are due in EUR and have been translated at the foreign exchange rate as of December 31, 2024, of $1.04 / €1.00

(2) Payments are due in CHF and have been translated at the foreign exchange rate as of December 31, 2024, of $1.10 / CHF1.00

10. Intangible assets, net and Goodwill

The following table presents the Company's acquired licenses, intangible asset related to the favorable supply terms under the CSA and acquired IPR&D as of December 31:

	At December 31, 2024		
	Gross Carrying Amount	Accumulated Amortization	Net
		(in thousands)	
Acquired licenses	$ 2,276	$ (1,117)	$ 1,159
Favorable supply terms under CSA	16,700	(2,454)	14,246
Total amortizable intangible assets	18,976	(3,571)	15,405
Acquired IPR&D intangible asset	55,638	—	55,638
Total intangible assets	**$ 74,614**	**$ (3,571)**	**$ 71,043**

	At December 31, 2023		
	Gross Carrying Amount	Accumulated Amortization	Net
		(in thousands)	
Acquired licenses	$ 2,419	$ (1,057)	$ 1,362
Total amortizable intangible assets	2,419	(1,057)	1,362
Acquired IPR&D intangible asset	59,119	—	59,119
Total intangible assets	**$ 61,538**	**$ (1,057)**	**$ 60,481**

As of December 31, 2024, the estimated future amortization expense for each of the five succeeding years and the period thereafter is as follows:

Years	Amount (in thousands)
2025	$ 5,689
2026	5,689
2027	3,234
2028	122
2029	122
Thereafter	549
Total	**$ 15,405**

a. Acquired licenses

All acquired licenses are owned by uniQure biopharma B.V, a subsidiary of the Company. The remaining weighted average life is 9.5 years as of December 31, 2024 (December 31, 2023 10.5 years).

The amortization expense related to acquired licenses for the year ended December 31, 2024 was $0.1 million (December 31, 2023: $0.1 million; December 31, 2022: $0.4 million).

b. Favorable supply terms under CSA

As part of the Lexington Transaction, the Company recognized an intangible asset related to its rights to purchase HEMGENIX® at terms considered favorable to market terms. Refer to Note 3 "*Divestment of commercial manufacturing activities"*. The intangible asset is amortized on a straight line basis over a three year period that commenced in July 2024.

The amortization expense related to the intangible asset for the year ended December 31, 2024 was $2.5 million (December 31, 2023 and 2022: nil).

c. Acquired in-process research and development

The IPR&D Intangible Asset was recorded as part of the Company's July 2021 acquisition of uniQure France SAS. Refer to Note 2.3.11.

d. Goodwill

The goodwill was recorded as part of the Company's July 2021 acquisition of uniQure France SAS. Refer to Note 2.3.11.

11. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities include the following items:

	December 31, 2024	December 31, 2023
	(in thousands)	
Personnel related accruals and liabilities	$ 12,583	$ 16,263
Accruals for goods received from and services provided by vendors-not yet billed	10,109	12,834
Current portion of firm purchase commitment liability (refer to Note 3 "Divestiture of commercial manufacturing activities")	1,582	-
Liability owed to the Purchaser pursuant to the Royalty Financing Agreement	4,951	1,437
Total	**$ 29,225**	**$ 30,534**

12. 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 December 31, 2024 under the 2024 Amended Facility was $50.0 million.

The Company is required to repay the residual principal balance on the Maturity Date. The interest rate is adjustable and is the greater of (i) 7.95% and (ii) 7.95% plus the prime rate less 3.25% per annum. 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) of the 2024 Amended Facility was $51.9 million as of December 31, 2024, compared to an amortized cost of $102.9 million as of December 31, 2023, and is recorded net of discount and debt issuance costs. The foreign currency loss on the loan was $4.1 million in 2024 (2023: gain of $3.0 million; 2022: loss of $5.8 million). The fair value of the loan approximates its carrying amount. Inputs to the fair value of the loan are considered Level 3 inputs.

Interest expense recorded during the years ended December 31 was as follows:

Years	Amount (in millions)
2024	$ 12.9
2023	14.6
2022	11.5

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 United States, equivalent to the lesser of (i) 65% of the outstanding balance of principal due or (ii) 100% of worldwide cash and cash equivalents. This restriction on cash and cash equivalents only relates to the location of the cash and cash equivalents, and such cash and cash equivalents can be used at the discretion of the Company. Beginning on April 1, 2024, the Company is required to keep a minimum of unrestricted cash of 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 $556.5 million, less $4.1 million of cash and cash equivalents and other current assets held by the Company and $80.5 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 December 31, 2024, the Company was in material compliance with all covenants and provisions.

The aggregate maturities of the loans, including $16.0 million of coupon interest payments and financing fees, for each of the 25 months after December 31, 2024, are as follows:

Years	Amount (in thousands)
2025	$ 8,616
2026	6,185
2027	51,218
Total	**$ 66,019**

13. Royalty Financing Agreement

On May 12, 2023, the Company entered into the Royalty Financing Agreement with 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 will be obligated to pay $25.0 million of the first worldwide sales milestone payment from CSL Behring, if received, to the Purchaser.

The Purchaser will receive 1.85 times the upfront payment (or $693.8 million) 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 payment through December 31, 2038 ("Second Hard Cap Date"). If, on or prior to the defined dates for each cap amount, the total amount of royalty payments received by the Purchaser equals or exceeds the cap amount applicable to such date, the Royalty Financing Agreement will automatically terminate and all rights to the HEMGENIX® royalty payments will revert back to the Company. The Company has no obligation to repay any amounts received from the Purchaser in the event that the applicable cap amount is not reached during the term of the Royalty Financing Agreement.

The Company has retained the rights to all other royalties, as well as commercial 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 balance sheet as of closing of the transaction on June 5, 2023. Following the initial recognition, the Company records the debt at amortized cost.

As of December 31, 2024 the Company expects to satisfy its commitment to the Purchaser prior to the Second Hard Cap Date. The Company until December 2024 assumed that it would satisfy the commitments to the Purchaser prior to the First Hard Cap Date. This change in assumption did not have a material impact on the amount of debt or interest expense recorded for the year ended December 31, 2024. The Company will record the difference of $473.7 million between the total expected payments of $843.8 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 Second Hard Cap Date. Based on the Company's projections the effective interest rate is expected to be within a range of 12.0% to 13.5% per annum, which is consistent with the range that was used prior to the change in assumption in December 2024. The Company would have recorded the following amounts:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Interest expenses at effective interest rate of 12.0% per annum	$ 50.7	$ 26.5	$ —
Interest recorded in the statement of operations and comprehensive loss and income	50.9	26.9	—
Interest expenses at effective interest rate of 13.5% per annum	57.8	29.9	—

The Company prospectively updates the effective interest rate at each reporting date based on updated cash flow 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 year ended December 31, 2024 and December 31, 2023:

	Amount of liability (in thousands)
Gross proceeds from royalty financing agreement on June 5, 2023	375,000
Debt issuance costs paid	(4,938)
Royalty payments to Purchaser	(1,317)
Interest expense for the period	26,933
Balance as of December 31, 2023 (includes $1.4 million presented as "Accrued expenses and other current liabilities)	**$ 395,678**
Royalty payments to Purchaser	(6,662)
Interest expense for the period	50,865
Balance as of December 31, 2024 (includes $5.0 million presented as "Accrued expenses and other current liabilities)	**$ 439,881**

14. Retirement benefits

Defined benefit pension plan

The Company operates a defined benefit pension plan for its Swiss employees (the "Swiss Plan") in accordance with local regulations and practices. The normal retirement age under the Swiss Plan is 65 years. All benefits are immediately vested. Under the Swiss Plan, a percentage of pensionable salary is contributed as a retirement credit with additional contributions being made for death and disability benefits. Under Swiss pension law, participants who are covered by the pension plan of another employer are required to transfer the termination benefit of that pension plan into the plan of the Company. When employment at the Company ends before reaching retirement, the termination benefit is transferred out of the defined benefit pension plan. At time of retirement the accumulated retirement credit can be converted into a life-long annuity or be paid-out as a lump-sum. Participants are also permitted to withdraw a part of the accumulated termination benefit in special circumstances before reaching retirement age for example for payments related to obtain home ownership.

The Company initially recognized its net projected benefit obligation as of December 31, 2023 at a carrying amount of CHF 2.1 million ($2.6 million), presented within other non-current liabilities in the consolidated balance sheets.

A summary of the changes in the projected benefit obligation ("PBO") and plan assets is presented below:

	December 31, 2024 (in thousands)
Beginning projected benefit obligation	$ 11,499
Service cost	551
Interest cost	167
Liabilities assumed from participants joining the plan	643
Actuarial losses	509
Liabilities extinguished through participants leaving the plan	(984)
Foreign currency exchange rate changes	(890)
Ending projected benefit obligation	**$ 11,495**

	December 31, 2024
	(in thousands)
Beginning fair value of plan assets	$ 8,946
Return on plan assets	690
Interest income	226
Contributions by the employer	643
Assets contributed to the plan from participants joining the plan	643
Assets distributed to participants leaving the plan	(984)
Foreign currency exchange rate changes	(664)
Ending fair value of plan assets	**$ 9,500**

Amounts recognized on the consolidated balance sheet, presented within other non-current liabilities, were as follows:

	December 31, 2024	December 31, 2023
	(in thousands)	
Fair value of plan assets	$ 9,500	$ 8,946
Present value of projected benefit obligation	(11,495)	(11,499)
Funded status: (net liability)	**$ (1,995)**	**$ (2,553)**
Accumulated benefit obligation as of December 31	**$ 11,075**	**$ 10,739**

Amounts recorded in accumulated other comprehensive (income) / loss:

	December 31, 2024
	(in thousands)
Actuarial loss - beginning of year	$ 2,540
Actuarial (gain) of current year	(241)
Amortization of prior service costs	(142)
Total	**$ 2,157**

Net pension expense related to the defined benefit plans included the following components:

	December 31, 2024
	(in thousands)
Service cost	$ 551
Interest cost	167
Interest income	(226)
Amortization of net loss	142
Net pension expense	**$ 634**

The assumptions related to the Swiss Plan are as follows:

Actuarial assumptions (% p.a.)	December 31, 2024	December 31, 2023
Discount rate	0.90%	1.50%
Expected return on plan assets	1.80%	2.60%
Expected inflation rate	0.70%	1.60%
Interest credit rate	1.25%	1.25%
Long-term expected rate of salary increases	0.70%	1.60%
Pension increase	0.00%	0.00%

Future benefits expected to be paid are as follows:

	December 31, 2024	December 31, 2023
	(in thousands)	
Year 1	$ 490	$ 533
Year 2	409	610
Year 3	417	528
Year 4	440	529
Year 5	480	540
Next 5 years	4,747	4,992
Other disclosure items:		
Next year's expected employer contribution	**$ 575**	**$ 552**

The Company's investment strategy for its pension plan is to optimize the long-term investment return on plan assets in relation to the liability structure to maintain an acceptable level of risk while minimizing the cost of providing pension benefits and maintaining adequate funding levels in accordance with the applicable rules in each jurisdiction. The Company does not manage any assets internally. The plan assets relate to assets being held by the Swiss pension foundations in which the Company's pension plan is set-up.

The allocation of plan assets is presented below:

	December 31, 2024	December 31, 2023
Bonds	61%	61%
Equities	25%	25%
Real estate	10%	10%
Others	4%	4%

The fair value of the plan assets is determined based on Level 2 inputs.

15. Shareholders' (deficit) / equity

As of December 31, 2024, the Company's authorized share capital is €4.0 million (or $4.2 million when translated at an exchange rate as of December 31, 2024, of $1.04/ €1.00), divided into 80,000,000 ordinary shares, each with a nominal value of €0.05.

All ordinary shares issued by the Company were fully paid. The minimum amount of share capital to be held under Dutch law is EUR 0.0 million. Under the Company's Articles of Association, the Company is required to maintain a minimum amount of share capital in reserve. In addition, the Company is only permitted to make distributions on its ordinary shares to the extent that its shareholders' (deficit) / equity exceeds the sum of the paid-up and called-up capital and the reserves it is required to maintain under Dutch law. There are no other distribution restrictions applicable to the Company's shares. As the Company's equity is negative as of December 31, 2024 the Company cannot distribute any equity.

As of December 31, 2024, and 2023 and 2022 the Company's other comprehensive result was restricted for payment of dividends for an accumulated other comprehensive loss of $52.8 million in 2024, an accumulated other comprehensive loss of $53.6 million in 2023, and an accumulated other comprehensive loss of $58.3 million in 2022.

The Company recorded a $0.8 million increase of additional paid-in capital in the year ended December 31, 2022 resulting from the release of valuation allowance for the tax benefit of share issuance costs incurred in 2018, 2019 and 2021 within the Netherlands.

16. Share-based compensation

Share-based compensation expense recognized by classification included in the consolidated statements of operations and comprehensive loss was as follows:

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Cost of manufacturing services revenue	$ 1,035	$ 826	$ 323
Research and development	9,295	16,881	18,402
Selling, general and administrative	11,928	17,386	15,479
Total	**$ 22,258**	**$ 35,093**	**$ 34,204**

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

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Award type/ESPP			
Share options	$ 9,178	$ 13,302	$ 13,425
Restricted share units	11,490	18,524	15,486
Performance share units	1,580	3,234	5,267
Employee share purchase plan	10	33	26
Total	**$ 22,258**	**$ 35,093**	**$ 34,204**

As of December 31, 2024, the unrecognized compensation cost related to unvested awards under the various share-based compensation plans were:

	Unrecognized share-based compensation expense	Weighted average remaining period for recognition
	(in thousands)	(in years)
Award type		
Share options	$ 9,439	2.09
Restricted share units	9,873	1.54
Performance share units	3,013	0.97
Total	**$ 22,324**	**1.80**

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's share-based compensation plans include the 2014 Amended and Restated Share Option Plan as approved by the shareholders in 2014, (the "2014 Plan") and inducement grants under Rule 5653(c)(4) of The Nasdaq Global Select Market with terms similar to the 2014 Plan (together the "2014 Plans").

The shareholders have approved amendment to the 2014 Plan from time to time to increase the shares authorized for issuance. At an extraordinary general meeting of shareholders in November 2023, an additional 1,750,000 shares were authorized for issuance. At the annual general meeting of shareholders in June 2024, the Company's shareholders authorized an additional 1,500,000 shares for issuance. As of December 31, 2024, a total of 3,912,283 ordinary shares remain available for issuance under the 2014 Plan.

Share options

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

2014 Plans

The following tables summarize option activity under the Company's 2014 Plans for the year ended December 31, 2024:

	Options			
	Number of ordinary shares	Weighted average exercise price	Weighted average remaining contractual life	Aggregate intrinsic value
			in years	(in thousands)
Outstanding at December 31, 2023	**4,974,030**	**23.25**	**6.71**	**$ 182**
Granted	1,093,080	$ 5.47		
Forfeited	(316,056)	$ 16.69		
Expired	(613,996)	$ 25.04		
Exercised	(169,898)	$ 13.39		
Outstanding at December 31, 2024	**4,967,160**	**$ 19.87**	**5.91**	**19,196**
Thereof, fully vested, and exercisable on December 31, 2024	3,128,557	$ 24.82	4.48	5,923
Thereof, outstanding and expected to vest after December 31, 2024	1,838,603	$ 11.46	8.34	13,273
Outstanding and expected to vest after December 31, 2023	2,235,435	$ 19.78		

Total weighted average grant date fair value of options issued during the period (in $ millions)		$ 3.5	
Granted to directors and officers during the period (options, grant date fair value $ in millions)	626,880	$ 2.0	
Proceeds from option sales during the period (in $ millions)		$ 2.1	

The following table summarizes information about the weighted average grant-date fair value of options during the years ended December 31:

	Options	Weighted average grant-date fair value
Granted, 2024	1,093,080	$ 3.19
Granted, 2023	1,650,030	10.57
Granted, 2022	1,426,966	9.04
Vested, 2024	992,777	12.21
Forfeited, 2024	(316,056)	9.74

The following table summarizes information about the weighted average grant-date fair value of options at December 31:

	Options	Weighted average grant-date fair value
Outstanding and expected to vest, 2024	1,838,603	$ 6.66
Outstanding and expected to vest, 2023	2,235,435	11.50

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:

	Year ended December 31,		
	2024	2023	2022
Assumptions			
Expected volatility	70%	70%	70%
Expected terms	10 years	10 years	10 years
Risk free interest rate	3.7% - 4.3%	3.7% - 4.8%	2.1% - 4.2%
Expected dividend yield	0%	0%	0%

The Hull & White option model captures early exercises by assuming that the likelihood of exercises will increase when the share price reaches defined multiples of the strike price. This analysis is performed over the full contractual term.

The following table summarizes information about options exercised during the years ended December 31:

	Exercised during the year	Intrinsic value (in thousands)
2024	169,898	$ 248
2023	14,070	154
2022	138,356	1,848

Restricted Share Units

The following table summarizes the RSU activity for the year ended December 31, 2024:

	RSUs	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2023	**2,264,369**	**$ 18.07**
Granted	1,321,360	$ 5.57
Vested	(931,450)	$ 19.49
Forfeited	(994,381)	$ 12.44
Non-vested at December 31, 2024	**1,659,898**	**$ 10.71**
Total weighted average grant date fair value of RSUs granted during the period (in $ millions)		$ 7.4
Granted to directors and officers during the period (shares, $ in millions)	355,060	$ 1.9

The following table summarizes information about the weighted average grant-date fair value of RSUs granted during the years ended December 31:

	Granted during the year	Weighted average grant-date fair value
2024	1,321,360	$ 5.57
2023	1,770,025	17.88
2022	1,604,533	16.10

The following table summarizes information about the total fair value of RSUs that vested during the years ended December 31:

	Total fair value (in thousands)
2024	$ 5,603
2023	13,729
2022	5,104

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

Performance Share Units

The following table summarizes the PSU activity for the year ended December 31, 2024:

	PSUs	
	Number of ordinary shares	Weighted average grant-date fair value
Non-vested at December 31, 2023	**222,550**	**$ 28.09**
Granted	65,000	$ 15.40
Vested	(42,759)	$ 29.35
Forfeited	(94,671)	$ 28.63
Non-vested at December 31, 2024	**150,120**	**$ 21.65**
PSUs awarded but not yet earned	115,000	**$** 17.66
Total non-vested and discretionary PSUs	265,120	**$** 19.92
Total weighted average grant date fair value of PSUs granted during the period (in $ millions)		$ 1.0

The Company granted shares to certain employees in September and December 2021 and various dates during the year ended December 31, 2022 and December 31, 2024 that will be earned upon achievement of defined milestones. Earned shares vested upon the later of a minimum service period of three years, or the achievement of defined milestones, subject to the grantee's continued employment. In addition, portions of the December 2021 granted to executives and other members of senior management were subject to achieving a minimum total shareholder return relative to the Nasdaq biotechnology index. As of December 31, 2024, four milestones had been achieved and vested in either 2022, 2023 or 2024. As of December 31, 2024, two milestones were considered probable. The Company recognizes the compensation cost related to these grants to the extent it considers achievement of the milestones to be probable.

The Company awarded PSUs to certain employees in December 2024 that will be earned upon the Board of Directors' (the "Board") assessment of the level of achievement of agreed upon performance targets through December January 2, 2026

The following table summarizes information about the weighted average grant-date fair value of the PSUs determined as of the grant date for the years ended December 31:

	Granted during the year	Weighted average grant-date fair value
2024	65,000	$ 15.40
2023	—	$ —
2022	34,700	$ 15.11

The following table summarizes information about the total fair value of PSUs that vested during the years ended December 31:

	Total fair value (in thousands)
2024	$ 319
2023	1,474
2022	4,450

Employee Share Purchase Plan ("ESPP")

In June 2018, the Company's shareholders adopted and approved an ESPP allowing the Company to issue up to 150,000 ordinary shares. The ESPP is intended to qualify under Section 423 of the Internal Revenue Code of 1986. Under the ESPP, employees are eligible to purchase ordinary shares through payroll deductions, subject to any plan limitations. The purchase price of the shares on each purchase date is equal to 85% of the lower of the closing market price on the offering date or the closing market price on the purchase date of each three-month offering period. During the year ended December 31, 2024, 10,150 ordinary shares have been issued (December 31, 2023: 19,198 and December 31, 2022: 11,242). As of December 31, 2024, a total of 86,712 ordinary shares remain available for issuance under the ESPP plan.

17. Segment reporting

The Company is advancing a pipeline of innovative gene therapies seeking to deliver to patients suffering from rare and other devastating diseases single treatments with potentially curative results. The Company manages the operations related to these research and development activities within one operating segment because they rely on a common set of infrastructure, resources and technology of the products and production processes, types of customers, distribution methods and regulatory environment.

The leadership team is identified as the CODM.

The CODM allocates resources to research projects and clinical candidates based on scientific data as well as quantitative and qualitative expected risk adjusted returns on investment. The CODM uses segment operating loss to monitor that cash operating losses remain within the approved budget.

The Company does not evaluate performance or allocate resources based on segment asset data and therefore such information is not presented. Refer to Note 8 "*Property, plant and equipment, net*" and Note 9 "*Right-of-use asset and lease liabilities*" for geographic information related to long-lived assets.

The accounting policies of the operating segment are the same as those described in the summary of significant accounting policies.

	Years ended December 31,		
	2024	2023	2022
		(in thousands)	
Revenue	$ **27,119**	$ **15,843**	$ **106,483**
Less:			
Employee related expenses	(75,184)	(98,903)	(85,292)
Laboratory and development expenses	(47,848)	(44,346)	(52,231)
Professional fees	(8,503)	(16,918)	(10,884)
Facility expenses	(14,247)	(21,550)	(16,066)
Consumables	(9,172)	(19,029)	(19,896)
Other segment items[a] [b]	(12,482)	(28,299)	(14,099)
Segment operating loss	**(140,317)**	**(213,202)**	**(91,985)**
Reconciliation			
Depreciation, amortization and impairment expense	(12,641)	(11,900)	(8,537)
Share-based compensation expense	(22,258)	(35,093)	(34,204)
Fair value gain / (loss) - contingent consideration and derivative financial instrument	1,817	(15,895)	(4,320)
Foreign currency (losses) / gains, net	(10,507)	(1,691)	23,235
Interest income	21,415	19,562	609
Interest expense - Royalty Financing Agreement	(50,865)	(26,934)	—
Interest expense - Hercules debt facility	(12,876)	(14,623)	(11,704)
Other reconciling items[c] [d]	(10,895)	(6,781)	(1,353)
Consolidated loss before income tax (expense) / benefit	**$ (237,127)**	**$ (306,557)**	**$ (128,259)**

[a] Other segments items included in segment operating loss include costs related to intellectual property, information technology and insurance offset by income related to payments received from European authorities to subsidize the Company's research and development in the Netherlands and France.

[b] For the year ended December 31, 2023, other segment items include $10.0 million related to the upfront consideration paid to Apic Bio for the global licensing agreement for AMT-162.

[c] For the year ended December 31, 2024, other reconciling items include costs related to the divestment of the Company's commercial manufacturing activities and the August 2024 reorganization.

[d] For the year ended December 31, 2023, other reconciling items include costs related to the October 2023 reorganization and professional fees related to the Apic Bio transaction.

18. Collaboration arrangements and concentration of credit risk

Revenues recorded for the years ended December 31, are as follows:

	Years ended December 31,		
	2024	2023	2022
		(in thousands)	
License revenue (royalty payments) from CSL Behring	$ 10,133	$ 2,758	$ —
License revenue (milestone payments) from CSL Behring	—	—	100,000
Contract manufacturing revenue from CSL Behring	6,114	10,835	1,717
Collaboration revenue from CSL Behring	10,872	2,250	3,014
Collaboration revenue from BMS	—	—	1,752
Total	**$ 27,119**	**$ 15,843**	**$ 106,483**

License revenue (milestone payments) from CSL Behring

The Company recorded $100.0 million in variable milestone revenue related to a first sale of HEMGENIX® in the U.S. during the year ended December 31, 2022 as the Company considered the occurrence of this event to be probable following the November 2022 BLA approval of HEMGENIX®. The Company collected the $100.0 million payment from CSL Behring in July 2023 following the first sale of the Product in the U.S in June 2023.

Contract manufacturing revenue from CSL Behring

The Company provided contract manufacturing services to CSL Behring from April 2022 until the July 2024 divestment of the commercial manufacturing activities to Genezen. 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.

The Company's development and commercial supply agreement requires the Company to supply HEMGENIX® to CSL Behring until such time that these capabilities are transferred to CSL Behring or a contract manufacturing organization designated by CSL Behring. On September 6, 2022, CSL Behring notified the Company of its intent to transfer manufacturing technology related to HEMGENIX® in the coming years to a third-party contract manufacturer designated by CSL Behring.

The Company generated $6.1 million, $10.8 million and $1.7 million contract manufacturing revenue from sales to CSL Behring during the years ended December 31, 2024, 2023 and 2022. The Company incurred $17.1 million, $13.6 million and $2.1 million of costs in relation to its contract manufacturing activities during the years ended December 2024, 2023 and 2022.

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 as well as 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 from CSL Behring

The Company provides on-demand development services and other services to CSL Behring. These activities are reimbursed at an agreed full-time-employee rate and CSL Behring also reimbursed agreed third-party expenses incurred in relation to performing these activities.

The Company recognized $10.9 million of collaboration revenue in the year ended December 31, 2024, compared to $2.3 million and $3.0 million in the same periods in 2023 and 2022.

Accounts receivable

As of December 31, 2024, the Company had accounts receivable of $5.7 million 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.

19. Other income

Other income during the year ended December 31, 2024 was $7.9 million compared to $6.1 million and $7.2 million during the same periods in 2023 and 2022.

	Years ended December 31,		
	2024	2023	2022
		(in thousands)	
Research and development grants from Dutch and French authorities	$ 5,602	$ 5,293	$ 6,084
Gain on sale of commercial manufacturing facility	1,150	—	—
Sublease income	1,073	609	763
Other	101	157	324
Total	**$ 7,926**	**$ 6,059**	**$ 7,171**

20. Other expense

Other expense during the year ended December 31, 2024 was $4.6 million compared to $1.7 million and $0.8 million during the same periods in 2023 and 2022, respectively.

	Years ended December 31,		
	2024	2023	2022
	(in thousands)		
Supply of HEMGENIX® to CSL Behring	$ 3,215	$ —	$ —
Sublease expense	1,358	900	820
Fair value loss related to equity stake in VectorY B.V.	—	790	—
Total	**$ 4,573**	**$ 1,690**	**$ 820**

In the year ended December 31, 2024, the Company recognized $3.2 million net (nil in periods ended December 31, 2023 and 2022) in other expense 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 the favorable supply terms under the CSA and credits from the release of liabilities related to expected net losses associated with the minimum purchase commitments under the CSA.

21. Income taxes

a. Income tax (benefit) / expense

Due to the uncertainty surrounding the realization of favorable tax attributes in future tax returns, the Company has recorded a valuation allowance against the Company's net deferred tax assets in the Netherlands and a partial valuation allowance against the Company's net deferred tax assets in France.

There are no significant unrecognized tax benefits as of December 31, 2024 and 2023.

For the years ended December 31, 2024, 2023 and 2022, (loss) / income before income tax benefit / (expense) consists of the following:

	Years ended December 31,		
	2024	2023	2022
	(in thousands)		
Dutch operations	$ (215,251)	$ (282,530)	$ (96,872)
U.S. operations	(1,133)	(6,903)	(14,934)
Other	(20,743)	(17,124)	(16,453)
Total	**$ (237,127)**	**$ (306,557)**	**$ (128,259)**

The income tax (expense) / benefit for the years ended December 31, 2024, 2023 and 2022, consists of the following:

	Years ended December 31,		
	2024	2023	2022
	(in thousands)		
Current tax expense			
Other	$ (145)	$ (110)	$ (24)
Total current income tax expense	$ (145)	$ (110)	$ (24)
Deferred tax (expense) / benefit			
Dutch operations	$ —	$ —	$ (808)
U.S. operations	(2,275)	(2,708)	(1,075)
Other	(9)	897	3,377
Total deferred tax (expense) / benefit	$ (2,284)	$ (1,811)	$ 1,494
Total income tax (expense) / benefit	**$ (2,429)**	**$ (1,921)**	**$ 1,470**

b. Tax benefit recognized in other comprehensive income

The reconciliation of the amount of income tax (loss) / benefit recognized in Other comprehensive income / (loss) for the years ended December 31, 2024 and December 31, 2023 is as follows:

	Year ended December 31, 2024			Year ended December 31, 2023		
	Before tax	Tax	Net of tax	Before tax	Tax	Net of tax
		(in thousands)			(in thousands)	
Unrecognized (loss) / gain related to defined benefit pension plan liability	$ 384	$ (57)	$ 327	$ (2,553)	$ 417	$ (2,136)
Total	**$ 384**	**$ (57)**	**$ 327**	**$ (2,553)**	**$ 417**	**$ (2,136)**

No income tax benefit or expense has been recognized in Other Comprehensive Loss for the year ended December 31, 2022.

c. Tax rate reconciliation

The reconciliation of the amount of income tax (expense) / benefit that would result from applying the Dutch statutory income tax rate to the Company's reported amount of loss before income tax (expense) / benefit for the years ended December 31, 2024, 2023 and 2022, is as follows:

	Years ended December 31,		
	2024	2023	2022
		(in thousands)	
Loss before income tax (expense) / benefit for the period	$ (237,127)	$ (306,557)	$ (128,259)
Expected income tax benefit at the 25.8% tax rate enacted in the Netherlands	61,179	79,092	33,091
Difference in tax rates between the Netherlands and other foreign countries	(149)	(124)	99
Other net change in valuation allowance	(57,550)	(67,004)	(20,591)
Non-deductible expenses	(5,909)	(13,885)	(11,129)
Income tax (expense) / benefit	**$ (2,429)**	**$ (1,921)**	**$ 1,470**

Non-deductible expenses predominantly relate to share-based compensation expenses. These expenses affected the effective tax rate by an amount of $5.6 million in 2024 (2023: $9.0 million; 2022: $8.5 million). The fair value gain on contingent consideration affected the effective tax rate by an amount of $0.5 million in 2024 ($4.1 million and $1.9 million in 2023 and 2022, respectively).

d. Significant components of deferred taxes

The tax effects of temporary differences and carryforwards that give rise to significant portions of deferred tax assets and deferred tax liabilities as of December 31, 2024 and 2023 are as follows:

	Years ended December 31,	
	2024	2023
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 178,421	$ 145,826
Liability from Royalty Financing agreement	19,476	6,155
Intangibles	4,702	6,417
Operating lease liabilities	3,846	9,790
Accrued expenses and other current liabilities	3,069	1,435
Interest carryforwards	2,956	3,711
Property, plant and equipment	365	—
Defined benefit pension plan liability	260	406
Inventory	—	497
Total deferred tax assets	**$ 213,095**	**$ 174,237**
Less valuation allowance	(191,864)	(145,191)
Deferred tax assets, net of valuation allowance	**$ 21,231**	**$ 29,046**
Acquired IPR&D intangible asset	(14,341)	(15,242)
Operating lease right-of-use assets	(3,864)	(8,159)
Property, plant and equipment	(165)	(719)
Other current assets and receivables	(48)	(193)
Deferred tax liability	**$ (18,418)**	**$ (24,313)**
Net deferred tax asset	**$ 2,813**	**$ 4,733**

Changes in the valuation allowance were as follows:

	Years ended December 31,		
	2024	2023	2022
		(in thousands)	
January 1,	$ 145,191	$ 74,547	$ 60,289
Changes recorded in the statement of operations	57,550	67,004	20,593
Changes recorded in equity	—	—	(972)
Other changes including currency translation adjustments	(10,877)	3,640	(5,363)
December 31,	**$ 191,864**	**$ 145,191**	**$ 74,547**

The valuation allowance of $191.9 million as of December 31, 2024 is primarily related to EUR 178.7 million ($185.6 million) deferred tax assets in the Netherlands resulting from net operating loss carryforwards of EUR 153.1 million ($159.1 million), liability from Royalty Financing Agreement of EUR 18.8 million ($19.5 million), intangible assets of EUR 3.6 million ($3.8 million), interest carryforwards of EUR 2.8 million ($3.0 million) and property, plant and equipment of EUR 0.4 million ($0.4 million).

Netherlands

As of December 31, 2024, the total amount of net operating losses carried forward under the Dutch tax regime was EUR 593.6 million ($616.5 million) (December 31, 2023: EUR 446.4 million ($492.7 million)). The Company has historically recorded a full valuation allowance. The Company evaluates all positive and negative evidence in assessing the need for a full valuation allowance. Management considers reversing taxable temporary differences, projected future taxable income and tax-planning strategies in making this assessment. The Company concluded that as of December 31, 2024, and December 31, 2023 it is more likely than not that the remaining deferred tax assets will not be realized. The Company's Dutch net operating tax losses carried forward relate to 2019, 2022, 2023 and 2024.

As of December 31, 2024, the tax treatment of the Royalty Agreement has not been agreed with the Dutch tax authorities. A different tax treatment could result in a different categorization of temporary differences and an offsetting deferred tax asset.

A portion of the valuation allowance for deferred tax assets recorded as of December 31, 2024 continues to relate to follow-on offering costs incurred in 2019. Any subsequently recognized tax benefits will be credited directly to contributed capital. As of December 31, 2024, that amount was EUR 3.0 million ($3.2 million) and EUR 3.0 million ($3.4 million) as of December 31, 2023.

The Dutch corporate tax rate is 25.8% from 2022 onwards.

Net operating loss carryforwards subject to a limit of offsetting taxable profit in excess of EUR 1.0 million to 50% of the taxable profit can be carried forward indefinitely.

The fiscal periods from 2022 onwards are still open for inspection by the Dutch tax authorities.

United States of America

The federal corporate tax rate in the U.S. is 21.0%. In addition, the Company is subject to state income taxes resulting in a combined tax rate of 27.3% for its U.S. operation. As of December 31, 2024, an estimated $22.9 million of net operating losses remain to be carried forward. These net operating losses carried forward will expire in 2036 and 2037 except for $0.7 million which can be carried forward indefinitely with a deduction limited to 80% of taxable income in a given year.

The Company's U.S. operations have been generating taxable income since 2018 with the exception of 2022. The Company expects to continue to generate taxable income in the U.S. during the foreseeable future.

Under the provision of the Internal Revenue Code, the U.S. net operating losses carried forward may become subject to an annual limitation in the event of certain cumulative exchange in the ownership interest of significant shareholders over a three-year period in excess of 50 percent, as defined under Section 382 and 383 of the Internal Revenue Code. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation.

The fiscal periods from 2021 are still open for inspection by the Internal Revenue Service ("IRS"). To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the IRS or Massachusetts Department of Revenue to the extent utilized in a future period. The Company is currently not under examination by the IRS for any tax years.

France

The French corporate tax rate for fiscal year 2024 was 25.0%. In addition, the Company is subject to a surcharge of 3.3% of the 25.0% standard corporate tax rate resulting in a combined rate of 25.8%.

The Company's French operations have incurred losses since incorporation and are expected to continue incurring tax losses for the foreseeable future. The French operations as of December 31, 2024 have an estimated EUR 48.9 million ($50.8 million) (December 31, 2023: EUR 35.9 million ($39.6 million)) of net operating losses that are available for carry forward indefinitely. The Company recorded a partial valuation allowance during the years ended December 31, 2024 and 2023. No such valuation allowance was recorded in the years ended December 31, 2022 or 2021. The Company evaluates all positive and negative evidence including future income from reversing taxable temporary differences (particularly from reversing the deferred tax liability related to the acquired IPR&D intangible asset), projected future taxable income subject to the loss limitation rules applicable in France and tax-planning strategies in making this assessment.

22. Basic and diluted earnings per ordinary share

Basic net loss per ordinary share is computed by dividing net loss for the period by the weighted average number of ordinary shares outstanding during the period. Diluted earnings per ordinary share are calculated by adjusting the weighted average number of ordinary shares outstanding, assuming conversion of all potentially dilutive ordinary shares. As the Company has incurred a loss in the years presented, all potentially dilutive ordinary shares for these years would have an antidilutive effect, if converted, and thus have been excluded from the computation of loss per share.

	Year ended December 31,		
	2024	2023	2022
	(in thousands, except share amounts)		
Numerator:			
Net loss attributable to ordinary shares	$ (239,556)	$ (308,478)	$ (126,789)
Denominator:			
Weighted-average number of ordinary shares outstanding - basic and diluted	48,649,129	47,670,986	46,735,045

The following table presents ordinary share equivalents that were excluded from the calculation of diluted net loss per ordinary share for the years presented as the effect of their inclusion would have been anti-dilutive:

	Year ended December 31,		
	2024	2023	2022
Anti-dilutive ordinary share equivalents			
Stock options under 2014 Plans and previous plan	4,967,160	4,974,030	4,237,917
Non-vested RSUs and PSUs	1,810,018	2,486,919	2,219,464
ESPP	—	3,640	1,048
Total anti-dilutive ordinary share equivalents	**6,777,178**	**7,464,589**	**6,458,429**

The anti-dilutive ordinary shares are presented without giving effect to the application of the treasury method or exercise prices that exceeded the price of the Company's ordinary shares as of December 31, 2024, December 31, 2023 and December 31, 2022.

23. Commitments and contingencies

In the course of its business, the Company enters as a licensee into contracts with other parties regarding the development and marketing of its pipeline products. Among other payment obligations, the Company is obligated to pay royalties to the licensors based on future sales levels and milestone payments whenever specified development, regulatory and commercial milestones are met. As both future sales levels and the timing and achievement of milestones are uncertain, the financial effect of these agreements cannot be estimated reliably. The Company also has obligations to make future payments that become due and payable upon the collection of milestone payments from CSL Behring. The achievement and timing of these milestones is not fixed and determinable. Relevant commitments and contingencies are further discussed in other sections of this form 10-K, such as, Note 3 "*Divestiture of manufacturing facility*" and Note 18 "*Collaboration arrangements and concentration of credit risk*", amongst others.

24. Related party transaction

None.

25. Subsequent events

In January 2025, the Company received net proceeds of $70.1 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company, through a follow-on public offering of 4.4 million ordinary shares at a public offering price of $17.00 per ordinary share.

In February 2025, the Company received an additional $10.6 million in net proceeds upon the underwriters' exercise of their option to purchase an additional 0.7 million ordinary shares at the public offering price.

EXHIBIT INDEX

Exhibit No.	Description
2.1†	Sale and Purchase Agreement, executed June 21, 2021, by and between uniQure N.V. and Corlieve Therapeutics SAS (incorporated by reference to Exhibit 2.1 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended June 30, 2021 filed with the SEC on July 26, 2021).
3.1	Amended Articles of Association of the Company (incorporated by reference to Exhibit 3.1 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended June 30, 2021 filed with the SEC on July 26, 2021).
4.1*	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934.
10.1t	2014 Share Incentive Plan (incorporated by reference to Exhibit 4.3 of the Company's Registration Statement on Form S-8 (file no. 333-225629) filed with the SEC on June 14, 2018).
10.2t	Amended and Restated 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K (file no. 001-36294) filed with the SEC on November 17, 2023).
10.3t	Amended and Restated 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K (file no. 001-36294) filed with the SEC on June 20, 2024).
10.4t	Form of Share Option Agreement, effective December 8, 2021, under the 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.65 of the Company's Annual Report on Form 10-K for the year ended December 31, 2021 (file no. 001-36294) filed with the SEC on February 25, 2022).
10.5t	Form of Restricted Stock Unit Award, effective December 8, 2021, under the 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.66 of the Company's Annual Report on Form 10-K for the year ended December 31, 2021 (file no. 001-36294) filed with the SEC on February 25, 2022).
10.6†t	Form of Performance Stock Unit Award, effective December 8, 2021 under the 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.67 of the Company's Annual Report on Form 10-K for the year ended December 31, 2021 (file no. 001-36294) filed with the SEC on February 25, 2022).
10.7t	Employee Share Purchase Plan (incorporated by reference to Exhibit 4.2 of the Company's Registration Statement on Form S-8 (file no. 333-225629) filed with the SEC on June 14, 2018).
10.8t	Employment Agreement between uniQure, Inc. and Matthew Kapusta, dated December 9, 2014 (incorporated by reference to Exhibit 10.6 of the Company's Annual Report on Form 10-K (file no. 001-36294) for the year ended December 31, 2016 filed with the SEC on March 15, 2017).
10.9t	Amendment to the Employment Agreement between uniQure, Inc. and Matthew Kapusta, dated March 14, 2017 (incorporated by reference to Exhibit 10.7 of the Company's Annual Report on Form 10-K (file no. 001-36294) for the year ended December 31, 2016 filed with the SEC on March 15, 2017).
10.10t	Amendment to the Employment Agreement between uniQure, Inc. and Matthew Kapusta, dated October 26, 2017 (incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended September 30, 2017 filed with the SEC on November 1, 2017).
10.11t	Amended and Restated Employment Agreement, effective June 15, 2021, by and between uniQure biopharma B.V. and Christian Klemt (incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended June 30, 2021 filed with the SEC on July 26, 2021).
10.12t	Employment Agreement, effective May 17, 2021, by and between uniQure biopharma B.V. and Pierre Caloz (incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended June 30, 2021 filed with the SEC on July 26, 2021).

10.13t Equity Side Letter, effective May 17, 2021, by and between uniQure N.V. and Pierre Caloz (incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended June 30, 2021 filed with the SEC on July 26, 2021).

10.14t Termination Agreement, dated July 22, 2024, by and between uniQure biopharma B.V. and Pierre Caloz (incorporated by reference to Exhibit 10.5 of the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2024 (file no. 001-36294) filed with the SEC on August 1, 2024).

10.15t Employment Agreement dated June 13, 2023 between uniQure, Inc. and Jeannette Potts (incorporated by reference to Exhibit 10.77 of the Company's Annual Report on Form 10-K for the year ended December 31, 2023 (file no. 001-36294) filed with the SEC on February 28, 2024).

10.16t* Employment Agreement dated June 26, 2023 between Corlieve Therapeutics AG and Walid Abi-Saab.

10.17 Lease relating to 113 Hartwell Avenue, Lexington, Massachusetts, dated as of July 24, 2013, by and between uniQure Inc. and King 113 Hartwell LLC (incorporated by reference to Exhibit 10.28 of the Company's Registration Statement on Form F-1 (file no. 333-193158) filed with the SEC on January 2, 2014).

10.18 First Amendment Lease relating to 113 Hartwell Avenue, Lexington, Massachusetts, dated as of July 24, 2013, by and between the Company and King113 Hartwell LLC (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K (file no. 001-36294) filed with the SEC on November 15, 2018).

10.19 Second Amendment Lease relating to 113 Hartwell Avenue, Lexington Massachusetts, dated as of June 17, 2019, by and between the Company and King 113 Hartwell LLC (incorporated by reference to Exhibit 10.42 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended June 30, 2019 filed with the SEC on July 29, 2019).

10.20 Landlord Consent to Assignment and Assumption of Lease and Third Amendment to Lease, dated June 28, 2024, by and among Hartwell Innovation Campus, LLC, uniQure, Inc. and Genezen MA, Inc. (incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ending June 30, 2024 filed with the SEC on August 1, 2024).

10.21 Assignment and Assumption of Lease, dated July 22, 2024, by and between uniQure, Inc. and Genezen MA, Inc. (incorporated by reference to Exhibit 10.4 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ending June 30, 2024 filed with the SEC on August 1, 2024).

10.22 Lease relating to Paasheuvelweg 25, dated as of March 7, 2016, by and between 52 IFH GmbH & Co. KG and uniQure biopharma B.V. (incorporated by reference to Exhibit 10.36 of the Company's Annual Report on Form 10-K (file no. 001-36294) for the year ended December 31, 2016 filed with the SEC on March 15, 2017).

10.23 Lease Agreement relating to 91 Hartwell Avenue, Lexington, Massachusetts, dated as of February 1, 2022, by and between uniQure Inc. and NRL 91 Hartwell LLC (incorporated by reference to Exhibit 10.70 of the Company's Annual Report on Form 10-K for the year ended December 31, 2021 (file no. 001-36294) filed with the SEC on February 25, 2022).

10.24 Lease Agreement relating to Peter Merian-Weg 4, 4052 Basel, Switzerland, dated as of November 1, 2023, by and between Corlieve Therapeutics AG and Stiftung Sympany.

10.25 Business Acquisition Agreement, dated as of February 16, 2012, by and among Amsterdam Molecular Therapeutics (AMT) Holding N.V., the Company and the other Parties listed therein (incorporated by reference to Exhibit 10.29 of the Company's Registration Statement on Form F-1 (file no. 333-193158) filed with the SEC on January 2, 2014).

10.26 Deed of Assignment of Certain Assets and Liabilities of Amsterdam Molecular Therapeutics (AMT) Holding N.V., dated as of April 5, 2012, by and among Amsterdam Molecular Therapeutics (AMT) Holding B.V., Amsterdam Molecular Therapeutics (AMT) Holding IP B.V. and Amsterdam Molecular Therapeutics (AMT) Holding N.V. (incorporated by reference to Exhibit 10.30 of the Company's Registration Statement on Form F-1 (file no. 333-193158) filed with the SEC on January 2, 2014).

10.27	Agreement for Transfer of Certain Assets and Liabilities of Amsterdam Molecular Therapeutics (AMT) Holding N.V., dated as of February 16, 2012, by and among Amsterdam Molecular Therapeutics (AMT) Holding B.V., Amsterdam Molecular Therapeutics (AMT) Holding IP B.V. and Amsterdam Molecular Therapeutics (AMT) Holding N.V. (incorporated by reference to Exhibit 10.31 of the Company's Registration Statement on Form F-1 (file no. 333-193158) filed with the SEC on January 2, 2014).
10.28†	Assignment and License Agreement dated April 17, 2017 between Professor Paolo Simioni and uniQure biopharma B.V. (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K (file no. 001-36294) filed with the SEC on October 19, 2017).
10.29†	Commercialization and License Agreement by and between uniQure biopharma B.V. and CSL Behring LLC dated June 24, 2020 (incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q (file no. 001-36294) for the period ended June 30, 2020 filed with the SEC on July 30, 2020).
10.30†	Third Amended and Restated Loan and Security Agreement as of December 15, 2021, by and among uniQure biopharma B.V., uniQure Inc., uniQure IP B.V., the Company and Hercules Capital Inc (incorporated by reference to Exhibit 10.68 of the Company's Annual Report on Form 10-K for the year ended December 31, 2021 (file no. 001-36294) filed with the SEC on February 25, 2022).
10.31†	Amendment No. 1 to Third Amended and Restated Loan and Security Agreement, dated of May 12, 2023, by and among uniQure biopharma, B.V., uniQure, Inc., uniQure IP B.V., the Company and Hercules Capital, Inc. (incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2023 (file no. 001-36294) filed with the SEC on August 1, 2023).
10.32†	Consent and Amendment No. 2 to Third Amended and Restated Loan and Security Agreement, dated June 28, 2024, by and among uniQure biopharma B.V., uniQure, Inc., uniQure IP B.V., the Company and Hercules Capital, Inc. (incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2024 (file no. 001-36294) filed with the SEC on August 1, 2024).
10.33†	Royalty Purchase Agreement, dated May 12, 2023, by and between uniQure biopharma B.V. and HemB SPV, L.P. (incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2023 (file no. 001-36294) filed with the SEC on August 1, 2023).
10.34†	Asset Purchase Agreement, by and among uniQure, Inc., uniQure biopharma B.V., Genezen Holdings Inc. and Genezen MA, Inc., dated as of June 29, 2024 (incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2024 (file no. 001-36294) filed with the SEC on August 1, 2024).
14.1*	Code of Ethics.
19.1*	Insider Trading Policy.
21.1*	Subsidiaries of the Company.
23.1*	Consent of Independent Registered Public Accounting Firm – KPMG Accountants N.V.
24.1*	Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K).
31.1*	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer.
31.2*	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer.
32.1**	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1	Compensation Clawback Policy (incorporated by reference to Exhibit 97.1 of the Company's Annual Report on Form 10-K for the year ended December 31, 2023 (file no. 001-36294) filed with the SEC on February 28, 2024).

101* The following materials from the Company's Annual Report on Form 10-K for the year ended December 31, 2024, formatted in Inline XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Income (Loss), (iii) Consolidated Statements of Shareholders' (Deficit) / Equity, (iv) Consolidated Statements of Cash Flows and (v) Notes to Consolidated Financial Statements.

104* The cover page from the Company's Annual Report on Form 10-K for the year ended December 31, 2024 has been formatted in Inline XBRL.

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

* Filed herewith.

** Furnished herewith.

t Indicates a management contract or compensatory plan or arrangement.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

UNIQURE N.V.

Date: February 27, 2025

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

Date: February 27, 2025

By: /s/ CHRISTIAN KLEMT
Christian Klemt
Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Matthew Kapusta and Christian Klemt, jointly and severally, his or her attorney-in-fact, with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
/s/ MATTHEW KAPUSTA Matthew Kapusta	Chief Executive Officer and Director (Principal Executive Officer)	February 27, 2025
/s/ CHRISTIAN KLEMT Christian Klemt	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 27, 2025
/s/ MADHAVAN BALACHANDRAN Madhavan Balachandran	Director	February 27, 2025
/s/ ROBERT GUT Robert Gut	Director	February 27, 2025
/s/ RACHELLE JACQUES Rachelle Jacques	Director	February 27, 2025
/s/ JACK KAYE Jack Kaye	Director	February 27, 2025
/s/ DAVID MEEK David Meek	Director	February 27, 2025
/s/ LEONARD POST Leonard Post	Director	February 27, 2025
/s/ JEREMY P. SPRINGHORN Jeremy P. Springhorn	Director	February 27, 2025