Annual Report 2021

uniQure N.V.

Amsterdam, April 29, 2022

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A Report of the Board of Directors

1 Introduction

a) Forward-looking statements

This Annual Report and the Consolidated Financial Statements (this "Annual Report") contain "forward-looking statements" as defined under U.S. 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, which include, but are not limited to, statements related to the COVID-19 coronavirus pandemic, our collaboration and license agreements, our beliefs about our competitive advantage and the capabilities of our manufacturing facility, our cash runway, the advancement of our clinical trials, our intellectual property portfolio, and the impact of regulatory actions on our regulatory submission timelines, may be found in Part 2, Part 3, Part 4 and other sections of this Annual Report.

Forward-looking statements are only predictions based on management's current views and assumptions and involve risks and uncertainties, and actual results could differ materially from those projected or implied. The most significant factors known to us that could materially adversely affect our business, operations, industry, financial position or future financial performance include those described under "Risk Factors" and elsewhere in this Annual Report and in our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the U.S. Securities and Exchange Commission on February 25, 2022, 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 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 under "Risk Factors" and elsewhere in this Annual Report 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. We do not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of this Annual Report to reflect later events or circumstances or to reflect the occurrence of unanticipated events. All forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements.

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

b) History and development of uniQure

We were 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 (AMT) Holding N.V ("AMT"). In 2012, AMT undertook a corporate reorganization, pursuant to which uniQure B.V. acquired the entire business and assets of AMT and completed a share-for-share exchange with the shareholders of AMT. Effective February 10, 2014, in connection with our initial public offering, we converted into a public company with limited liability (naamloze vennootschap) and changed our 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) in Amsterdam, the Netherlands under number 54385229. Our headquarters are in Amsterdam, the Netherlands, and our registered office is located at Paasheuvelweg 25, Amsterdam 1105 BP, the Netherlands and our telephone number is +31 20 240 6000. Our website address is www.uniqure.com. Our ordinary shares are listed on the Nasdaq Global Select Market ("Nasdaq") and trade under the symbol "QURE".

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.

*c) **Business overview***

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

Key events

Acquisition of Corlieve Therapeutics

On June 21, 2021, we entered into a share and purchase agreement ("SPA") to acquire all outstanding ordinary shares of Corlieve Therapeutics SAS ("Corlieve"), a privately held French gene therapy company (together, the "Corlieve Transaction"). Upon the closing of the Corlieve Transaction on July 30, 2021 ("Acquisition Date"), we acquired 97.7% of the outstanding ordinary shares of Corlieve in return for EUR 44.9 million ($53.3 million as of the Acquisition Date). As contractually required in the SPA, we acquired the remaining outstanding ordinary shares on February 9, 2022 following the expiration of a minimum holding period ("Mandatorily Redeemable Shares"). We recorded a liability related to these Mandatorily Redeemable Shares for an amount of EUR 0.7 million ($0.9 million) as of the Acquisition Date. We financed the Corlieve Transaction from cash on hand.

Following its formation in November 2019, Corlieve obtained exclusive licenses to certain patents from two French research institutions that continue to collaborate with Corlieve and us. Corlieve also obtained an exclusive license from Regenxbio Inc. ("Regenxbio") for the use of AAV9 to deliver any sequence that affects the expression of the Glutamate inotropic receptor kainate type subunit 2 ("GRIK 2") gene sequence in humans. Corlieve and Regenxbio simultaneously entered into a collaboration plan related to agreed joint preclinical research and development activities. At the Acquisition Date, Corlieve and its Swiss subsidiary, Corlieve Therapeutics AG, employed seven employees.

Corlieve's gene therapy program, ("AMT-260"), employs micro ribonucleic acid ("miRNA") silencing technology to target suppression of aberrantly expressed kainate receptors in the hippocampus of patients with temporal lobe epilepsy ("TLE"). TLE affects approximately 1.3 million people in the U.S. and Europe alone, of which approximately 0.8 million patients are unable to adequately control acute seizures with currently approved anti-epileptic therapies. Patients with refractory TLE experience increased morbidity, excess mortality, and poor quality of life.

In addition to the payments to acquire 100% of the outstanding ordinary shares, Corlieve's former and remaining shareholders are eligible to receive up to EUR 35.8 million (or $40.6 million as of December 31, 2021) upon the achievement of development milestones through Phase I/II and EUR 143.1 million (or $162.3 million as of December 31, 2021) upon the achievement of milestones associated with Phase III development and obtaining approval to commercialize AMT-260 in the United States of America and the European Union. We may elect to pay up to 25% of such milestone payments through the issuance of our ordinary shares. We recorded a EUR 20.2 million ($24.0 million) liability related to these contingent consideration payments as of the Acquisition Date.

Total consideration of EUR 65.8 million ($78.1 million), which consisted of the cash paid upon the Acquisition Date, the payment for the Mandatorily Redeemable Shares and the contingent consideration payments, was allocated to identifiable intangible assets related to the in-process research and development of AMT-260 ("IPR&D Intangible Asset"). The IPR&D Intangible Asset's fair value was determined at EUR 53.6 million ($63.6 million) as of the Acquisition Date. We also recognized a EUR 13.4 million ($15.9 million) deferred tax liability in relation to this IPR&D Intangible Asset. The total consideration in excess of the net assets acquired was EUR 23.9 million ($28.4 million) and was allocated to goodwill.

CSL Behring commercialization and license agreement

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

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

CSL Behring is responsible for the development and commercialization of the Product. We agreed to complete the validation of the current manufacturing process as well as to the development and validation of a next generation manufacturing process. We will be entitled to receive a development milestone payment if we complete these activities in accordance with an agreed development plan and timeline. CSL Behring is responsible for global regulatory submissions and commercialization requirements for the Product. Certain clinical development and regulatory activities performed by us are reimbursed by CSL Behring.

On the Signing Date, 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 at an agreed-upon price commensurate with the stand-alone selling price ("SSP"). We will be responsible to supply the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization.

Other than under the CSL Behring Agreement, neither we nor CSL Behring may perform any clinical trials, with the exception of trials required to extend the label or gain marketing authorization outside the United States or the European Union, for any gene therapy product, gene-editing product, or any other product comprising an AAV vector to conduct nucleotide transfer (including deoxyribonucleic acid ("DNA") and ribonucleic acid ("RNA")) for the treatment, prevention, or cure of hemophilia B for a period commencing on June 24, 2020 and continuing for a period of four years following the first commercial sale of the Product in the United States, and neither we nor CSL Behring may commercialize such a product for a period commencing as of June 24, 2020 and continuing for a period of seven years following the first commercial sale of the Product in the United States. This exclusivity commitment would not bind an acquirer of us that owns or controls such a product so long as certain precautions are followed to ensure that CSL Behring's confidential information and our proprietary technology related to the Product are not used or accessed by personnel of such acquirer who are developing or commercializing such competing product.

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.

The effectiveness of the transactions contemplated by the CSL Behring Agreement was contingent on completion of review under antitrust laws in the United States, Australia, and the United Kingdom, and certain provisions of the CSL Behring Agreement did not become effective until after we had received all such regulatory approvals and after the waiting period under the HSR Act expired on May 5, 2021.

Following the Closing, we recorded $462.4 million, including a $450.0 million upfront cash payment, as license revenue. Upon the Closing, we contractually owed to our licensors $15.5 million of the upfront payment received from CSL Behring.

We are eligible to receive more than $0.3 billion in regulatory, development, and first commercial sale milestones, $1.3 billion in additional commercial milestones, and tiered double-digit royalties of up to a low-twenties percentage of net product sales arising from the collaboration. As of December 31, 2021, the Company recorded accounts receivable of $2.9 million from CSL Behring related to clinical development services as well as a contract asset of $55.0 million associated with milestone payments due upon CSL Behring's global regulatory submissions for etranacogene dezaparvovec, which were deemed to be probable. In March 2022, CSL Behring submitted the global regulatory submissions, and as of March 31, 2022, the Company collected $20.0 million of the total $55.0 million owed. As of March 31, 2022, the Company had accounts receivable of $38.3 million from CSL Behring, $35.0 million of which were related to the uncollected milestone payment associated with the global regulatory submissions. The remaining $35.0 million was received in April 2022.

Hemophilia B program – Etranacogene dezaparvovec (AMT-061)

Etranacogene dezaparvovec is our lead gene therapy candidate and includes an AAV serotype 5 ("AAV-5") vector incorporating the functional human Factor IX ("FIX") Padua variant. We are currently conducting, on behalf of CSL Behring, a pivotal Phase III study in 54 patients with severe and moderately-severe hemophilia B ("HOPE-B Study").

The U.S. Food and Drug Administration ("FDA") has agreed that etranacogene dezaparvovec will fall under the existing Breakthrough Therapy Designation and IND for AMT-060 (our first-generation hemophilia B gene therapy), and the European Medicines Agency ("EMA") has also agreed that etranacogene dezaparvovec will fall under the priority medicines ("PRIME") designation.

On December 9, 2021, we announced the achievement of the pre-specified primary endpoint of non-inferiority in annualized bleeding rate ("ABR") 18-months following administration compared to baseline Factor IX prophylactic therapy ("FIX") in the HOPE-B Study. ABR for all bleeds after stable FIX expression, assessed at 18 months, was 1.51 compared with the ABR of 4.19 for the lead-in period of at least six months, achieving the primary non-inferiority endpoint and a secondary superiority endpoint ($p=0.0002$) in the HOPE-B Study. ABR for investigator-adjudicated FIX-treated bleeds was 0.83 compared with lead-in ABR of 3.65 ($p<0.0001$). All participants continued to demonstrate durable, sustained increases in FIX activity at 18-months post-infusion with a mean FIX activity of 36.9 percent of normal, as measured by a one-stage activated partial thromboplastin time-based ("aPTT-based") clotting assay, compared to a mean FIX activity of 39.0 percent of normal at 26-weeks of follow-up. Etranacogene dezaparvovec was generally well-tolerated with over 80% of adverse events considered mild.

Huntington's disease program (AMT-130)

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

In June 2020, we announced the initiation of patient dosing in the U.S. Phase I/II study of AMT-130. The trial is a randomized, controlled, double-blinded, dose-escalation study of AMT-130. The study includes two dose cohorts of 26 patients randomized to either treatment with AMT-130 or to an imitation surgical procedure. The first dose cohort includes 10 patients, of which 6 patients receive treatment with AMT-130 and 4 patients receive imitation surgery. The second dose cohort includes 16 patients, of which 10 patients receive treatment with AMT-130 and 6 patients receive imitation surgery. A third cohort, which will include up to 18 additional randomized patients receiving the higher dose, will explore the use of alternative stereotactic navigation systems to simplify placement of catheters for infusions of AMT-130.

On April 5, 2021, we announced the completion of enrollment of the 10-patient low-dose cohort of the U.S. Phase I/II study of AMT-130. On December 16, 2021, we announced initial 12-month observations on the first four patients enrolled in the low-dose cohort of the U.S. Phase I/II study. Two of the four enrolled patients received AMT-130, and two patients received Sham surgery as a control. AMT-130 was generally well tolerated in the treated patients, with no serious adverse events related to AMT-130. Neurofilament light chain ("NfL"), a biomarker of injury in the brain, increased as expected immediately following the surgical procedure and returned to baseline in the treated patients. NfL remained relatively constant in the two untreated control patients. Structural magnetic resonance imaging did not reveal any clinically meaningful safety findings in either treated or control patients at one year of follow-up. Measurements of total and mutant HTT protein in the cerebral spinal fluid of the four patients were highly variable and inconclusive.

On February 7, 2022, we announced the initiation of patient dosing in our 15-patient, open-label, Phase Ib/II study of AMT-130 in the EU.

On March 21, 2022, we announced the completion of enrollment of the 16-patient high-dose cohort of the U.S. Phase I/II study of AMT-130.

Financing

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

On January 29, 2021, we and Hercules amended the 2018 Amended Facility ("2021 Amended Facility"). Pursuant to the 2021 Amended Facility, Hercules agreed to an additional Facility of $100.0 million ("Tranche B") increasing the aggregate principal amount of the term loan facilities from $35.0 million to up to $135.0 million. On January 29, 2021, we drew down $35.0 million of the Tranche B. Advances under Tranche B bore interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance of $70.0 million and all accrued but unpaid interest on advances under Tranche B was due on June 1, 2023. The back-end fee in respect of advances under the 2021 Amended Facility ranged from 1.65% to 6.85%, depending on the repayment date. In addition to Tranche B, the 2021 Amended Facility also extended the interest only payment period of the previously funded $35.0 million term loan ("Tranche A") from January 1, 2022 to June l, 2023.

On December 15, 2021, we and Hercules amended and restated the 2021 Amended Facility ("2021 Restated Facility"). Pursuant to the 2021 Restated Facility, Tranche A and Tranche B of the 2021 Amended Facility with a total outstanding balance of $70.0 million were consolidated into one tranche with a total commitment of $100.0 million. We drew down an additional $30.0 million, resulting in total principal outstanding as of December 31, 2021 of $100.0 million. The 2021 Restated Facility extended the loan's maturity date from June 1, 2023 until December 1, 2025. The interest-only period is extended from January 1, 2023 to December 1, 2024, or December 1, 2025 if, prior to June 30, 2024, either (a) the Biologics License Application ("BLA") for AMT-061 is approved by the FDA or (b) AMT-130 is advanced into a pivotal trial. The interest rate is adjustable and is the greater of (i) 7.95% and (ii) 7.95% plus the prime rate less 3.25% per annum. Under the 2021 Restated Facility, we owe a back-end fee of 4.85% of the outstanding debt. We are required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. We continue to owe a $2.5 million back-end fee related to the 2021 Amended Facility which is due on June 1, 2023.

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

In March and April of 2021, we issued 921,730 ordinary shares at a weighted average price of $33.52 per ordinary share, with net proceeds of $29.6 million, after deducting underwriting discounts and net of offering expenses.

Facilities

In February 2021, we commenced the expansion of our Amsterdam site to build additional laboratories to support the expansions of our research and development activities as well as the construction of a cleanroom capable of manufacturing cGMP materials at a 500-liter scale. The construction and validation of the cleanroom and the additional laboratories were completed in December 2021. In May 2021, we entered into a sublease agreement to let an additional approximately 1,080 square meters of office space at our Amsterdam site to accommodate the hiring of additional full-time employees. The lease expires in October 2028 and includes an option to break the lease on October 31, 2023.

In December 2021, we entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 13,501 square feet of space. The lease is expected to commence in the first half of 2022, is set for seven years starting from the rent commencement date and is non-cancellable. The lease is renewable for one five-year term.

In February 2022, we also entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 12,716 square feet. The lease is expected to commence in the second half of 2022 and is set for a non-cancellable period of seven years and four months. The lease is renewable for one five-year term.

Organization

On May 17, 2021, Pierre Caloz was appointed as Chief Operating Officer. Mr. Caloz oversees all manufacturing operations, global CMC development and innovation, supply chain, and facilities.

On June 15, 2021, Christian Klemt was appointed as Chief Financial Officer. Mr. Klemt was our Chief Accounting Officer from August 2017 to June 2021, and he will continue to serve as general manager of our Amsterdam site. Matthew Kapusta, who has been our Chief Executive Officer since December 2016 and had been our Chief Financial Officer from January 2015 to June 2021, will continue to serve as our Chief Executive Officer. In connection with his transition to Chief Financial Officer, Mr. Klemt will also serve as our Principal Financial Officer.

On June 16, 2021, our shareholders voted to approve the reappointment of Mr. David Meek and Ms. Paula Soteropoulos as non-executive directors of the Board of Directors. Mr. Meek has been appointed chairman of the Board. Mr. Philip Astley-Sparke did not stand for reappointment and retired from the Board on June 16, 2021.

On October 21, 2021, we held an Extraordinary General Meeting of our shareholders and Rachelle Jacques was appointed to the Board of Directors (the "Board"). Ms. Jacques will also serve as a member of the Audit Committee of the Board effective as of October 21, 2021.

Intellectual Property

On May 11, 2021, Pfizer, Inc. filed three petitions at the United States Patent & Trademark Office ("USPTO") seeking Inter Partes Review of U.S. Patent Nos. 9,982,248 (the "'248 Patent") and 10,465,180 (the "'180 Patent" and together with the '248 Patent, the "Patents"). The petitions collectively seek to invalidate all claims of the Patents. In August 2021, we filed our responses asking the USPTO to deny institution of the IPR proceedings. On November 17, 2021, the PTAB issued decisions granting institution on all three IPR proceedings. Our response to the petition was filed on March 3, 2022. Pfizer's reply to our response is due no later than June 17, 2022.

Covid pandemic

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

a) Workplace and employees

Throughout the pandemic, we have been implementing measures to address the impact of Covid on our business. We have implemented a series of protocols governing the operations of our Lexington facility to comply with the requirements of the various orders and guidance from the Commonwealth of Massachusetts and other related orders, guidance, laws, and regulations. We continue to monitor local government rules and recommendations and office protocols will be aligned with these rules and recommendations.

Effective March 1, 2022, we have implemented our base Covid-19 Protocol within the Lexington facility which requires only unvaccinated employees to wear facemasks and apply social distancing at the office. All non-essential Lexington employees are allowed to return to the office as space at the office allows and there is no longer a limitation on in-person meetings, although meetings organizers should still provide remote options for employees. This protocol will remain in place until July 1, 2022, unless extended or otherwise amended.

Effective February 28, 2022, the Amsterdam location is open to all employees and visitors, in line with the most updated Dutch government measures. We will continue to comply with additional Dutch measures, which amongst others is recommended for employers to make agreements with employees that allow working from home to continue to the extent applicable.

b) Business impact

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

Russian-Ukrainian war

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

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:

In collaboration with our partner, achieve regulatory approvals and the commercial launch of etranacogene dezaparvovec (AMT-061). Etranacogene dezaparvovec is a one-time administered gene therapy that combines the potential advantages of AAV5 with an enhanced Padua-FIX transgene, and may provide clinical and tolerability benefits to nearly all patients with hemophilia B. In June 2020, we entered into a commercialization and license agreement with CSL Behring pursuant to which CSL Behring received exclusive global rights to etranacogene dezaparvovec. We are responsible for the manufacturing of etranacogene dezaparvovec and CSL Behring is responsible for the development and commercialization of the Product. In September 2021, we completed the last patient's 78-week follow-up visit in the HOPE-B Phase III pivotal study, which enrolled a total of 54 patients.

Advance the development 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 to enter clinical development for Huntington's disease. It consists of an AAV5 vector carrying an artificial micro-RNA specifically tailored to silence the huntingtin gene and leverages our proprietary miQURE™ silencing technology. The therapeutic goal of AMT-130 is to inhibit the production of the mutant protein ("mHTT"). Patient enrollment is ongoing in two clinical trials of AMT-130 being conducted in the U.S. and Europe.

Build a pipeline of gene therapy programs focused on rare, liver-directed and central-nervous system ("CNS") diseases. Beyond our lead clinical program in Huntington's disease and our late-stage program in hemophilia B now partnered with CSL Behring, we have a pipeline of additional AAV-based gene therapy programs in various stages of preclinical development focused on larger market opportunities and built on validated targets and technologies. We are leveraging novel vectors, promoters, and manufacturing capabilities, to develop gene therapies that have the potential to be best or first in class and are primarily focused on rare, monogenic liver-directed, and CNS disorders as well as cardiovascular and muscle diseases.

Maintain our leadership position in commercial-scale AAV manufacturing. We have established cGMP, commercial-scale manufacturing capabilities for AAV-based gene therapies in our state-of-the-art Lexington, Massachusetts facility and begun construction of a second cGMP manufacturing facility in our Amsterdam, the Netherlands facility that will complement our work in Lexington. We seek to establish larger scale and highly cost-effective capabilities to address more prevalent disorders, and we believe the modularity of our platform provides us with distinct advantages, including the potential for reduced development risk and faster times to market.

Leverage the favorable immunogenicity profile of AAV5-based gene therapies to develop multiple products. We have developed extensive experience with our AAV5-based gene therapies, including in five clinical trials in multiple liver-directed and CNS diseases. During these clinical trials, no patient treated with AAV5-based gene therapies experienced a confirmed immune response to the AAV5 capsid or complications associated with T-cell activation. Additionally, the AAV5 capsid has demonstrated a low avidity to pre-existing neutralizing antibodies ("Nab"), which may enable all, or nearly all patients to be eligible for treatment with AAV5-based gene therapies. We are now in the process of developing Smart AAV capsids that combine the advantages of AAV5 with antibody-directed delivery to move cargo across the blood brain barrier and to improve transduction of cells in the CNS.

Invest in next-generation technologies with the goal of enhancing safety, improving efficacy, and expanding the applicability of gene therapy to patients. We are developing proprietary 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 (i) miQURE, our one-time administered gene silencing platform, (ii) goQURE for simultaneous silencing of a disease gene and replacement with a healthy gene, (iii) AbQURE, using the power of AAV5 to deliver therapeutic antibodies systemically from the liver or into the CNS from cells in the brain, (iv) QUREDose for dosing through neutralizing antibodies and re-dosing technology; along with other tailored vectors, promoters, and novel transgenes. These technologies are developed both in-house by our experienced research team in Amsterdam, the Netherlands, as well as via collaborations with third parties.

Continue to expand our intellectual property portfolio. We have established what we believe is a leading intellectual property portfolio covering various aspects of our technology and programs, including (i) elements of our gene therapy constructs, such as AAV vectors, promoters and transgenes (ii) innovative delivery technologies, such as re-administration of AAV gene therapy; and (iii) proprietary manufacturing processes covering key components of our upstream and downstream capabilities. We expect to continue to expand our intellectual property portfolio by aggressively seeking patent protection for promising aspects of our technology platform and product candidates.

Our Product Candidates

A summary of our key development programs is provided below:

	Preclinical	Phase I/II	Phase III	
Liver-directed/Rare Diseases **Hemophilia B** etranacogene dezaparvovec **(AMT-061)**			✓	CSL Behring partnership
Fabry disease (AMT-191)	✓			Proprietary programs
Other undisclosed programs	✓			
CNS Diseases **Huntington's disease (AMT-130)**		✓		
Temporal lobe epilepsy (AMT-260)	✓			
Parkinson's disease (AMT-210)	✓			
Amyotrophic lateral sclerosis (AMT-161)	✓			
Autosomal dominant alzheimer's disease (AMT-240)	✓			
Other undisclosed programs	✓			
Cardiovascular Diseases & Muscle Diseases **4 Collaboration Targets**	✓			Bristol-Myers Squibb partnership

Liver-directed diseases

Hemophilia B (etranacogene dezaparvovec)

Hemophilia B Disease and Market Background

Hemophilia B is a serious and rare inherited disease in males characterized by insufficient blood clotting. The condition can lead to repeated and sometimes life-threatening episodes of external and internal bleeding following accidental trauma or medical interventions. Severe hemophilia is characterized by recurrent episodes of spontaneous joint bleeds that cause long-term damage to the joints resulting in disabling arthropathy. Bleeds may be fatal if they occur in the brain. The deficient blood clotting results from the lack of functional human Factor IX ("hFIX"). Treatment of hemophilia B today consists of prophylactic or on-demand protein replacement therapy, in which one to three times weekly intravenous administrations of plasma-derived or recombinant hFIX are required to prevent bleeding and once daily infusions in case bleeding occurs. Hemophilia B occurs in approximately 1 out of 30,000 live male births.

CSL Behring collaboration

On June 24, 2020, we entered into the CSL Behring Agreement pursuant to which CSL Behring received exclusive global rights to etranacogene dezaparvovec. The transaction became fully effective on May 6, 2021, one day after the waiting period under the HSR Act expired.

CSL Behring is responsible for the development and commercialization of the Product. We agreed to complete the validation of the current manufacturing process as well as to the development and, if requested by CSL Behring, the validation of a next generation manufacturing process. We will be entitled to receive a development milestone payment if we complete these activities in accordance with an agreed development plan and timeline. CSL Behring is responsible for global regulatory submissions and commercialization requirements for the Product. Certain clinical development and regulatory activities performed by us are reimbursed by CSL Behring.

On the Signing Date, 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 at an agreed-upon price commensurate with the SSP. We will be responsible to supply the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization.

Development of etranacogene dezaparvovec for Hemophilia B

We believe we have substantially completed the development of etranacogene dezaparvovec, a gene therapy for patients with hemophilia B that is designed to restore FIX activity, an essential protein for blood clotting. Etranacogene dezaparvovec includes an AAV5 vector incorporating the FIX-Padua variant ("FIX-Padua").

Etranacogene dezaparvovec is intended to be delivered by intravenous ("IV")-infusion, without immunosuppressant therapy, through the peripheral vein in a single treatment session for approximately 30 minutes.

Our goal for etranacogene dezaparvovec was to develop a gene therapy with the following profile:

- long-term safety, including a favorable immunogenicity profile;
- predictable, sustained and potentially curative increases in FIX activity;
- significant reductions in both bleeding rates and the need for FIX replacement therapy; and
- broad patient eligibility, including the potential to treat all or nearly all patients with hemophilia B.

AAV5-based gene therapies have been used in a multitude of clinical trials, including five clinical trials conducted by us in patients with hemophilia B and other disorders. No patient treated in clinical trials with our AAV5-based gene therapies has experienced any confirmed, cytotoxic T-cell-mediated immune response to the capsid. An independent clinical trial has demonstrated that AAV5 has the lowest prevalence of pre-existing neutralizing antibodies compared to other AAV vectors. Data from our clinical, preclinical, and nonclinical studies suggest that all, or nearly all patients may be eligible for treatment with etranacogene dezaparvovec.

In March 2020, we completed enrollment of our HOPE-B Phase III pivotal trial of etranacogene dezaparvovec. The trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of etranacogene dezaparvovec. Fifty-four adult hemophilia B patients, who were classified as severe or moderately severe, were enrolled in a six-month observational period prior to dosing during which time they continued to use their current standard of care to establish a baseline control. After the six-month lead-in period, patients received a single IV-administration of etranacogene dezaparvovec. Patients enrolled in the HOPE-B trial were tested for the presence of pre-existing neutralizing antibodies to AAV5 but not excluded from the trial based on their titers.

On December 9, 2021, we announced the achievement of the pre-specified primary endpoint of non-inferiority in ABR 18-months following administration compared to baseline FIX prophylactic therapy in the HOPE-B study. ABR for all bleeds after stable FIX expression, assessed at 18 months, was 1.51 compared with the ABR of 4.19 for the lead-in period of at least six months, achieving the primary non-inferiority endpoint and a secondary superiority endpoint ($p=0.0002$) in the HOPE-B Study. ABR for investigator-adjudicated FIX-treated bleeds was 0.83 compared with lead-in ABR of 3.65 ($p<0.0001$). All participants continued to demonstrate durable, sustained increases in FIX activity at 18-months post-infusion with a mean FIX activity of 36.9 percent of normal, as measured by a one-stage aPTT-based clotting assay, compared to a mean FIX activity of 39.0 percent of normal at 26-weeks of follow-up. Etranacogene dezaparvovec was generally well-tolerated with over 80% of adverse events considered mild.

On March 28, 2022, CSL Behring announced that EMA had accepted the Marketing Authorization Application ("MAA") for etranacogene dezaparvovec under its accelerated assessment procedure. By the date of this Annual Report, we received $55.0 million in milestone payments owed to us by CSL Behring related to their global regulatory submissions for etranacogene dezaparvovec.

The FDA has agreed that etranacogene dezaparvovec will fall under Breakthrough Therapy Designation, and the EMA has also agreed that etranacogene dezaparvovec will fall under the PRIME designation.

Intellectual Property for etranacogene dezaparvovec

In 2017, we acquired intellectual property from Professor Paolo Simioni ("Dr. Simioni"), a hemophilia expert at the University of Padua, Italy. The intellectual property includes U.S. Patent Number 9,249,405, (the "'405 Patent"). The '405 Patent was subject to *Inter Partes Review* ("IPR") proceedings at the Patent Trials and Appeal Board ("PTAB") of the USPTO. Ultimately, the challenged claims of the '405 Patent were withdrawn but the unchanged claims remain in force. The '405 Patent thus covers compositions of FIX-Padua polypeptides (proteins), their therapeutic uses as well as nucleic acid sequences encoding FIX-Padua. The FIX Padua variant is a FIX protein carrying a leucine at the R338 position, often called the "FIX-Padua" or "Padua mutant".

On May 29, 2018, the USPTO granted us a second patent, U.S. Patent Number 9,982,248, which covers methods of treating coagulopathies (bleeding disorders), including hemophilia B, using AAV-based gene therapy with nucleic acid encoding the hyperactive FIX Padua variant.

On November 5, 2019, the USPTO granted us a third patent, U.S. Patent Number 10,465,180, which covers any AAV comprising a nucleic acid encoding a FIX-Padua protein, and promoter sequences, transcription termination and control elements. The claims also cover FIX-Padua variants with at least 70% sequence identity to FIX-R338L.

In addition to the U.S. patents, on February 20, 2018, the Canadian Intellectual Property Office granted Patent Number 2,737,094, which covers FIX-Padua nucleic acids for use in gene therapy and FIX-Padua polypeptides for use in FIX replacement therapy.

In Europe, European Patent 2337849 directed to a FIX polypeptide protein was withdrawn during opposition proceedings with the European Patent Office ("EPO"). In addition, EP 3252157, a refused divisional European patent application was withdrawn. We are still pursuing a European divisional patent application that was filed on May 14, 2019. Both in the U.S. and in Europe, we have pending divisional applications still in prosecution phases.

On May 11, 2021, Pfizer, Inc. filed three petitions at the USPTO seeking *Inter Partes Review* of U.S. Patent Nos. 9,982,248 (the "'248 Patent") and 10,465,180 (the "'180 Patent" and together with the '248 Patent, the "Patents"). The petitions collectively seek to invalidate all claims of the Patents. In August 2021, we filed our responses asking the USPTO to deny institution of the IPR proceedings. On November 17, 2021, the PTAB issued decisions granting institution on all three IPR proceedings. Our response to the petition was filed on March 3, 2022. Pfizer's reply to our response is due no later than June 17, 2022.

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. 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

In September 2020, we selected a lead gene therapy candidate (AMT-191) for the treatment of Fabry disease to advance into Investigational New Drug-enabling studies ("IND-enabling studies"). The lead candidate is a one-time administered AAV5 gene therapy incorporating the GLA transgene. In preclinical studies comparing multiple product candidates, including constructs incorporating a modified alpha-N-acetylgalactosaminidase transgene (modNAGA), AMT-191 demonstrated the most robust and sustained increases in GLA activity.

In October 2021, we presented preclinical data for AMT-191 at the European Society of Gene and Cell Therapy ("ESGCT"), confirming efficiency and cross correction in a Fabry mouse model, with increased gamma-linolenic acid in the liver, kidney, heart, and brain and normalized lysoglobotriaosylceramide-3 levels in main target organs.

Central Nervous System diseases

Huntington's Disease

Huntington's Disease and Market Background

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 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. Despite the ability to identify Huntington's disease mutation carriers 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. AMT-130 utilizes our proprietary, gene-silencing miQURE platform and incorporates an AAV vector carrying a miRNA specifically designed to silence the huntingtin gene and the potentially highly toxic exon 1 protein fragment. We are currently conducting a Phase I/II clinical trial for AMT-130 in the U.S. and a Phase Ib/II study in the EU. Together, these studies are intended to establish safety, proof of concept, and the optimal dose of AMT-130 to take forward into Phase III development or into a confirmatory study should an accelerated registration pathway be feasible. AMT-130 has received Orphan Drug and Fast Track designations from the FDA and Orphan Medicinal Product Designation from the EMA.

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.

On June 19, 2020, we announced the initiation of patient dosing in the U.S. Phase I/II study of AMT-130. The trial is a randomized, controlled, double-blinded, dose-escalation study of AMT-130. The study includes two dose cohorts of 26 patients randomized to either treatment with AMT-130 or to an imitation surgical procedure. The first dose cohort includes 10 patients, of which six patients receive treatment with AMT-130 and four patients receive imitation surgery. The second dose cohort includes 16 patients, of which ten patients receive treatment with AMT-130 and six patients receive imitation surgery. A third cohort, which will include up to 18 additional randomized patients receiving the higher dose, will explore the use of alternative stereotactic navigation systems to simplify placement of catheters for infusions of AMT-130.

On April 5, 2021, we announced the completion of enrollment of the 10-patient low-dose cohort of the U.S. Phase I/II study of AMT-130. On December 16, 2021, we announced initial 12-month observations on the first four patients enrolled in the low-dose cohort of the U.S. Phase I/II study. Two of the four enrolled patients received AMT-130, and two patients received Sham surgery as a control. AMT-130 was generally well tolerated in the treated patients, with no serious adverse events related to AMT-130. Neurofilament light chain ("NfL"), a biomarker of injury in the brain, increased as expected immediately following the surgical procedure and returned to baseline in the treated patients. NfL remained relatively constant in the two untreated control patients. Structural magnetic resonance imaging did not reveal any clinically meaningful safety findings in either treated or control patients at one year of follow-up. Measurements of total and mutant HTT protein in the cerebral spinal fluid of the four patients were highly variable and inconclusive.

On February 7, 2022, we announced the initiation of patient dosing in our 15-patient, open-label, Phase Ib/II study of AMT-130 in the EU.

On March 21, 2022, we announced the completion of enrollment of the 16-patient high-dose cohort of the U.S. Phase I/II study of AMT-130.

Temporal Lobe Epilepsy Program (AMT-260)

Temporal Lobe Epilepsy Disease and Market Background

TLE affects approximately 1.3 million people in the U.S. and Europe alone, of which approximately 0.8 million patients are unable to adequately control acute seizures with currently approved anti-epileptic therapies. Patients with refractory TLE experience increased morbidity, excess mortality, and poor quality of life.

Our Development of AMT-260 for Temporal Lobe Epilepsy

AMT-260 is being developed based on exclusive licenses to certain patents obtained in 2020 from two French research institutions that continue to collaborate with us.

AMT-260 is a gene therapy using an AAV9 vector. The use of AAV9 to deliver any sequence that affects the expression of the Glutamate inotropic receptor kainate type subunit 2 ("GRIK 2") gene sequence in humans has been exclusively licensed from Regenxbio. Regenxbio provides contractually agreed research and development services up to the transfer of manufacturing activities to a designated contract manufacturer.

AMT-260, employs miRNA silencing technology to target suppression of aberrantly expressed kainate receptors in the hippocampus of patients with TLE.

In October 2021, we presented preclinical data for AMT-260 at the ESGCT. AMT-260 reduces the expression of the Glutamate receptor kainate subunit 2 ("GluK2") in cortical neurons, reduces epileptiform activity and hyperlocomotion in a preclinical model of epilepsy and blocks epileptiform discharges in organotypic slices from patients with TLE.

Parkinson's Disease (AMT-210)

AMT-210 is our preclinical product candidate for the treatment of Parkinson's disease, targeting alpha-synuclein as a potential treatment for Parkinson's disease.

Parkinson's disease is a progressive neurodegenerative disorder that leads to motor deterioration and debilitating non-motor symptoms. It is the second most common neurodegenerative disorder after Alzheimer's disease, and no disease-modifying therapies are available.

Parkinson's disease is believed to be caused through the presence of toxic alpha-synuclein aggregates, affecting dopaminergic circuits. AMT-210 is a one-time, brain-targeting AAV gene therapy incorporating the Company's miQURE gene silencing technology. It is designed to halt misfolded alpha-synuclein and subsequent fibril formation in familial and sporadic Parkinson's disease patients.

Alzheimer's Disease (AMT-240)

AMT-240 is our preclinical product candidate for the treatment autosomal dominant Alzheimer's disease. Alzheimer's disease is the most prevalent neurodegenerative disease, causing dementia and subsequent gradual loss of ability to function with disease progression. Apolipoprotein E (APOE) is believed to potentially be an important factor in the pathogenesis of Alzheimer's disease. APOE consists of 3 major isoforms that are structurally and functionally different. The APOE4 isoform is believed to potentially be the largest risk factor to develop Alzheimer's. In contrast to the toxic properties of APOE4, clinical case studies indicate a potentially protective role of other APOE variants.

AMT-240 is a one-time gene therapy using the Company's miQURE gene-silencing technology to silence the toxic APOE variant, in combination with overexpressing a protective APOE variant as treatment for autosomal dominant Alzheimer's disease patients.

Amyotrophic Lateral Sclerosis (AMT-160)

AMT-161 is our preclinical product candidate utilizing our miQURE gene silencing technology to target toxic C9ORF72 as a potential treatment for amyotrophic lateral sclerosis (ALS).

ALS is caused by degeneration of upper and lower motor neurons, resulting in muscle weakness and atrophy. This rapid progressive loss of motor neurons typically starts at mid-life and median survival from disease manifestation is no more than two to four years.

The most prevalent genetic defect causing ALS is a G4C2 hexanucleotide repeat expansion in the C9ORF72 gene, which acquires toxic properties resulting in degeneration starting in motor neurons in the spinal cord. AMT-161 is designed to be a one-time, intrathecally-administered AAV gene therapy using the miQURE silencing technology to target repeat-expanded C9ORF72 to lower toxic RNA aggregates and prevent dipeptide protein formation.

Spinocerebellar Ataxia, Type 3 (AMT-150)

After conducting a comprehensive review of our product candidates, we decided in December 2021 to deprioritize the preclinical development of AMT-150, shifting resources and focus to our other research programs.

BMS Partnered Research Programs

We and Bristol-Myers Squibb ("BMS") entered into a collaboration and license agreement in May 2015 ("BMS CLA"). The BMS CLA provides BMS with exclusive access to our gene therapy technology platform for four targets primarily in cardiovascular diseases. On December 1, 2020, we and BMS entered into an amended BMS CLA ("amended BMS CLA").

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 DNA; (ii) the promoter, or the DNA sequence that drives the expression of the transgene; and (iii) the transgene, or therapeutic gene.

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; and (iii) enhanced safety. We believe we have significant expertise in vector engineering and have created promising genetically engineered capsids using a "rational design" approach.

We are focusing our efforts on rationally engineering the AAV capsids to target them to specific cells and/or tissues. These engineered viruses contain antibody fragments or peptides that target them to specific tissues or cells and to diminish potential off target effects.

We work extensively on designing synthetic promoters with the potential of enabling higher levels of protein expression in specific tissue types. A "promoter" is an essential component of a gene therapy construct that controls expression of a therapeutic protein. Synthetic promoters, that do not exist in nature, are optimally tailored to drive gene expression at a desired level and specificity.

To further tailor and optimize gene therapies to address certain disorders we may also incorporate specific modifications into the transgenes of our gene therapy constructs. For example, we incorporated the Padua-FIX variant into our hemophilia B gene therapy to substantially increase the resulting FIX activity and potentially improve clinical outcomes. For other programs, such as our gene therapy construct for Fabry disease, we have also utilized modified transgenes with the goal of enhancing efficacy, durability, and safety, as well as expanding the access of gene therapies to patients with inhibitors.

We are developing methods for delivering multiple doses of a gene therapy to a patient using a combination of immune modulation and antibody neutralization. The ability to deliver multiple doses of an AAV to a patient could potentially increase our ability to deliver the correct dose of a virus to a patient and might enable us to re-administer our gene therapies to patients that have lost expression of a transgene.

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.

Commercial-Scale Manufacturing Capabilities

The ability to reliably produce at a high quality and at commercial scale is a critical success factor in AAV gene therapy. We produce our gene therapies at our state-of-the-art, Lexington, Massachusetts-based manufacturing facility using a proprietary baculovirus expression vector system.

We believe our integrated manufacturing capabilities provide us several potential advantages, including:

(1) *Know-how.* Since our founding in 1998, we have invested heavily in developing optimized processes and methods to reliably and reproducibly manufacture AAV-based gene therapies at commercial scale. During this time, we have accumulated significant internal experience and knowledge of the underlying production technology and critical quality attributes of our products. These learnings have been essential in developing a modular, third generation production system that can be used to produce all our gene therapy products.

(2) *Flexibility.* Controlling cGMP manufacturing allows us to rapidly adapt our production schedule to meet the needs of our business. By controlling our manufacturing, we do not rely on contract manufacturers, nor do we require costly and time-consuming technology transfers to third parties. Our facility is designed to commercially supply multiple products and are flexibly designed to accommodate expansion and scale up as our needs change.

(3) *Faster Path to Market.* We believe our manufacturing platform enables us to rapidly produce new products for clinical investigation, minimize time between clinical phases and complete scale-up as product candidates advance into late-stage development and commercialization. For example, in transitioning our hemophilia B program from AMT-060 to AMT-061, we were able to rapidly demonstrate manufacturing comparability and produce clinical material for our ongoing Phase III pivotal study.

(4) *High Purity.* The baculovirus system eliminates the risk of introducing mammalian cell derived impurities.

(5) *Scalability.* We have demonstrated our manufacturing process is reproducible at volumes ranging from 2 liters to 500 liters and believe it is possible to achieve higher scale production with our insect-cell, baculovirus system.

(6) *Low Cost of Goods.* We believe our ability to scale production has the potential to significantly reduce unit costs. Our manufacturing process also utilizes fully disposable components, which enables faster change-over times between batches and lower costs associated with cleaning and sterilization. Additionally, our production system does not require the use of plasmids, which can be a costly raw material.

Intellectual Property

Introduction

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection in the United States, Europe, and other countries for novel components of gene therapies, the chemistries, 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 additional licenses 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 United States 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.

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 both Europe and the United States. For the same technologies, we typically file international patent applications under the PCT within a year. 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.

As of December 31, 2021, our intellectual property portfolio included 105 issued patents (including 27 U.S. patents and 10 patents granted by the European Patent Office ("EPO") and 120 pending patent applications (including 24 U.S. patent applications and 23 EPO patent applications.

These patents relate to a variety of technologies including our product candidates that are in development and our manufacturing and technology platform.

Our Patent Portfolio Related to Certain Development Programs

Hemophilia B (AMT-061)

We own a patent family, including patents and patent applications, directed to the use of the Padua mutation in hFIX for gene therapy in etranacogene dezaparvovec.

Huntington's disease (AMT-130)

We own two patent families directed to gene therapy treatment of Huntington's disease, including with AMT-130. This miQURE gene silencing technology platform is designed to degrade disease-causing genes, without off-target toxicity, and induce silencing of the entire target organ through secondary exosome-mediated delivery.

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.

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. The standard 20-year patent term for the licensed patents expires in 2031.

In 2018, we entered into an amendment of the license agreement with CSHL that expanded the license to include the diagnosis, treatment, or prevention of all CNS diseases in the Field, including but not limited to Huntington's disease. In addition, under the amended license agreement CSHL granted to us an exclusive license for a three-year term to develop and commercialize therapeutic products for the additional disease classifications in the Field of liver diseases, neuromuscular diseases, and cardiovascular diseases. If we meet certain diligence milestones during the initial three-year development term, we may include exclusively additional disease classifications within the additional Fields on similar terms and conditions as the CNS diseases.

Under this license agreement, annual fees, development milestone payments and future single-digit royalties on net sales of a licensed product are payable to CSHL.

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 licensed technology in the field of AAV-based gene therapy.

National Institutes of Health—AAV production

In 2007, we entered into a non-exclusive license agreement with the NIH, which we amended in 2009 and 2013. The patents under this license cover technology to produce AAV vectors in insect cells. We may only grant sublicenses under this agreement with the NIH's consent, which may not be unreasonably withheld. The standard 20-year term for the underlying patents will expire in 2022.

Payment obligations to the NIH under this license agreement include a low single-digit percentage royalty on the net sales of licensed products by us or on our behalf; development and regulatory milestone payments; and an annual maintenance fee creditable against royalties. We do not have to pay royalties or milestone fees under this agreement if we must pay royalties or milestone fees under our 2011 agreement with the NIH, described below, for the same product. Under the license agreement, we have agreed to meet benchmarks in our development efforts, including as to development events, clinical trials, and marketing approval, within specified timeframes.

The NIH may terminate this agreement in specified circumstances relating to our insolvency or bankruptcy. We may terminate this agreement for any reason, in any territory, subject to a specified notice period.

National Institutes of Health—AAV5

In 2011, we entered into another license agreement with the NIH, superseding the 2007 agreement. This agreement was amended in 2016. Under this agreement, the NIH granted us an exclusive, worldwide license to patents relating to AAV5 for use in therapeutic products to be delivered to the brain or liver for treatment of human diseases originating in the brain or liver but excluding arthritis-related diseases, and a non-exclusive, worldwide license to patents relating to AAV5 for all other diseases. We refer to the products licensed under this agreement as AAV5 products. We may grant sublicenses under this agreement only with the NIH's consent, which may not be unreasonably withheld. The last patent under this license expired in July 2021.

Payment obligations to the NIH under this license agreement include royalties equal to a low single-digit percentage of net sales of AAV5 products; development and regulatory milestone payments; and an annual maintenance fee creditable against royalties. If an AAV5 product is also covered by our 2007 agreement with the NIH, our obligation to pay royalties on net sales and our obligation to pay milestone fees only apply under this 2011 agreement and not the 2007 agreement. We have agreed to meet benchmarks in our development efforts, including as to development events, clinical trials, and marketing approval, within specified timeframes.

Technology Used for Specific Development Programs

Hemophilia B

Padua

On April 17, 2017, we entered into an Assignment and License Agreement with Dr. Simioni (the "Padua Assignment"). Pursuant to the Padua Assignment, we acquired from Dr. Simioni all right, title and interest in a patent family covering the variant of the FIX gene, carrying an R338L mutation (FIX-Padua; "Padua IP"). Under the Padua Assignment, we have also licensed certain know-how included in the Padua IP. We have provided Dr. Simioni with an initial license fee and reimbursement of past expenses. Under the agreement, additional payments may come due upon the achievement of certain milestone events related to the development of the Padua IP or as royalties on a percentage of certain revenues. We have granted a license of the Padua IP back to Dr. Simioni for therapeutic or diagnostic use of a modified Factor IX protein (other than in connection with gene therapy) and any application for non-commercial research purposes. We have agreed to indemnify Dr. Simioni for claims arising from our research, development, manufacture, or commercialization of any product making use of the Padua IP, subject to certain conditions. The Padua Assignment will remain in effect, unless otherwise terminated pursuant to the terms of the Padua Assignment, until the later of (i) the expiration date of the last of the patents within the Padua IP and (ii) the expiration of the payment obligations under the Padua Assignment.

St. Jude Children's Research Hospital

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. In addition, we have a first right of negotiation regarding any patent applications that are filed by St. Jude for any improvements to the patent rights licensed to us. The U.S. patent rights will expire in 2028 and the European patents will expire in 2025.

We have agreed to pay St. Jude a royalty equal to a low single-digit percentage of net sales, if any, by us or our sublicensees of products covered by the licensed patent rights, and a portion of certain amounts we receive from sublicensees ranging from a mid-single digit to a mid-teen double-digit percentage of such amounts. 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.

We have also agreed to pay St. Jude a one-time milestone of $5.0 million upon the BLA and MAA approval, and an annual maintenance fee creditable against royalties and milestones in the same year.

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.

Temporal Lobe Epilepsy

Regenxbio

In June 2020, Corlieve entered into an agreement, subsequently amended in June 2021, with Regenxbio for an exclusive (in the field of using AAV9 to expression of the GRIK 2 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 "Background Technology"). 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, Corlieve has certain diligence obligations and Regenxbio has certain obligations related to the pre-clinical development of manufacturing technology.

Inserm Transfert

In January 2020, Corlieve 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, Corlieve 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. Corlieve 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.

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 United States and the European Union. 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 research institutions and governmental agencies and public and private research institutions.

We face worldwide competition from larger pharmaceutical companies, specialty pharmaceutical companies and biotechnology firms, universities and other research institutions and government agencies that are developing and commercializing pharmaceutical products. Our key competitors focused on developing therapies in various indications, include among others, Pfizer, Freeline Therapeutics, Intellia Therapeutics, Sangamo Biosciences, Voyager Therapeutics, Passage Bio, Roche, PTC Therapeutics, Prilenia Therapeutics, Triplet Therapeutics, CombiGene, AvroBio, Caritas Therapeutics, and 4D Molecular Therapeutics.

We also compete with existing standards of care, therapies, and symptomatic treatments, as well as any new therapies 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 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 allow us to reach market in a number of indications ahead of our competitors, and to capture the markets in these indications.

Government Regulation and Reimbursement

Government authorities in the United States, European Union and other countries extensively regulate, among other things, the approval, research, development, preclinical 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. For other countries outside of the United States and the European Union, marketing approval and pricing and reimbursement requirements vary from country to country. If we fail to comply with applicable regulatory requirements, we may be subject to, among other things, fines, 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 United States, 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, in March 2020, the U.S. Congress passed the Coronavirus Aid, Relief, and Economic Security Act, ("CARES Act"), which includes various provisions regarding FDA drug shortage reporting requirements, as well as provisions regarding supply chain security, such as risk management plan requirements, and the promotion of supply chain redundancy and domestic manufacturing. The FDA has also issued a number of guidance documents concerning how sponsors and investigators may address COVID-19 challenges, including challenges specific to gene therapies. These guidance documents are continually evolving.

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 United States must typically undertake the following:

- completion of preclinical 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 United States
- approval by an independent institutional review board ("IRB") and 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 current Good Clinical Practice ("cGCP") to establish substantial evidence of the safety and efficacy proposed biological product for each indication;
- preparation and submission to the FDA of a BLA;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with 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 United States or under an IND, investigational product sponsors must first complete pre-clinical studies. Preclinical 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 Good Laboratory Practices ("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. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of an IND. INDs include preclinical 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 United States 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 must 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. 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 3 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 3 clinical study plus confirmatory evidence or a single large multicenter trial without confirmatory evidence.

In addition, under the Pediatric Research Equity Act, or 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 United States are also subject to regulation by the FDA. Further, the export of investigational products outside of the United States 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 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; 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 documents specific to gene therapies during the COVID-19 public health emergency, including one on manufacturing considerations and the conduct of risk assessments. FDA has further issued guidance focused on the development of gene therapies for the treatment of rare 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, or CARES, Act to include the volume of drugs produced during the prior year. Establishments may be subject to periodic unannounced inspections 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, among other consequences. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are 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 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 eligible for rolling review, intensive guidance on an efficient development program beginning as early as Phase 1 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. 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. 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 preclinical 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 for each. 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. The PDUFA action date is only a goal, thus, the FDA does not always meet its PDUFA dates. Additionally, this review period may change as the PDUFA statute must be reauthorized by Congress by September 2022.

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 the facility or facilities where the product is manufactured, referred to as a Pre-Approval Inspection. 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 are adequate to assure consistent production of the product within required specifications. Additionally, before approving a marketing application the FDA will inspect one or more clinical trial sites to assure compliance with GCPs.

After evaluating the marketing application and all related information, including the advisory committee recommendation, if any, and 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 IV clinical trials, 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 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 health care 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 BCPIA, a manufacturer may submit an application 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 thereafter. 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 market 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. Additionally, under a newly enacted statute related to biological product patent transparency, 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 United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a biological product available in the United States 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 will 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. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. The FDA has granted orphan drug designation to AMT-130 for the treatment of Huntington's disease as well as for etranacogene dezaparvovec; meaning that they would receive orphan drug exclusivity if they are the first products approved for their respective indications.

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 exclusivity against biosimilars. 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 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. Once approved or cleared, the device component sponsor (or the combination product sponsor, if both components are covered by one application) must comply with the FDA's post-market device requirements, 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 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 approved, 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 required for moderate-risk devices classified as Class II; and a de novo request may be used for novel devices not previously classified by the FDA that are low or moderate risk. 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.

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. 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 claims relating to a product that are 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 approved by the FDA. Biopharmaceutical companies, however, are required to promote their products only for the approved indications and in accordance with the provisions of the approved label. 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 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.

In addition, the distribution of prescription biopharmaceutical samples is subject to the Prescription Drug Marketing Act (the "PDMA"), which regulates the distribution of samples at the federal level. Both the PDMA and state laws limit the distribution of prescription biopharmaceutical product. Certain reporting related to samples is also required and laws and regulations impose requirements to ensure accountability in distribution. Free trial or starter prescriptions provided through pharmacies are also subject to regulations under the Medicaid Drug Rebate Program and potential liability under anti-kickback and false claims laws.

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. Sponsors must also verify that purchasers of the sponsors' products are appropriately licensed. Further, under this legislation, manufactures have product 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, fines, consent decrees, corporate integrity agreements, suspension and debarment from government procurement and non-procurement programs, and refusal of orders under existing government contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement, or civil or criminal penalties, 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 United States 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 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 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 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 Anti-Kickback Statute 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 Anti-Kickback Statute 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 Anti-Kickback Statute. 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 Anti-Kickback Statute 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 federal Anti-Kickback Statute is grounds for the government or a whistleblower to assert that a claim 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") recently promulgated a regulation 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 pharmacy benefit manager will not be protected under the anti-kickback discount safe harbor. Recent legislation delayed implementation of this portion of the rule until January 1, 2026, and further proposed legislation would permanently prohibit implementation of the rule beginning in 2026.

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 discovering the overpayment, even if the overpayment was not caused by a false or fraudulent act. In addition, conviction, or 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 or regulations similar to the federal anti-kickback law and false claims laws, 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 statute 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 Centers of 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 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 their immediate family. Payments made to principal investigators and research institutions at teaching hospitals 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 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 penalties 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. In addition, other federal and state laws, such as the California Consumer Privacy Act, 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 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. 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 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 criminal and significant civil monetary penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, corporate integrity agreements, suspension and debarment from government procurement and non-procurement programs, and 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, 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, recent legislation will restart the reductions, which will thereafter remain in effect through 2031 unless additional congressional action is taken. 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 United States 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 United States, 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 United States. 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 current 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 via (in the case of the CTD) implementation through national legislation of the member states. 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 CTD 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 uniQure's 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 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). This results in some EU member states, the GMO application must be approved before the Clinical Trial Application (CTA) is submitted, in some after approval of the CTA and in some 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 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—currently 28—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 MAA the applicant must properly and sufficiently demonstrate the quality, safety, and efficacy of the drug. 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 preclinical 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 EMA 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 marketing authorization may be converted into a standard marketing authorization (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 EMA through scientific advice or protocol assistance and discuss their development plan well in advance of the submission of a marketing-authorization application. Other stakeholders (e.g., health technology assessment bodies) can be included.

In addition, the 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 marketing authorization 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 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 they are approved preventing 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.

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.

Manufacturing and promotion

Pursuant to 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 and approval.

Other Regulatory Requirements

A holder of a marketing authorization 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 good manufacturing practices, 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 marketing authorization'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 marketing authorizations 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 etranacogene dezaparvovec for the treatment of hemophilia B as well as for AMT-130 for the treatment of Huntington's disease subject to the conditions applicable to orphan drug exclusivity in the European Union. Regulation (EC) No 141/2000, as amended, 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 marketing authorization application.

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 application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, 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 marketing authorization may be granted, for the same therapeutic indication, to a similar drug if:

- the holder of the marketing authorization for the original orphan drug has given its consent to the second applicant;
- the holder of the marketing authorization 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 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.

Human Capital Resources

As of December 31, 2021, we had a total of 463 employees, 250 of whom are based in The Netherlands, 206 in the United States of America, and seven in other European countries. As of December 31, 2021, 142 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.

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. In 2021 we initiated activities to coordinate our various ongoing activities and initiatives within an environmental, social and governance ("ESG") framework.

2 Financial results

Acquisition of Corlieve Therapeutics

On June 21, 2021, we entered into the Corlieve Transaction. Upon the Acquisition Date, we acquired 97.7% of the outstanding ordinary shares of Corlieve in return for EUR 44.9 million ($53.3 million as of the Acquisition Date). As contractually required in the SPA, we acquired the Mandatorily Redeemable Shares on February 9, 2022. We recorded a liability related to these Mandatorily Redeemable Shares for an amount of EUR 0.7 million ($0.9 million) as of the Acquisition Date. We financed the Corlieve Transaction from cash on hand.

In addition to the payments to acquire 100% of the outstanding ordinary shares, Corlieve's former and remaining shareholders are eligible to receive up to EUR 35.8 million (or $40.6 million as of December 31, 2021) upon the achievement of development milestones through Phase I/II and EUR 143.1 million (or $162.3 million as of December 31, 2021) upon the achievement of milestones associated with Phase III development and obtaining approval to commercialize AMT-260 in the United States of America and the European Union. We may elect to pay up to 25% of such milestone payments through the issuance of our ordinary shares. We recorded a EUR 20.2 million ($24.0 million) liability related to these contingent consideration payments as of the Acquisition Date.

Total consideration of EUR 65.8 million ($78.1 million), which consisted of the cash paid upon the Acquisition Date, the payment for the Mandatorily Redeemable Shares and the contingent consideration payments, was allocated to identifiable intangible assets related to the IPR&D Intangible Asset. The IPR&D Intangible Asset's fair value was determined at EUR 53.6 million ($63.6 million) as of the Acquisition Date. We also recognized a EUR 13.4 million ($15.9 million) deferred tax liability in relation to this IPR&D Intangible Asset. The total consideration in excess of the net assets acquired was EUR 23.9 million ($28.4 million) and was allocated to goodwill.

CSL Behring Agreement

On the Signing Date, uniQure biopharma B.V., a wholly-owned subsidiary of uniQure N.V., entered into the CSL Behring Agreement, as amended, with CSL Behring pursuant to which CSL Behring received exclusive global rights to the Product.

The transaction became fully effective on May 6, 2021, one day after the waiting period under the HSR Act expired on May 5, 2021.

CSL Behring is responsible for the development and commercialization of the Product. We agreed to complete the validation of the current manufacturing process as well as to the development and validation of a next generation manufacturing process. We will be entitled to receive a development milestone payment if we complete these activities in accordance with an agreed development plan and timeline. CSL Behring is responsible for global regulatory submissions and commercialization requirements for the Product. Certain clinical development and regulatory activities performed by us are reimbursed by CSL Behring.

On the Signing Date, 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 at an agreed-upon price commensurate with the SSP. We will be responsible to supply the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization.

Following the Closing, we recorded $462.4 million, including a $450.0 million upfront cash payment, as license revenue. Upon the Closing, we contractually owed to our licensors $15.5 million of the upfront payment received from CSL Behring.

We are eligible to receive more than $0.3 billion in regulatory, development, and first commercial sale milestones, $1.3 billion in additional commercial milestones, and tiered double-digit royalties of up to a low-twenties percentage of net product sales arising from the collaboration. As of December 31, 2021, we accrued revenue of $55.0 million related to milestone payments we are entitled to receive under the CSL Behring Agreement for global regulatory submissions.

Financing

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

Pursuant to the 2021 Amended Facility, Hercules agreed to Tranche B, increasing the aggregate principal amount of the term loan facilities from $35.0 million to up to $135.0 million. On January 29, 2021, we drew down $35.0 million of the Tranche B. Advances under Tranche B bore interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance of $70.0 million and all accrued but unpaid interest on advances under Tranche B was due on June 1, 2023. The back-end fee in respect of advances under the 2021 Amended Facility ranged from 1.65% to 6.85%, depending on the repayment date. In addition to Tranche B, the 2021 Amended Facility also extended the interest only payment period of the previously funded $35.0 million term loan ("Tranche A") from January 1, 2022 to June l, 2023.

On December 15, 2021, we and Hercules amended and restated the 2021 Amended Facility. Pursuant to the 2021 Restated Facility, Tranche A and Tranche B of the 2021 Amended Facility with a total outstanding balance of $70.0 million were consolidated into one tranche with a total commitment of $100.0 million. We drew down an additional $30.0 million, resulting in total principal outstanding as of December 31, 2021 of $100.0 million. The 2021 Restated Facility extended the loan's maturity date from June 1, 2023 until December 1, 2025. The interest-only period is extended from January 1, 2023 to December 1, 2024, or December 1, 2025 if, prior to June 30, 2024, either (a) the BLA for AMT-061 is approved by the FDA or (b) AMT-130 is advanced into a pivotal trial. The interest rate is adjustable and is the greater of (i) 7.95% and (ii) 7.95% plus the prime rate less 3.25% per annum. Under the 2021 Restated Facility, we owe a back-end fee of 4.85% of the outstanding debt. We are required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. We continue to owe a $2.5 million back-end fee related to the 2021 Amended Facility which is due on June 1, 2023.

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

In March and April of 2021, we issued 921,730 ordinary shares at a weighted average price of $33.52 per ordinary share, with net proceeds of $29.6 million, after deducting underwriting discounts and net of offering expenses.

Facilities

In February 2021, we commenced the expansion of our Amsterdam site to build additional laboratories to support the expansions of our research and development activities as well as the construction of a cleanroom capable of manufacturing cGMP materials at a 500-liter scale. The construction and validation of the cleanroom and the additional laboratories were completed in December 2021. In May 2021, we entered into a sublease agreement to let an additional approximately 1,080 square meters of office space at our Amsterdam site to accommodate the hiring of additional full-time employees. The lease expires in October 2028 and includes an option to break the lease on October 31, 2023.

In December 2021, we entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 13,501 square feet of space. The lease is expected to commence in the first half of 2022, is set for seven years starting from the rent commencement date and is non-cancellable. The lease is renewable for one five-year term.

In February 2022, we also entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 12,716 square feet. The lease is expected to commence in the second half of 2022 and is set for a non-cancellable period of seven years and four months. The lease is renewable for one five-year term.

Results of operations

The following table presents a comparison of the twelve months ended December 31, 2021, and 2020:

	Years ended December 31,		
	2021	2020	2021 vs 2020
		$ in thousands	
License revenues	517,400	37,319	1286%
Collaboration revenues	6,602	195	3286%
Total revenues	**524,002**	**37,514**	**1297%**
Cost of revenues	(27,807)	—	100%
Gross profit	**496,195**	**37,514**	**1397%**
Operating expenses:			
Research and development expenses	(144,594)	(118,519)	(22)%
Selling, general and administrative expenses	(55,983)	(43,954)	(27)%
Total operating expenses	**(200,577)**	**(162,473)**	**(23)%**
Other income	15,155	3,342	353%
Other expense	(876)	(1,302)	33%
Profit / (Loss) from operations	**309,897**	**(122,919)**	**352%**
Finance income	29,821	4,033	639%
Finance expense	(11,485)	(21,401)	(46)%
Finance income / (expense), net	**18,336**	**(17,368)**	**206%**
Profit / (loss) before income tax (expense) / benefit	**328,233**	**(140,287)**	**334%**
Income tax (expense) / benefit	(3,021)	16,806	(118)%
Net income / (loss)	**325,212**	**(123,481)**	**363%**

Revenues

CSL Behring

Following the Closing of the CSL Behring agreement, we recognize license revenue related to the License Sale of the global rights to the Product. We determined that our performance obligation related to the License Sale was satisfied on the Closing. We recognized $517.4 million of license revenue for the year ended December 31, 2021. We did not recognize any license revenue related to the CSL Behring Agreement during the year ended December 31, 2020. The license revenue recognized in 2021 of $517.4 million resulted from a fixed upfront payment of $450.0 million, $12.4 million we received in relation to the product that we continued to develop between the Signing Date and the Closing and certain reimbursable activities to fulfil the transfer of global rights ("Additional Covenants") allocated to License sale as well as a total of $55.0 million related to milestone payments owed following CSL Behring's submission of marketing and license applications for etranacogene dezaparvovec in March 2022. We will recognize additional license revenue in relation to the License Sale when it becomes highly probable that regulatory and sales milestone events will be achieved as well as when royalties on sales of Product have been earned.

We recognize collaboration revenues associated with development services that will be reimbursed by CSL Behring relating to clinical development activities. These services are provided by our employees. Collaboration revenue related to these contracted services is recognized when the performance obligations are satisfied.

We recognized $2.4 million of collaboration revenue for the year ended December 31, 2021 and no such income in 2020. The increase in collaboration revenue in 2021 of $2.4 million compared to 2020 was primarily related to the revenues related to FTE recharges from the CSL Behring Agreement.

BMS

We recognize collaboration revenues (providing pre-clinical research activities) associated with Collaboration Target-specific pre-clinical analytical development and process development activities that are reimbursable by BMS under the BMS CLA and the December 1, 2021, amended BMS CLA ("amended BMS CLA") as well as other related agreements. Collaboration Revenue related to these contracted services is recognized when performance obligations are satisfied.

We recognized license revenues associated with the amortization of the non-refundable upfront payment and target designation fees we received from BMS in 2015 until December 1, 2020. We evaluated our outstanding performance obligation following the amendment of the BMS CLA on December 1, 2020 and determined that our remaining performance obligation is immaterial. We updated our measure of progress accordingly and amortized the remaining balance of unrecognized revenue of $27.8 million as of December 1, 2020. In accordance with the amended BMS CLA, we continue to be eligible to receive research, development, and regulatory milestone payments as well as sales milestone payments and royalties for each of the four active Collaboration Targets if defined milestones are achieved in relation to the license to our technology and know-how. We will recognize revenue from these payments when earned or as sales occur.

We recognized $37.3 million of license revenue for the year ended December 31, 2020 (nil for same period in 2021), which includes the $27.8 million of license revenue that we recognized as of the December 1, 2020 effective date of the amended BMS CLA as well as $4.4 million research milestone payment that we recorded in December 2020 following the designation of one of the four Collaboration Targets as a candidate to advance into IND-enabling studies.

We recognized $4.2 million and $0.2 million of collaboration revenue for the years ended December 31, 2021 and 2020, respectively. The increase in collaboration revenue in 2021 of $4.0 million compared to 2020 was primarily related to the revenues recognized from the amended BMS CLA.

Cost of Contract revenues

We expense contract fulfillment costs associated with license revenue recognized under the CSL Behring Agreement as costs of contract revenues. These expenses primarily consist of payments we owe to our licensors in relation to license payments we received from CSL Behring. We incurred $27.8 million of such cost in the year ended December 31, 2021. We did not incur such costs in the year ended December 31, 2020.

Research and development expenses

Research and development expenses for the year ended December 31, 2021 were $144.6 million, compared to $118.5 million for the year ended December 31, 2020. Other research and development expenses are separately classified in the table below. These are not allocated as they are deployed across multiple projects under development.

	Year ended December 31,		
	2021	2020	2021 vs 2020
	$ in thousands		
Etranacogene-dezaparovec (AMT-060/061)	$ 8,738	$ 21,458	$ (12,720)
Huntington's disease (AMT-130)	10,529	6,905	3,624
Programs in preclinical development and platform related expenses	9,758	6,518	3,240
Total direct research and development expenses	**$ 29,025**	**$ 34,881**	**$ (5,856)**
Employee and contractor-related expenses	55,725	41,694	14,031
Facility expenses	16,559	15,086	1,473
Share-based compensation expense	16,095	13,501	2,594
Disposables	14,679	10,203	4,476
Fair value changes related to contingent consideration	6,683	—	6,683
Other expenses	5,828	3,154	2,674
Total other research and development expenses	**$ 115,569**	**$ 83,638**	**$ 31,931**
Total research and development expenses	**$ 144,594**	**$ 118,519**	**$ 26,075**

Direct research and development expenses

Hemophilia B (AMT-060/061)

In the years ended December 31, 2021 and 2020, the external costs for our hemophilia B program were primarily related to the execution of our Phase III clinical trial. During 2020 and up to the Closing, we also incurred costs related to the preparation of global regulatory submissions and for commercialization of the Product. We also incurred costs for Manufacturing Development. After the Closing, CSL Behring is responsible for the clinical and regulatory development and commercialization of the Product, with the Company managing the existing trials on behalf of CSL Behring. Direct research and development expenses related to clinical development incurred in the year ended December 31, 2021 are presented net of reimbursements due from CSL Behring.

In the same period, we also incurred costs related to the long-term follow-up of patients in our Phase I/II clinical trial of AMT-060 and our Phase IIb clinical trial of etranacogene dezaparvovec. Our Phase IIb dose-confirmation study was initiated in January 2018 and dosing occurred in July and August 2018. Patients were dosed as part of our Phase I/II clinical trial of AMT-060 in 2015 and 2016.

Huntington disease (AMT-130)

In the years ended December 31, 2021 and 2020, our external costs for the development of Huntington's disease were primarily related to the execution of our Phase I/II clinical trial in the United States as well as the preparation of a Phase I/IIb clinical trial in Europe.

Preclinical programs and platform development

In the year ended December 31, 2021, we incurred $9.8 million of costs primarily related to our preclinical activities associated with product candidates for the treatment of Spinocerebellar Ataxia type 3 ("SCA3") (AMT-150), Fabry disease (AMT-191) and temporal lobe epilepsy (AMT-260), as well as various other research programs and technology innovation projects compared to $6.5 million in 2020. The expenses for the year ended December 31, 2020 include costs related to our product candidate for Hemophilia A (AMT-180), which was deprioritized in June 2020.

Other research and development expenses

- We incurred $55.7 million in employee and contractor expenses in the year ended December 31, 2021 compared to $41.7 million in 2020. Our cost increased in 2021 by $14.0 million compared to 2020 as a result of the recruitment of personnel to support the preclinical and clinical development of our product candidates;
- We incurred $16.6 million in operating expenses and depreciation expenses related to our rented facilities in the year ended December 31, 2021 compared to $15.1 million in 2020. The increase in 2021 compared to 2020 of $1.5 million primarily related to the expansion of our Amsterdam facility;
- We incurred $16.1 million in share-based compensation expenses in the year ended December 31, 2021 compared to $13.5 million in 2020. The increase in 2021 compared to 2020 of $2.6 million was primarily driven by grants to newly recruited personnel offset by share-based compensation expenses recorded in relation to the termination of one of our executives in 2020;
- We incurred $14.7 million in disposables costs in the year ended December 31, 2021 compared to $10.2 million in the year ended December 31, 2020 related to miscellaneous other costs we incurred as a result of expanding our organization;
- We incurred $6.7 million of expenses for the year ended December 31, 2021 related to an increase in the fair value of contingent consideration associated with the Corlieve Transaction, compared to nil for the year ended December 31, 2020; and
- We incurred $5.8 million in other expenses in the year ended December 31, 2021 compared to $3.2 million in 2020. The increase in 2021 compared to 2020 of $2.7 million is due to professional fees as a result of expanding the organization and to support the cGMP validation of our Lexington facility.

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 include employee expenses as well as professional fees related to the preparation of a commercial launch of etranacogene dezaparvovec and advisory fees related to obtaining the CSL Behring Agreement.

Selling, general and administrative expenses for the year ended December 31, 2021 were $56.0 million, compared to $44.0 million for the year ended December 31, 2020.

- We incurred $16.0 million in personnel and contractor expenses in 2021 compared to $13.6 million in 2020. The increase of $2.4 million in 2021 compared to 2020 was primarily related to the recruitment of personnel to support our growth;
- We incurred $12.7 million of share-based compensation expenses in 2021 compared to $11.4 million in 2020. The increase in 2021 compared to 2020 of $1.3 million was primarily related to the increase in awards granted, including those to newly recruited personnel;
- We incurred $9.4 million in professional fees in 2021 compared to $8.0 million in 2020. We regularly incur accounting, audit and legal fees associated with operating as a public company. Additionally, in the years ended December 31, 2021 and December 31, 2020, we incurred professional fees in relation to our licensing transaction with CSL Behring and our acquisition of Corlieve; and
- We incurred $5.1 million in financial advisory fees in relation to our licensing transaction with CSL Behring in the year ended December 31, 2021, compared to nil in the same period in 2020.

Other items, net

We recognized $3.0 million in other income in relation to the equity stake received in VectorY B.V. in conjunction with a settlement agreement that the Company and VectorY B.V. entered into in April 2021 in the year ended December 31, 2021, compared to no such income for the same period in 2020.

We recognized $2.6 million in other income of employee retention credit under the U.S. CARES Act in the year ended December 31, 2021, compared to no such income for the same period in 2020.

In 2021, we recognized $2.8 million in other income derived from a net modification gain resulting from the amendments to the Company's loan agreements under the 2021 Amended Facility and 2021 Restated Facility. Refer to Note 9 "Borrowings" for further details. No such income was recorded for the same period in 2020.

In 2021, we recognized $5.3 million in income related to payments received from European authorities to subsidize our research and development efforts in the Netherlands compared to $1.9 million in 2020.

Other income for the years ended December 31, 2021 and 2020 also includes income from the subleasing of a portion of our Amsterdam facility. We present expenses related to such income as other expense.

Finance expense, net

Our Finance income / (expense), net, for the years ended December 31, 2021, and 2020 was as follows:

	Years ended December 31,		
	2021	2020	2021 vs 2020
		$ in thousands	
Finance income:			
Foreign exchange income, net	29,659	—	29,659
Derivative gains	—	3,095	(3,095)
Interest income on cash and cash equivalents	162	938	(776)
Total finance income:	**29,821**	**4,033**	**25,788**
Finance expense:			
Foreign exchange losses, net	—	(13,613)	13,613
Interest expense on leases	(3,982)	(3,898)	(84)
Interest expenses on Hercules borrowing	(7,245)	(3,722)	(3,523)
Interest expense on cash and cash equivalents	(258)	(169)	(89)
Total finance expense:	**(11,485)**	**(21,401)**	**9,916**
Finance income / (expense), net	**18,336**	**(17,368)**	**35,704**

We issued warrants to BMS in 2015 (the "BMS Warrants"). We recognize changes in the fair value of these warrants within finance income / expense. As a result of the termination of the BMS Warrants on December 1, 2020, we no longer recognize changes in the fair value of these warrants within finance income / expense. In 2020, we recognized a $3.1 million net gain related to fair value changes of derivative financial instruments, which includes an $0.8 million gain that we recognized related to the derecognition of the BMS Warrants.

We recognized $0.2 million interest income in 2021 and $0.9 million in 2020. Our interest income in 2021 decreased by $0.7 million compared to 2020 due to a reduction in market interest rates.

We recognized $7.2 million interest expense on Hercules borrowing in 2021 and $3.7 million in 2020. Our interest expense in 2021 primarily increased by $3.5 million compared to 2020 due to the additional $35.0 million we drew down on our loan facility from Hercules in January of 2021.

In 2021, we recognized a net foreign currency gain of $29.7 million related to our borrowings from Hercules and our cash and cash equivalents as well as loans between entities within the uniQure group, compared to a net loss of $13.6 million in 2020.

Income tax (expense) / benefit

We recognized $3.0 million of deferred tax expenses in 2021, compared to $16.8 million of deferred tax income in 2020. Deferred tax expense recorded in 2021 results from the consumption of net operating tax losses carried forward by our U.S. entity as well as deferred tax expense resulting from the release of valuation allowance for the tax benefit of share issuance costs within the Netherlands. Deferred tax income recorded in 2020 results from the recognition of net deferred tax assets by our U.S. entity following our determination that it became probable that taxable profit that would be available against which existing temporary differences (including net operating losses carried forward) can be utilized.

Cash Flow and Cash Position

As of December 31, 2021, we had cash and cash equivalents of $556.3 million, which include payments received from CSL Behring following the Closing. Until such time, if ever, as we can generate substantial cash flows from successfully commercializing our proprietary product candidates, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution, and licensing arrangements. We believe that our cash and cash equivalents will fund our operations into the first half of 2025 assuming achievement of $175.0 million related to first commercial sales milestones under the CSL Behring Agreement. The table below summarizes our consolidated cash flow data for the years ended December 31:

	Years ended December 31,		
	2021	2020	2021 vs 2020
		$ in thousands	
Cash and cash equivalents at the beginning of the period	244,932	377,793	(132,861)
Net cash generated from / (used in) operating activities	289,431	(132,713)	422,144
Net cash used in investing activities	(67,084)	(9,235)	(57,849)
Net cash generated from financing activities	92,676	5,329	87,347
Foreign exchange impact	(3,699)	3,758	(7,457)
Cash and cash equivalents at the end of the period	**556,256**	**244,932**	**311,324**

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. As a result of receiving the upfront payment upon the Closing, we generated $289.4 million cash flows from operating activities during the year ended December 31, 2021. We recorded net income of $325.2 for the year ended December 31, 2021, and a net loss of $123.5 million in 2020. As of December 31, 2021, we had an accumulated deficit of $458.0 million.

Net Cash generated from / (used in) operating activities

Net cash generated from operating activities was $289.4 million for the year ended December 31, 2021, and consisted of net income of $325.2 million adjusted for non-cash items, including depreciation and amortization expense of $13.2 million, share-based compensation expense of $28.8 million, an increase in fair value of contingent consideration of $6.7 million, unrealized foreign exchange losses of $32.5 million, a change in deferred taxes of $3.0 million and other non-cash items, net, of $2.8 million. Net cash generated from operating activities also included unfavorable changes in operating assets and liabilities of $45.8 million, which includes $55.0 million recognized as a contract asset related to highly probable CSL Behring milestone payments. Additionally, these changes also related to a net increase in accounts receivable, prepaid expenses, and other current assets and receivables of $4.1 million primarily related to an increase in various prepaids, including those related to clinical trials, partially offset by decrease in receivables as a result of collection of the BMS milestone that was recorded as of December 31, 2020 and collection of the CSL Behring receivables recorded as of December 31, 2020 for expenses for which we had a right of reimbursement and a net increase in accounts payable, accrued expenses, other liabilities, and operating leases of $13.3 million primarily related to an increase in various accruals for goods received from and services provided by vendors and an increase in personnel accruals. Net income primarily consisted of $462.4 million license revenue recognized on the Closing and $55.0 million license revenue related to milestone payments associated with CSL Behring's global regulatory submissions for etranacogene dezaparvovec, which occurred prior to the approval of this Annual Report.

Net cash used in operating activities was $132.7 million for the annual period ended December 31, 2020, and consisted of a net loss of $123.5 million adjusted for non-cash items, including depreciation and amortization expense of $10.3 million, share-based compensation expense of $24.9 million, interest expense on leases, net of $3.9 million, fair value gain of derivative financial instruments of $3.1 million, unrealized foreign exchange loss of $15.2 million, deferred tax income of $16.8 million and a decrease in unamortized deferred revenue of $33.6 million. Net cash used in operating activities also included unfavorable changes in operating assets and liabilities of $2.8 million. These changes primarily related to a net increase in accounts receivable, prepaid expenses, and other current assets of $8.0 million and a net increase in accounts payable, accrued expenses, other liabilities, and operating leases of $5.2 million. There was also interest paid, net of $7.1 million primarily related to leases and the Hercules borrowing.

Net cash used in investing activities

In 2021, we used $67.1 million in our investing activities compared to $9.2 million in 2020.

	Years ended December 31,	
	2021	2020
	$ in thousands	
Acquisition of Corlieve, net of cash acquired	(49,949)	—
Build out of Amsterdam site	(12,412)	(4,534)
Build out of Lexington site	(5,026)	(2,737)
Acquisition of licenses and patents	—	(2,213)
Receipt of bank deposit	303	249
Total investments	**(67,084)**	**(9,235)**

We paid EUR 42.1 million ($49.9 million), net of EUR 2.8 million ($3.3 million) of cash acquired, during the year ended December 31, 2021 to acquire 97.7% of the outstanding ordinary shares of Corlieve on July 30, 2021.

In 2021, we invested $12.4 million in the build out of our Amsterdam site compared to $4.5 million in 2020. Our investments in 2021 primarily relate to the construction of additional laboratories to support the expansion of our research and development activities as well as the construction of a cleanroom designed to be capable of manufacturing cGMP materials at a 500-liter scale.

In 2021, we invested $5.0 million in our facility in Lexington compared to $2.7 million in 2020.

Net cash generated from financing activities

	Years ended December 31,	
	2021	2020
	$ in thousands	
Proceeds from loan increment, net of transaction costs	64,067	—
Proceeds from public offering of ordinary shares, net	29,565	—
Proceeds from issuance of ordinary shares related to employee stock option and purchase plans	2,798	7,444
Payments for principal portion of lease liability	(2,182)	(2,115)
Repayments of debts acquired through acquisition of Corlieve	(1,572)	—
Net cash generated from financing activities	**92,676**	**5,329**

In January 2021, we received $34.6 million net proceeds from the 2021 Amended Facility and in December 2021 we received $29.5 million net proceeds from the 2021 Restated Facility for combined net proceeds of $64.1 million.

We received net proceeds of $29.6 million associated with our ATM offering in March and April 2021, consisting of gross proceeds of $30.9 offset by $1.3 million of issuance costs.

In 2021, we received $2.8 million from the exercise of options to purchase ordinary shares issued in accordance with our share incentive plans, compared to $7.4 million in 2020.

In 2021, we paid $2.2 million to repay our lease liabilities compared to $2.1 million in 2020.

Upon the acquisition of Corlieve, Corlieve held loans with an outstanding amount equal to EUR 1.4 million ($1.6 million). During the year ended December 31, 2021, the loans were repaid in their entirety.

Equity

Shareholders' equity at December 31, 2021, amounted to $599.2 million compared to $247.9 million for December 31, 2020; a total of 46.3 million ordinary shares were issued and outstanding at December 31, 2021.

We had a net income of $325.2 million in 2021 and a net loss of $123.5 million in 2020. As of December 31, 2021, we had an accumulated deficit of $458.0 million.

Outlook 2022

Hemophilia B – Etranacogene dezaparvovec (AMT-061)

On March 28, 2022, CSL Behring announced that the EMA has accepted the MAA for etranacogene dezaparvovec under its accelerated assessment procedure. As of the date of this Annual Report, we collected $55.0 million owed to us by CSL Behring related to their global regulatory submissions for etranacogene dezaparvovec.

Huntington product candidate ("AMT-130")

On December 16, 2021, we announced the initiation of patient screening in our 15 patient, open-label, Phase Ib/II study of AMT-130 in the EU, as well our plans to initiate a third cohort in the ongoing U.S. Phase I/II clinical trial. In February 2022, the first two patients were dosed in this European open-label Phase Ib/II study of AMT-130. The first and second dose cohorts will include 6 patients and 9 patients, respectively.

On March 21, 2022, we announced the completion of the enrollment of all 26 patients in the first two cohorts of our randomized, double-blinded, Phase I/II clinical trial of AMT-130 taking place in the U.S. In the study, patients are randomized to either treatment with AMT-130 or to an imitation surgical procedure. The first dose cohort includes 10 patients, of which six patients received treatment with AMT-130 and four patients received imitation surgery. The second dose cohort includes 16 patients, of which 10 patients received treatment with AMT-130 and six patients received imitation surgery. The Phase I/II clinical trial consists of a blinded 12-month period followed by unblinded long-term follow-up for five years. The treated patients have received a single administration of AMT-130 using MRI-guided, convection-enhanced stereotactic neurosurgical delivery directly into the striatum (caudate and putamen). The third cohort, which will include up to 18 additional randomized patients receiving the higher dose, will explore the use of alternative stereotactic navigation systems to simplify placement of catheters for infusions of AMT-130. We expect to provide an update in the second quarter of this year from the 12-month interim analysis of the 10 patients in the first cohort, including safety, mutant HTT protein ("mHTT") and NfL data.

Preclinical programs

We expect to advance our gene therapy product candidates for Fabry disease and refractory temporal lobe epilepsy into IND-enabling toxicology studies, and we expect to initiate at least two new gene therapy programs targeting the liver and CNS during the year.

Expansion footprint

In December 2021, the Company entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 13,501 square feet of space. The lease is expected to commence in the first half of 2022, is set for seven years starting from the rent commencement date and is non-cancellable. The lease is renewable for one five-year term.

In February 2022, we also entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 12,716 square feet. The lease is expected to commence in the second half of 2022 and is set for a non-cancellable period of seven years and four months. The lease is renewable for one five-year term.

COVID-19 measures

The Covid caused by the Sars-CoV 2 virus was characterized as a pandemic by the WHO on March 11, 2020. Since then, various variants of the Sars-CoV 2 virus causing Covid have been identified.

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

3 Risk Factors

Risk appetite

We are developing gene therapy products. The development of commercial gene therapy products is a multi-year process involving a multitude of risk that can result in delays or even termination of product development efforts. None of our product candidates are currently approved for commercial sale. Advancing our product candidates to the commercial stage requires considerable financial resources. We believe our cash and cash equivalents as of December 31, 2021 and the collection of $55.0 million collected from CSL Behring related to the global regulatory submissions filed by the date of the issuance of this Annual Report will fund our operations, including our debt repayment obligations, as they become due, into the first half of 2025 assuming achievement of $175.0 million related to first commercial sales milestones under the CSL Behring Agreement. We will likely need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations, which could have a material adverse effect on our business, financial conditions, results of operations and cash flow. As a development stage biotechnology company, acceptance of these industry risks forms part of our strategy.

We strive to mitigate these industry risks by ensuring that we strictly comply with the rules and regulations governing our highly regulated industry. We have established and maintain adequate internal controls over financial reporting to provide reasonable assurance regarding the reliability of our financial reporting as well as processes to ensure that we comply with the rules and regulations defined by the United States Securities and Exchange Commission ("SEC") as well as Nasdaq listing standards. Compliance with these rules and regulations is necessary for us to maintain access to external funding, which may be critical for us.

a) Summary Risk Factors

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

- Our business, operations and supply chain have been, and may continue to be, materially and adversely affected by the ongoing Covid pandemic.
- We have encountered, and may continue to encounter, delays in, and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates.
- We may not be successful in our efforts to use our gene therapy technology platform to build a pipeline of additional product candidates, and we may not be successful in our efforts to create innovative programs, platform technologies or other technologies to be competitive with others.
- We may not be successful in our efforts to in-license or acquire product candidates that align with our research and development strategy.
- Our manufacturing facility is subject to significant government regulations and approvals. If we fail to comply with these regulations or to maintain these approvals our business could be materially harmed.
- Our resources might be adversely affected if we are unable to successfully complete pre-approval inspections required by regulators or meet our supply needs and obligations, which could adversely affect our ability to sufficiently meet our future production needs or regulatory filing or approval timelines.
- We cannot predict when or if we will obtain marketing approval to commercialize any of our product candidates, or whether they will be commercially successful once approved.
- We are exposed to a number of external factors such as competition, insurance coverage of and pricing and reimbursement for our product candidates that may adversely affect our product revenue and that may cause our business to suffer. We also have experienced and could continue to experience increased competition for and compensation expenses associated with employee recruiting and employee retention, which could adversely affect our business.
- If we are unable to successfully commercialize our product candidates or experience significant delays in doing so, our business could be materially harmed.

- We rely, and expect to continue to rely, on third parties to conduct, supervise, and monitor our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or failing to comply with regulatory requirements.
- We rely on licenses of intellectual property from third parties, and such licenses may not provide adequate rights or may not be available in the future on commercially reasonable terms or at all, and our licensors may be unable to obtain and maintain patent protection for the technology or products that we license from them.
- If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our ability to successfully commercialize our products may be impaired.
- Our reliance on third parties may require us to share our trade secrets, which could increase the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.
- Our acquisition strategy may not produce the cash flows expected or could result in additional costs and challenges.
- We will likely need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations which could have a material adverse effect on our business, financial condition, results of operations, and cash flows.
- Our relationships with customers and third-party payers will be subject to applicable anti-kickback, anti-bribery, fraud and abuse and other laws and regulations, which, if we are found in violation thereof, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.
- We are subject to laws governing data protection in the different jurisdictions in which we operate. The implementation of such data protection regimes is complex, and should we fail to fully comply, we may be subject to penalties that may have an adverse effect on our business, financial condition, and results of operations.
- Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches or other errors or disruptions, which could result in a material disruption of our product development programs, such as potential issues with data integrity or loss of data.
- If we fail to maintain an effective system of internal controls, we may be unable to accurately report our results of operations or prevent fraud or fail to meet our reporting obligations, and investor confidence and the market price of our ordinary shares may be materially and adversely affected.

b) Internal risk management and control system

We have developed an internal risk management and control system that is tailored to the risk factors that are relevant to us. Our controls frequently entail involvement of the Board and Senior Management. The internal risk management and control systems are discussed in the Board.

The Board is responsible for designing, implementing and operating our internal risk management and control systems. The objective of these systems is to manage in an effective and efficient manner the significant risks to which we are exposed. Our internal risk management and control systems are designed to provide reasonable assurance that these objectives are met. Such systems can never provide absolute assurance regarding achievement of our objectives, nor can they provide absolute assurance that material errors, losses, fraud, and the violation of laws or regulations will not occur. A summary of the risks that could have prevented us from realizing our objectives is included in the section 'Risk Factors' of this report.

Our internal risk management and control systems make use of various measures including:

- Annual strategic evaluations of the business;
- Periodic operational review meetings of the Leadership Team comprising the executive directors of the Board and Senior Management;
- Quarterly review of the financial position and prospects as part of the Board meeting;

- A planning and control cycle consisting of annual, quarterly and monthly procedures, including subsequent follow-up on achievements of targets set;
- A system of internal controls and procedures;
- An Audit Committee that meets regularly with the executives and Senior Management as well as the independent auditors.

We maintain controls and procedures designed to:

- Ensure that records are maintained, in reasonable detail, accurately and fairly reflect the transactions and disposition of the assets of the Company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with IFRS, and that receipts and expenditures of the Company are being made only by authorized employees in accordance with documented authorizations; and
- 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 for future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

Based on the evaluation of our Company's disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer ("CEO") and Chief Financial Officier ("CFO") concluded that our company's disclosure controls and procedures were effective.

Director's Annual Report on Internal Control Over Financial Reporting

The Board 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 U.S. Exchange Act of 1934, as amended ("Exchange Act") and in accordance with the Dutch Corporate Governance Code. This rule defines internal control over financial reporting as a process designed by, or under the supervision of, a company's CEO 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, 2021. 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, 2021, based on criteria established in the COSO 2013 framework.

Additional information

In addition to the information contained in this Annual Report, we also filed Consolidated Financial Statements for 2021 of uniQure N.V. prepared in accordance with generally accepted accounting principles in the United States ("U.S. GAAP") with the SEC on February 25, 2022, as part of our Annual Report on Form 10-K for the year ended December 31, 2021, which is available on the Company's website.

4 Governance and compliance

We monitor and assess applicable Dutch and U.S. federal and state corporate governance codes, rules, and regulations. We apply the 2016 Dutch Corporate Governance Code (the "Code"). We also are required to comply with all applicable U.S. securities laws and regulations, including the rules and regulations promulgated by the SEC pursuant to the U.S. Exchange Act of 1934 and the U.S. Sarbanes-Oxley Act of 2002, as well as the Nasdaq listing rules.

Our corporate governance structure is based on the requirements of the Dutch Civil Code, the Company's Articles of Association and the rules and regulations applicable to companies listed on Nasdaq. These procedures include a risk management and control system, as well as a system of assurance of compliance with laws and regulations.

When in this chapter a reference is made to Articles of Association, this shall be a reference to the Company's Articles of Association, as amended by deed on June 22, 2021. The articles of association do not provide for anti-takeover measures.

a) Board

All members of the Board, both the executive directors and the non-executive directors, are collectively responsible for the management performed by the one-tier Board and the general policy and strategy of the Company. The executive directors manage the day-to-day management of the Company. The non-executive directors focus on the supervision on the policy and functioning of the executive directors and the general state of affairs within the Company. The division of tasks and responsibilities, the manner in which decisions are taken and all other manners concerning the Board are laid down in the Corporate Governance Guidelines and Rules for the Board of Directors, which is effective as of April 14, 2017 and published on the Company's website. The Board is supported by a Secretary, who is appointed by the Board. The executive directors and non-executive directors are appointed as such at the annual general meeting of the shareholders (the "General Meeting") at the binding nomination of the non-executive directors. The General Meeting may at all times overrule a binding nomination by a resolution adopted by at least a two-thirds majority of the votes cast, provided such majority represents more than half the issued share capital. The Board determines the number of executive directors and non-executive directors, provided that the number of executive directors shall at all times be less than the number of non-executive directors. Only natural persons can be non-executive directors. The General Meeting shall at all times be entitled to suspend or dismiss a Board member. The Board shall also at all times be entitled to suspend (but not dismiss) an executive director.

The Board shall appoint an executive director as CEO. The Board shall furthermore appoint a non-executive director to be Chairman of the Board for such period as the Board may decide.

The Board, as well as two executive directors acting jointly, are authorized to represent the Company. In case only one Executive Director is in office, such Executive Director is authorized to represent the Company independently.

Under the Company's Articles of Association, members of the Board are appointed for a maximum term of four (4) years, provided that, unless a Board Member resigns earlier, his term shall end at the close of the General Meeting to be held in the fourth year after the date of his appointment. A Board Member may be reappointed with due observance of the preceding sentence. The Articles of Association provide that the Board shall draw up a retirement schedule for the directors of the Board.

The current practice of the Board is to nominate members for terms of three years. Pursuant to that practice, all Board Members except one are currently serving three-year terms. The following table sets out information with respect to the executive and non-executive directors of the Board, and their ages and position at the Company as of the date of this annual report. The business address of the executive and non-executive directors of the Board is our registered office address at Paasheuvelweg 25, 1105 BP, Amsterdam, The Netherlands.

Name	Age[1)]	Nationality	Position	Member Since	Term Expires
Mr. Matthew Kapusta	49	American	Executive Director	2016	2022
Mr. David Meek	58	American	Non-Executive Director, Chairman of the Board	2018	2024
Mr. Madhavan Balachandran	71	American	Non-Executive Director	2017	2023
Mr. Robert Gut	57	American	Non-Executive Director	2018	2022
Mr. Jack Kaye	78	American	Non-Executive Director	2016	2023
Ms. Rachelle Jacques	50	American	Non-Executive Director	2021	2024
Mr. Leonard Post	69	American	Non-Executive Director	2020	2023
Ms. Paula Soteropoulos	54	American	Non-Executive Director	2013	2024
Mr. Jeremy P. Springhorn	59	American	Non-Executive Director	2017	2023

1) As of April 29, 2022

MATTHEW KAPUSTA. Matthew Kapusta, age 49, has been Chief Executive Officer of uniQure since December 2016, and currently serves on the Company's Board of Directors. Mr. Kapusta also served as our Chief Financial Officer from joining uniQure in January 2015 until June 2021. Prior to joining uniQure, Mr. Kapusta was Senior Vice President at AngioDynamics (Nasdaq: ANGO) from 2011 to 2014, responsible for corporate development, strategic planning, and national accounts. Prior to AngioDynamics, he served as Vice President, Finance and Strategic Planning and Analysis for Smith & Nephew Orthopaedics. Mr. Kapusta's career also includes more than a decade of investment banking experience focused on emerging life sciences companies. Mr. Kapusta was Managing Director, Healthcare Investment Banking at Collins Stewart, and held various positions at Wells Fargo Securities, Robertson Stephens, and PaineWebber. Mr. Kapusta holds a Master of Business Administration from New York University's Stern School of Business, a Bachelor of Business Administration from University of Michigan's Ross School of Business and earned his Certified Public Accountant license in 1996 while at Ernst & Young. We believe that Mr. Kapusta is qualified to serve as our Chief Executive Officer and an Executive Director due to his broad expertise in the biotechnology and finance industries.

DAVID MEEK. David Meek, age 58, has served as a member of our Board since June 2018 and as Chair of our Board since June 2021. Mr. Meek has more than 30 years of experience in the biopharma industry, where he has held various global executive positions in major pharmaceutical and biotechnology companies. Mr. Meek was appointed CEO and Director of Mirati Therapeutics (Nasdaq: MRTX), a public clinical stage oncology biotech company, in September 2021. From January 2020 to March 2021, Mr. Meek was President & CEO, Director of FerGene, a gene therapy biotech focused on the treatment of cancer. From July 2016 to December 2020, Mr. Meek was CEO and a member of the Board of Ipsen, a French public biopharma company. From July 2014 to June 2016, he was Executive Vice-President and President of the oncology division of Baxalta prior to being acquired by Shire. He spent two years as the Chief Commercial Officer of Endocyte from August 2012 to July 2014. Mr. Meek also spent eight years at Novartis as a global franchise head from January 2005 to June 2007, CEO of Novartis Canada from July 2007 to December 2009, and region head of oncology for northern, central and Eastern Europe from January 2010 to August 2012. He began his biopharma career at Johnson & Johnson and Janssen Pharmaceuticals where he worked from July 1989 to December 2004 and where he held increasingly senior levels of executive roles. Mr. Meek serves as a Director for Entasis Therapeutics (Nasdaq: ETTX). Mr. Meek holds a B.A. from the University of Cincinnati. We believe Mr. Meek is qualified to serve as a Non-Executive Director due to his extensive experience in the biotechnology industry.

MADHAVAN BALACHANDRAN. Mr. Balachandran, age 71, has served as a member of our Board since September 2017. Mr. Balachandran has been a director of Catalent (NYSE: CTLT) since May 2017. Mr. Balachandran was Executive Vice President, Operations of Amgen Inc., a global biotechnology company, from August 2012 until July 2016 and retired as an Executive Vice President in January 2017. Mr. Balachandran joined Amgen in 1997 as Associate Director, Engineering. He became Director, Engineering in 1998, and, from 1999 to 2001, he held the position of Senior Director, Engineering and Operations Services before moving to the position of Vice President, Information Systems from 2001 to 2002. Thereafter, Mr. Balachandran was Vice President, Puerto Rico Operations from May 2002 to February 2007. From February 2007 to October 2007, Mr. Balachandran was Vice President, Site Operations, and from October 2007 to August 2012, he held the position of Senior Vice President, Manufacturing. Prior to his tenure at Amgen, Mr. Balachandran held leadership positions at Copley Pharmaceuticals, now a part of Teva Pharmaceuticals Industries Ltd., and Burroughs Wellcome Company, a predecessor before mergers of GlaxoSmithKline plc. Mr. Balachandran holds a Master of Science degree in Chemical Engineering from The State University of New York at Buffalo and an MBA from East Carolina University. We believe Mr. Balachandran is qualified to serve as a Non-Executive Director due to his extensive experience in the biotechnology industry.

ROBERT GUT, M.D., Ph.D. Dr. Robert Gut, age 57, was elected to his current term as a Non-Executive Director in December 2020. Dr Gut first joined our Board in June 2018, and previously served as both a Non-Executive and an Executive Director. He also served as our Chief Medical Officer from August 2018 until October 2020. During his time as our Chief Medical Officer, Dr. Gut led clinical development, clinical operation and medical team activities that successfully initiated and executed our HOPE-B pivotal trial of etranacogene dezaparvovec for hemophilia B and our Phase 1/2 clinical trial of AMT-130 for the treatment of Huntington's Disease. In October 2020, he resigned as Chief Medical Officer and as executive director (because under Dutch law our executive directors must hold an executive position with the Company), and in December 2020, he was reappointed to the Board as a non-executive director. Dr. Gut has more than 23 years of experience in the biopharmaceutical industry-leading clinical development and medical affairs activities in rare disorders and other therapeutic areas. For most of his career, Dr. Gut worked at Novo Nordisk Inc. (NYSE: NVO), where he headed the company's U.S. Biopharm Medical organization with leading products in hemophilia, endocrinology, and women's health (NovoSeven®, Norditropin® and Vagifem®), totaling approximately $1.6 billion in U.S. revenue. Over his career, Dr. Gut's contributions have helped achieve six FDA product approvals and three additional new product indications. Dr. Gut has supported the launch of nine new products, overseeing medical activities including medical science liaison and health economics and outcomes research teams building. He has also served for the FDA's Center for Drug Evaluation and Research as a member of the Advisory Committees for Reproductive Health Drugs and Drug Safety and Risk Management. Dr. Gut was appointed the Chief Medical Officer of Versartis, Inc. in September 2017 and received his Doctor of Medicine degree from the Medical University of Lublin, and his Doctorate degree from Lublin Institute of Medicine, Poland. He attended numerous postgraduate programs at Wharton, Stanford, and Harvard Business School. We believe Dr. Gut is qualified to serve as a Non-Executive Director due to his extensive experience in the biotechnology industry.

RACHELLE JACQUES. Rachelle Jacques, age 50, has more than 25 years of industry experience, with strong global experience in strategic, cross-functional leadership roles spanning finance, business operations, manufacturing, and commercial, including the successful launches of several novel therapies for rare diseases. In March 2022, Ms. Jacques was appointed President and Chief Executive Officer of Akari Therapeutics, a late-stage biopharmaceutical company focused on innovative therapeutics to treat orphan autoimmune and inflammatory diseases. From February 2019 to March 2022, Ms. Jacques has served as the Chief Executive Officer of Enzyvant Therapeutics Inc, focusing on the development of transformative regenerative therapies for rare diseases. From August 2017 to February 2019, she served as the Senior Vice President and Global Complement Franchise Head at Alexion Pharmaceuticals, Inc., where she was responsible for global franchise strategy development and execution across the therapeutic areas of hematology, nephrology, and neurology. From January 2016 to June 2017, she was Vice President of U.S. Hematology Marketing at Baxalta Inc. and then Shire plc, following Shire's acquisition of Baxalta in 2016. From July 2015 to June 2016, she served as Vice President of Business Operations at Baxalta Inc. after its spinoff from Baxter International Inc. Ms. Jacques held multiple leadership positions at Baxter, including Vice President of Finance, U.S. BioScience Business. Earlier in her career, Ms. Jacques served in various roles at Dow Corning Corporation, including operational management positions in the U.S., Europe, and China. Ms. Jacques received her B.A. degree in business administration from Alma College. She has also served as a financial auditor for Ernst & Young and Deloitte and Touche. Since April 2019, Ms. Jacques has served on the Board of Directors of Corbus Pharmaceuticals (Nasdaq: CRBP), and from April 2020 to February 2021, she served on the Board of Directors of Viela Bio. She is a founding member of the Alliance for Regenerative Medicine (ARM) Action for Equality Task Force.

JACK KAYE. Jack Kaye, age 78, has served as a member of our Board since 2016. Mr. Kaye has also served as Chairman of the Audit Committee of Keryx Biopharmaceuticals, Inc. (Nasdaq: KERX) from 2006 to 2016, is currently chairman of the Audit Committee and a member of the Compensation Committee of Dyadic International, Inc. (OTC: DYAI), and chairman of the Audit Committee of DiaCarta Ltd. Mr. Kaye began his career at Deloitte LLP, an international accounting, tax and consulting firm, in 1970, and was a partner in the firm from 1978 until May 2006. At Deloitte, he was responsible for servicing a diverse client base of public and private, global, and domestic companies in a variety of industries. Mr. Kaye has extensive experience consulting with clients on accounting and reporting matters, private and public debt financings, SEC rules and regulations, corporate governance, and Sarbanes-Oxley matters. Prior to retiring, Mr. Kaye served as Partner-in-Charge of Deloitte's Tri-State Core Client practice, a position he held for more than 20 years. Mr. Kaye has a Bachelor of Business Administration from Baruch College and is a Certified Public Accountant. We believe that Mr. Kaye is qualified to serve as a Non- Executive Director due to his extensive accounting and financial experience.

LEONARD POST, Ph.D. Dr. Post, age 69, has over 35 years of experience in the pharmaceutical industry where he has held various global executive positions and has extensive experience in research and development of product candidates. Since July 2016, Dr. Post has served as Chief Scientific Officer of Vivace Therapeutics, an oncology company working on small molecules targeting the hippo pathway and is also Chief Scientific Officer of its sister company Virtuoso Therapeutics, a company working on bispecific antibodies for oncology. From February 2010 until June 2016, Dr. Post worked at BioMarin (Nasdaq: BMRN), in various positions including Chief Scientific Officer. During that time, he oversaw the initiation of BioMarin's first gene therapy project for hemophilia A. Prior to that, Dr. Post served as Chief Scientific Officer of LEAD Therapeutics, Senior Vice President of Research & Development at Onyx Pharmaceuticals, and Vice President of Discovery Research at Parke-Davis Pharmaceuticals. He is also currently an advisor to Canaan Partners. Dr. Post is a virologist by training and did early work on engineering of herpes simplex virus as a postdoctoral fellow. He has a Bachelor of Science degree in Chemistry from the University of Michigan, and a Doctorate degree in Biochemistry from the University of Wisconsin. We believe Dr. Post is qualified to serve as a Non-Executive Director due to his extensive experience in the biotechnology industry.

PAULA SOTEROPOULOS. Paula Soteropoulos, age 54, has served as a member of our Board since July 2013. Ms. Soteropoulos is an executive leader with more than 30 years of experience in the biopharma industry in areas of drug development, manufacturing, business development, global commercialization and company building. She currently serves as the Executive Chairman of Ensoma, a private venture-backed company. Since November 2020, she has served on the Board of Directors of Rallybio, LLC. Since March 2020 she also has served as a Strategic Advisor to 5AM Ventures. From January 2015 through September 2019, she served as President and Chief Executive Officer of Akcea Therapeutics (Nasdaq: AKCA). From July 2013 to December 2014, she served as Senior Vice President and General Manager, Cardiometabolic Business and Strategic Alliances at Moderna Therapeutics Inc. Prior to this, Ms. Soteropoulos worked at Genzyme Corporation, a biotechnology company, from 1992 to 2013, most recently as Vice President and General Manager, Cardiovascular, Rare Diseases. Ms. Soteropoulos holds a Bachelor of Science degree in chemical engineering and a Master of Science degree in chemical and biochemical engineering, both from Tufts University, and holds an executive management certificate from the University of Virginia, Darden Graduate School of Business Administration. Ms. Soteropoulos serves on the Advisory Board for the Chemical and Biological Engineering Department of Tufts University. We believe Ms. Soteropoulos is qualified to serve as a Non-Executive Director due to her extensive experience in the biotechnology industry.

JEREMY P. SPRINGHORN, Ph.D. Dr. Springhorn, age 59, has served as a member of our Board since September 2017. Since April 2021, Dr. Springhorn has been Chief Executive Officer of Nido Biosciences. Prior to taking his position at Nido, Dr. Springhorn was Chief Business Officer of Syros Pharmaceuticals, Inc. (Nasdaq: SYRS) from November 2017 until April 2021. Prior to taking his position at Syros, Dr. Springhorn served as Partner, Corporate Development at Flagship Pioneering from March 2015 until June 2017 where he worked with VentureLabs in helping companies in various strategic and corporate development capacities, creating next generation startups, and working with Flagship's Corporate Limited Partners. Prior to joining Flagship, Dr. Springhorn was one of the original scientists at Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) and was one of the original inventors of the drug Soliris®. At Alexion Pharmaceuticals, Dr. Springhorn was Vice President of Corporate Strategy and Business Development from 2006 until March 2015. Dr. Springhorn started at Alexion in 1992 where he served in various leadership roles in R&D before switching to Business Development in 2006. Prior to 1992, Dr. Springhorn received his Ph.D. from Louisiana State University Medical Center in New Orleans and his BA from Colby College. Dr. Springhorn currently serves on the Board of Directors for NMD Pharma, Board of Advisors for Mythic Therapeutics, and the Board of Visitors for Colby College. We believe Dr. Springhorn is qualified to serve as a Non-Executive Director due to his extensive experience in the biotechnology industry.

Meetings and board committees

We have established an Audit Committee ("Audit Committee", a Compensation Committee ("Compensation Committee"), a Nominating and Corporate Governance Committee ("Nominating and Corporate Governance Committee"), and a Research and Development Committee ("Research and Development Committee") (collectively, the "Committees"). The charter of the Compensation Committee and the Nominating and Corporate Governance Committee were amended in June 2018 and the charter of the Audit Committee was amended in September 2018. The charter of the Research and Development Committee was established in December 2019. The charters are published at our website.

Meetings

In 2021, the Board held six (6) meetings by means of a video conference call. During these meetings and also in informal communications among its members, extensive discussions were held to ensure the continuity of high-level management of the Company. The Chairman sets the agenda and ensures that the directors receive accurate information in time. During these formal meetings and discussions, the Board primarily focuses on the objectives and strategy of uniQure, the main risks of its business, the assessment made by the executive directors of the design and effectiveness of the internal risk management and control systems, the progress made on clinical development, corporate governance, the financial budgets, the operational plan and the annual and quarterly consolidated financial statements. Specifically, pursuant to the Company's Corporate Governance Guidelines and Board Rules, the Board is charged with assessing major risks facing the Company and reviewing options to mitigate such risks. The Board performs this oversight role by using several different levels of review. In connection with its reviews of the operations and corporate functions of the Company, the Board addresses the primary risks associated with those operations and corporate functions. In addition, the Board reviews the risks associated with the Company's business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies.

The Board has delegated certain risk oversight responsibilities to the Committees. Each of our Committees also oversees the management of the Company's risk that falls within each Committee's areas of responsibility. In performing this function, each Committee has full access to management, as well as the ability to engage advisors. For example, the Audit Committee is required to regularly review and discuss with management the Company's major financial risk exposures and the steps management has taken to monitor and control such exposures. The Nominating and Corporate Governance Committee is required to regularly review the corporate governance principles of the Company and recommend to the Board any proposed changes it may deem appropriate. The Compensation Committee considers risks related to the attraction and retention of professional talent and the implementation and administration of compensation and benefit plans affecting the Company's employees. The Research and Development Committee serves as an advisory body to the Board in matters related to the Company's technology and evaluates the function and effectiveness of the Company's research, development, manufacturing operations, clinical operations, and other technical, scientific and medical operations. All Committees are required, pursuant to their respective charters, to report regularly to the Board. The activities of the Audit, Nominating and Corporate Governance and Compensation as well as the Research and Development Committees are more fully described below.

Throughout 2021, the Board actively reviewed the progress and planning for the hemophilia B and Huntington's disease programs and other pipeline programs, as well as our collaborations with CSL Behring and BMS.

Attendance at the Board meetings during 2021 was as follows:

	Number of meetings	Meetings attended
David Meek (Chairman)	6	6
Philip Astley-Sparke (Former Chairman) [1)]	4	4
Matthew Kapusta	6	6
Paula Soteropoulus	6	6
Jack Kaye	6	5
Jeremy Springhorn	6	6
Madhavan Balachandran	6	5
Robert Gut	6	6
Rachelle Jacques [2)]	1	1
Leonard Post	6	6

(1) Term ended on June 16, 2021.
(2) Appointed on October 21, 2021

Audit Committee

Our Audit Committee currently consists of our non-executive directors Mr. Kaye (Chairman), Ms. Jacques and Dr. Springhorn. Following the 2021 General Meeting, Ms. Soteropoulos joined the committee to succeed Mr. Astley-Sparke (who did not stand for reelection at the June 2021 General Meeting) on an interim basis until Ms. Jacques joined the Audit Committee following her appointment to the Board in October 2021. Each member attended all meetings of the committee for the time they served on the committee. Each member satisfies the independence requirements of Nasdaq listing standards, and Ms. Jacques and Mr. Kaye qualify as an audit committee financial expert pursuant to Section 407 of the U.S. Sarbanes-Oxley Act of 2002 and as determined by the Board. The Audit Committee oversees our accounting and financial reporting processes, the funding of the Company and the audits of our consolidated financial statements. The Audit Committee is responsible for:

- Recommending the selection of our independent registered public accounting firm;
- Reviewing with the Company's independent registered public accounting firm the procedures for and results of their audits;
- Reviewing with the independent accountants and management our financial reporting, internal controls and internal audit procedures;
- Reviewing and approving related party transactions; and
- Reviewing matters relating to the relationship between the Company and our independent registered public accounting firm, including the selection of and engagement fee for our independent registered public accounting firm, and assessing the independence of the independent registered public accounting firm.

The Audit Committee has the authority to engage independent legal, accounting and other advisers, as it determines necessary to carry out its duties. The Audit Committee reviews regularly and discusses with management the Company's major financial, income tax and information technology related risk exposures and the steps management has taken to monitor and control such exposures. The Audit Committee met five (5) times during 2021. During these meetings, the committee discussed the reports of the Disclosure Committee, internal controls, related party transactions, the whistle blower hotline, the (interim) financial statements, the actual financial results of each of the quarters, securities filings and financial press releases as well as the audit approach and the budget for 2021 and 2022.

The Audit Committee annually reviews the independent registered public accounting firm's independence, including reviewing all relationships between the independent registered public accounting firm and us and any disclosed relationships or services that may impact the objectivity and independence of the independent registered public accounting firm, and the independent registered public accounting firm's performance.

Compensation Committee

Our Compensation Committee currently consists of our non-executive directors Mr. Balachandran (Chairman), Mr. Kaye and Mr. Meek. Each of them attended all meetings of the committee for the time they served on the committee. Each member satisfies the independence requirements of Nasdaq listing standards. The Compensation Committee assists the Board in reviewing and approving or recommending our compensation structure, including all forms of compensation relating to our non-executive and executive directors as well as senior management. Members of our senior management (other than the General Counsel) may not be present at any committee meeting while the compensation of that person is deliberated, and the practice of the committee is to hold discussions on the compensation of any executive director as well as other compensation matters in executive session. The Compensation Committee has the authority to retain compensation consultants and other outside advisors to assist in the evaluation of executive officer compensation.

Subject to the terms of the compensation policy approved by our General Meeting and as required by Dutch law, the compensation committee is responsible for:

- Reviewing and approving or recommending to the Board for approval, as appropriate, the compensation of our executive officers following consideration of corporate goals and objectives relevant to such executive officers;
- Overseeing the evaluation of the Company's senior executives;
- Reviewing and making recommendations to the Board regarding incentive compensation and equity-based plans; and
- Administering our stock option plans.

The Compensation Committee met seven (7) times during 2021. The committee discussed the long-term incentive grant guidelines, the compensation terms of our newly recruited executives, the terms and conditions of our executive compensation, and assessed the Company's 2021 corporate goals. The remuneration policy provides for fixed pay, incentives and benefits. The fixed pay is in cash and is paid monthly. The fixed pay is set at the median of the appropriate peer group. Benefits include provisions of death, disability and medical insurance cover, directors' liability insurance and tax returns preparation costs. The Company has established a long-term incentive plan and sets incentives on a year-to-year delivery basis in support of the strategic and corporate goals as part of the ongoing enhancement of shareholders value. The target annual bonus of the CEO is 60% of the fixed pay adjusted by the corporate factor. The corporate factor is the outcome of the assessment of the achievement of the corporate goals. Over 2021 the Board assessed the corporate factor at 100%.

Nominating and Corporate Governance Committee

Our Nominating and Corporate Governance Committee consists of our non-executive directors Mr. Springhorn (Chairman), Ms. Soteropoulos and Mr. Meek. Following the 2021 General Meeting, Mr. Meek joined the committee to succeed Mr. Astley-Sparke. Each of them attended all meetings of the committee for the time they served on the committee. Each member satisfies the independence requirements of Nasdaq listing standards. The Nominating and Corporate Governance Committee assists the board in selecting individuals qualified to serve as an executive or non-executive director of the board and in determining the composition of the board and its committees.

The Nominating and Corporate Governance Committee is responsible for, among other things:

- Identifying individuals qualified to become Board members and to recommend to the Board the nominees for director at annual general meetings of Shareholders;
- Recommending to the Board nominees for each committee; developing and recommending to the Board corporate governance principles applicable to the Company; and
- Leading the Board in its annual review of the Board's performance.

The Nominating and Corporate Governance Committee met six (6) times during 2021. The committee discussed the composition of the committees, the selection of new non-executive members, the appointment of an additional non-executive member, and conducted a review of the Company's policies related to corporate governance.

Research and Development Committee

Our Research and Development Committee consists of our non-executive directors Mr. Post, Dr. Gut, Ms. Soteropoulos and Mr. Springhorn. Dr. Gut was added to the committee in February 2021. Each of the members of the committee attended all of the meetings held in 2021 for the time they served on the committee. The members of this committee are not subject to independence requirements of Nasdaq listing standards. The Research and Development Committee serves as an advisory body to the Board in matters related to the Company's technology, research and development activities, product pipeline, and manufacturing platform (the "Company's Technology").

The Research and Development Committee is responsible for, among other things:

- Advising the Board on the strategic direction of the Company with respect to the Company's Technology;
- Evaluating the function and effectiveness of the Company's research, development, manufacturing operations, clinical operations, and other technical, scientific and medical operations;
- Conferring with officers and employees of the Company as needed on matters related to the Company's technology; and
- Performing other tasks customarily performed by research and development committees as may be reasonably required to effectively advise the Board on matters associated with the Company's Technology.

The Research and Development Committee met nine (9) times during 2021. The committee discussed the status of various programs, reviewed potential business development transactions, evaluated the Company's manufacturing, quality and clinical operations, and reviewed the Company's research and development pipeline.

b) Corporate governance

In addition to U.S. securities laws, Nasdaq listing standards and rules and regulations as promulgated by the SEC, as a Dutch company, our governance practices are governed by the Code, a copy of which is available at the website of the Monitoring Committee Corporate Governance Code, www.mccg.nl. The Code was published on December 8, 2016 and came into force as of the financial year starting after January 1, 2017 and contains a number of principles and best practices. The Code, contains an apply-or-explain principle, offering the possibility to deviate from the Corporate Governance Code and still comply, provided such deviations be explained. The Company, as a domestic filer under SEC rules, experiences that the Code and the SEC rules do not always align. In the event of non-alignment between applicable U.S. rules and the Code, it is permissible for the Company to deviate from the Code provided the Company explains such deviation. In essence, the Company complies with most of the principles and best practice provisions of the Code. In certain cases, the Company has not applied the Code's principles or best practice provisions and in those instances, we explain the non-application.

The Code also requires the Board to confirm, and the Board hereby confirms, that:

i. The Report of the Board provided sufficient insights into any failings in the effectiveness of the internal risk management and control systems;

ii. The aforementioned systems provided reasonable assurance that the financial reporting does not contain any material inaccuracies;

iii. Based on the current state of affairs, it is justified that the financial reporting is prepared on a going concern basis; and

iv. The Report states those material risks and uncertainties that are relevant to the expectations of the Company's continuity for the period of twelve months after the preparation of the Report.

We conduct our operations in accordance with internationally accepted principles of good governance and best practice, while ensuring compliance with the corporate governance requirements applicable in the countries in which we operate. There is considerable overlap between the requirements we must meet under U.S. rules and regulations and the provisions of the Code and we apply most of the provisions of the Code. For further clarity, we have listed below deviations from the Code and our reasons for deviating.

1.3.6 Absence of an internal audit department

The Audit Committee meets with the executive director of the Board prior to the release of the publicly disclosed financial reports, which enables the Audit Committee to monitor the quality and the completeness of such reports.

The Board 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 U.S. Exchange Act and in accordance with the Dutch corporate governance code. 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, 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. Under the direction and supervision of our CEO and CFO and based on criteria established in Internal Control—Integrated Framework (2013) issued by the COSO an assessment on the effectiveness of our internal control over financial reporting was performed. This included testing and evaluating the design and operating effectiveness of our internal controls.

The audit committee determined that due to the limited size and complexity of the Company no internal audit department had to be established in 2021.

2.1.5 – 2.1.6 Diversity Policy.

The Board applies the criteria for nominating executive and non-executive members of the Board as defined in the charter of the Nominating and Governance Committee. The Company publishes the personal information of a candidate nominated for the Company's Board at the Company's website and at the website of the SEC. Currently the Company's Board consists of nine members, one of whom is female. The Board believes, that whilst gender is an important part of diversity, members of the Board were and will continue to be selected on the basis of the criteria reflected in the charter and their experience, background, skills, knowledge and insight. The Board feels that this policy serves the interest of the Company and its stakeholders best.

3.1.2 Remuneration Policy.

> *vi. If shares are being awarded, the terms and conditions govern this. Shares should be held for at least five years after they are awarded.*
> *vii. If share options are being awarded, the term and conditions governing this and the terms and conditions subject to which the share options can be exercised. Share options cannot be exercised during the first three years after they are awarded.*

The stock options and restricted share units the Company grants to its executive and non-executive directors of the Board and to our senior management are issued under the 2014 Incentive Plan as amended and are exercisable pursuant to a vesting schedule before the fourth anniversary of the date of grant, which is contrary to best practices provision 3.1.2 of the Code. The vesting terms of options vary between one and four years, and begin vesting on the first anniversary of date of grant.

We believe our vesting schedules are in line with the practices of our peer group used for executive compensation purposes and necessary to attract and retain the best people.

3.2.3 Severance Payment.

The remuneration in the event of a dismissal of the executive director of the Board exceeds one year's salary. The terms and conditions triggering a higher severance amount have been approved following a review and recommendation by the compensation committee. In addition, we believe it is in line with the practice of our peer group used for executive compensation.

3.3 Remuneration of the non-executive Members of the Board.

The non-executive members of the Board are eligible to receive restricted share units and options grants, and, in case granted, will vest on the first anniversary of the grant date. We believe it is in line with the practice of our peer group used for non-executive compensation.

The Remuneration Policy provides guidelines for the compensation of non-executive directors. The non-executive directors are compensated for their services on the Board as follows:

- Each non-executive director receives an annual retainer of $40,000, pro-rated for service over the course of the year.
- The chairman of the Board receives an additional annual retainer of $35,000, and as such receives a total annual retainer of $75,000.
- Each non-executive director who serves as member of a committee of the Board receives additional compensation as follows:

    - Compensation Committee: members receive an annual retainer of $7,500; the chair receives an annual retainer of $15,000 in total.
    - Nominating and Corporate Governance Committee: members receive an annual retainer of $5,000; the chair receives an annual retainer of $10,000 in total.
    - Audit Committee: members receive an annual retainer of $10,000; the chair receives an annual retainer of $20,000 in total.
    - Research and Development Committee: members receive an annual retainer of $7,500; the chair receives an annual retainer of $15,000 in total.
    - Non-executive director receives an annual equity grant vesting after one year. The total fair value of the grant is divided equally by fair value between options to acquire our ordinary shares as well as restricted stock units. The size of the annual equity grant is determined by reference to our peer group companies.

    Each annual retainer for Board and committee services is payable semi-annually.

Each member of our Board is entitled to be reimbursed for reasonable travel and other expenses incurred in connection with attending meetings of the Board and any committee of the Board on which she or he serves.

3.4.1 Remuneration report.

The Company has not posted a comprehensive report on its website, but remuneration information is reported publicly in our filings with the SEC. We engaged an independent, third-party compensation expert to benchmark our remuneration of non-executive directors, executive directors and senior management compared to our peer group. Based on this evaluation, we believe our compensation is in line with market practice. The remuneration of the Board is disclosed in Note 20 "*Key management compensation*" to the consolidated financial statement.

3.4.2 Agreement of the executive member of the Board.

We do not disclose the main elements of the agreement with the executive director of the Board at the Company's website. As for the year ended December 31, 2021, the Company was a listed company on Nasdaq. The disclosures made by the Company under the applicable listing rules and which are published at http://www.sec.gov are deemed to be appropriate in this respect.

4.2.2 Policy on bilateral contacts with shareholders

The Company has not formulated a policy on bilateral contacts with shareholders. The Company regularly meets with shareholders in one-on-one situations, which it considers to be in the best interests of the Company and its stakeholders. In such meetings no price-sensitive or material, non-public financial information shall be disclosed.

The Company announces by press release most corporate presentations held at investor conferences and provides for real time participation via webcast. However, considering the Company's size, it would create an excessive burden to establish and maintain formal bilateral contacts with shareholders. The Company endeavors to facilitate its shareholders by announcing its business updates on its website and follow such updates, to the extent possible, via webcast. The Company does not issue press releases as a standard practice. The Company will undertake that presentations are posted on its website immediately after the meetings in question.

5.1.3 Independence of chairman of the Board.

The former chairman of the Board (Philip Astley-Sparke) was president of an affiliated company of the Company in the five years prior to his appointment as chairman of the Board. He was also affiliated with Forbion. Therefore, he was not independent within the meaning of the Code. However, the chairman met the independence requirements as set by Nasdaq. The Company believes this deviation was justified both by his specific knowledge and experience of the Company's business as well as the significant ownership interest Forbion has in the Company. The current chairman of the Board (David Meek) is independent within the meaning of the Code and under Nasdaq rules.

c) Related party transactions

Details of transactions between the Company and members of the Board and significant shareholders are set out in Note 19 "*Related party transactions*" to the consolidated financial statements and are within the meaning of clause 2.2.3 and clause 2.7.1 of the Code. There have been no material transactions with shareholders holding more than ten percent of the shares in the Company.

d) Functioning of the Board of Directors

The members of the Board have discussed their individual functioning, as well as that of the Board as a whole, on a continuing basis. The Board undertakes a self-assessment of its performance annually to identify, discuss and act on any areas of potential deficiency as well as for overall improvement. Additionally, the Nominating and Governance Committee addresses as a standing agenda item at each meeting the composition of the Board to determine whether the existing members of the Board collectively have the proper profile for the needs of the Company both at the present time and as are anticipated for the future, which are reported to and discussed with the full Board on a regular basis. In these discussions, also consideration was given to the composition and profile of the Board, as well as the functioning of its members and committees and the Board's tasks. The profile sets out the types of expertise the Board must possess. Annually, following the completion of the annual review of the Board's performance, the Board considers and discusses the recommendations by the nominating and corporate governance committee. The chairman of the Board reviews and assesses the performance of the executive director. As the Board devotes time and addresses the issues reported at regular scheduled Board meetings, the Board, in our view satisfies the defined requirements, and we consider the composition to be adequate for the proper performance of its duties. The Board has appointed from among its members four separate committees with special tasks, the Audit Committee, the Compensation Committee, the Research and Development Committee, and the Nominating and Corporate Governance Committee. These committees prepare the decision making of the Board on the relevant matters. The following regulations can be found on the Company's website: Corporate Governance Guidelines and Rules for the Board, Disclosure Policy, Expanded Access Policy, Insider Trading Policy, Code of Business Conduct and Ethics, Related Party Transaction Policy, Audit Committee Charter, Compensation Committee Charter, Nominating and Corporate Governance Committee Charter, Research and Development Committee Charter, Remuneration Policy and the Articles of Association of the Company.

e) Compensation of the executive director

This report sets out the remuneration policy operated by the Company in respect of its executive director.

In summary, the Company's compensation program is designed to be straightforward in nature with five core elements, the first three of which are compensation related and the last two are benefits reflecting local market practices for each executive officer.

Element	Purpose	Key Features
Base Salary	Provide market-competitive fixed compensation Attract exceptional talent in the relevant market	• Fixed cash compensation • Reviewed annually • Value informed by market levels for executives with comparable qualifications, experience, and responsibility, coupled with the nature, scope and impact of the role • Target approximately 50th percentile of market peers, considering the factors noted above
Short-Term Incentive (Annual Cash Bonus)	Reward for achievement of pre-defined criteria in areas of strategic importance to uniQure Align compensation with Company performance	• Subject to the approval of the Board in its discretion • Discretionary variable cash compensation of 60% of annual Base Salary in 2021 • Maximum opportunity capped at 150% of target • Weighting based solely on corporate performance for the Chief Executive Officer • Corporate and individual targets established in the beginning of each year • Assessment against the predetermined targets informs actual cash bonus that is awarded • Target opportunity informed by levels in the market, with reference to the 50th percentile
Long-Term Incentives (Equity Awards)	Align long-term interests with shareholders Reward sustainable value creation Encourage retention	• Annual awards subject to the approval of the Board in its discretion • Annual awards in 2021 were a mix of stock options and restricted stock units • Stock options have a ten-year term, with 25% vesting after one year and then ratably on a quarterly basis • Restricted stock units vest ratably on an annual basis over three years • Target opportunity informed by prior year performance and levels in the market with reference to the 50th percentile • One-time PSU award provided in 2021 with goals tied to the pipeline milestones and relative total shareholder return
Pension and Retirement Savings Plans	Provide market-competitive retirement benefits	• Based on local market practice • Eligible to participate in a qualified 401(k) Plan with matching of up to 3% of base salary
Other Benefits	Provide market competitive benefits focused on well-being	• An Employee Stock Purchase Plan ("ESPP") is offered to all eligible employees, which includes the executive director • ESPP allows for purchase of discounted ordinary shares through accumulated payroll deductions • Medical, dental and vision health care plans with premiums paid by the company • Up to four weeks of paid time off • Company-paid life insurance and short-term and long-term disability, with some employee contribution • Tuition reimbursement • Fitness membership reimbursement

f) Financial statements

The Annual Accounts have been prepared by our executive Board member and discussed within the full Board. The Report of the Independent Auditor, KPMG Accountants N.V., is included in 'D Other Information.' The financial statements are being presented for adoption by shareholders at the General Meeting. The Board recommends that shareholders adopt these financial statements.

g) Shareholders and the general meeting of shareholders

The General Meeting shall be held within six months after the end of each financial year. The Company's financial year is equal to a calendar year. The Board or those who are authorized by law or pursuant to the articles of association of the Company may convene the General Meeting. The Articles of Association provide that, unless another majority of votes or a quorum is required by virtue of law, all resolutions of the General Meeting shall be adopted by at least a simple majority cast, in a meeting where more than 33⅓% of the issued share capital is represented.

An Extraordinary General Meeting of Shareholders may be convened by the Board or by those who are authorized by law or pursuant to the articles of association of the Company.

In accordance with Dutch law and the articles of association, shareholders representing alone or in aggregate at least one-tenth of the Company's issued and outstanding share capital can petition a court for authorization to convene a General Meeting after first requesting the Company to convene a General Meeting.

A record date shall apply to establish which shareholders are entitled to attend and vote in the General Meeting. The Company applies as record date the date as set by the Dutch Civil Code, i.e., the twenty-eighth day prior to the date of the meeting.

Each of the Company's shares is entitled to one vote. Shareholders may vote by proxy. The voting rights attached to any of the shares held by the Company are suspended as long as they are held in treasury.

Amendment of the Articles of Association

The General Meeting may resolve to amend the articles of association at the proposal of the Board.

Issuance of ordinary shares, options, restricted share units and performance share units

The General Meeting, following a proposal by the Board, is authorized to issue shares or grant rights thereto. Following a proposal by the Board, the General Meeting can delegate this authority to the Board. On June 16, 2021, the General Meeting delegated the authority to the Board to issue ordinary shares in the share capital of the Company and to grant rights to subscribe for ordinary shares and to limit or exclude pre-emptive rights in connection therewith:

- For a period of 18 months with effect from June 16, 2021. The number of ordinary shares to be issued shall be up to a maximum of (i) the authorized share capital of the Company in the event of an underwritten public offering, or (ii) a maximum of 19.9% of the Company's aggregate issued capital at the time of issuance in connection with any other single issuances (or series of related issuances).

Acquisition of own shares

The Company may acquire its own fully paid shares at any time for nil consideration (*om niet*). Furthermore, subject to certain provisions of Dutch law and the articles of association, the Company may acquire fully paid shares in the Company's own capital, within the limits set by Dutch law.

Unless for nil consideration, shares may only be acquired subject to a resolution of the Board and authorized by the General Meeting. Such authorization from the General Meeting for the acquisition of the Company's shares shall specify the number of shares that may be acquired, the manner in which these shares may be acquired and the price range within which shares may be acquired. Such authorization shall be valid for a period of not more than 18 months and may be extended from time to time for a period of not more than 18 months. On June 16, 2021, the General Meeting furthermore authorized the Board to acquire the Company's own fully paid ordinary shares up to a maximum of ten percent of the Company's issued share capital within the limits set by Dutch law and the Company's articles of association through purchase on the public market or otherwise at a purchase price between the nominal value of the ordinary shares concerned and an amount equal to 110% of the highest price officially quoted for the ordinary shares on any of the official stock markets on which the Company's ordinary shares are listed during any of 30 banking days preceding the date the repurchase is effected or proposed.

No authorization from the General Meeting is required for the acquisition of fully paid shares for the purpose of transferring these shares to employees under a scheme applicable to such employees. Any shares the Company held in its own capital may not be voted or counted for voting quorum purposes.

Reduction of share capital

Subject to Dutch law, the General Meeting may resolve to reduce the Company's issued and outstanding share capital by (i) amending the Articles of Association to reduce the nominal value of the shares or (ii) canceling:

- shares which the Company holds itself in the Company's share capital, or
- all issued shares against repayment of the amount paid on those shares.

Dividends and other distributions

The Board may determine which part of the profits shall be added to the reserves. The part of the profit remaining after reservation shall be at the disposal of the General Meeting, which may resolve to carry it to the reserves or to distribute it among the Shareholders.

Under the Articles of Association, the Company may make distributions of profit to the Company's shareholders after adoption of the Company's annual accounts demonstrating that such distributions are legally permitted. With due observance of applicable law and the articles of association, the Board may resolve to make interim distributions to the Shareholders.

The General Meeting may, at the proposal of the Board, resolve to distribute to the Shareholders a dividend in the form of shares in the share capital of the Company. Each of the Company's shares entitled its holder to equal ranking rights to dividends and other distributions.

h) Company culture and Code of Conduct

The Company has established the following values: be passionate about the patient; act with integrity and respect; take ownership and act with urgency; collaborate for success; and innovate every day. These values were established to guide the Company and its employees in order to effectively execute the Company's mission and strategy. In order to assure that employees live up to these principles we have implemented various training and evaluation programs. By virtue of these programs and evaluations we create an environment in which the employees, with more than 20 different nationalities represented, can contribute to the growth and values of the Company.

The company has a Code of Business Conduct and Ethics in place which sets forth the legal and ethical standards of conduct for employees and directors. The Code of Business Conduct and Ethics is provided to every new employee and the Company annually requires confirmation from all employees and directors of their adherence.

5 Statement of the Board of Directors

The Board of Directors is responsible for the preparation of the Annual Accounts and the Annual Report of uniQure N.V. for the year ended December 31, 2021, in accordance with applicable Dutch law and International Financial Reporting Standards ("IFRS") as adopted by the European Union, ("EU").

RESPONSIBILITY STATEMENT PURSUANT TO SECTION 5:25C PARAGRAPH 2(C) OF THE DUTCH FINANCIAL MARKETS SUPERVISION ACT ('*Wet op het financieel toezicht'*)

Each of the Directors of the Board confirms that to the best of his or her knowledge:

- the uniQure N.V. 2021 Annual Accounts give a true and fair view of the assets, liabilities, financial position and profit or loss of uniQure N.V. and the entities included in the consolidation;
- the uniQure N.V. 2021 Annual Report gives a true and fair view of the state of affairs on December 31, 2021, the course of business during the financial year of uniQure N.V. and of the entities affiliated to it whose data are included in the 2021 Annual Accounts and that the 2021 Annual Report describes the substantial risks with which uniQure N.V. is confronted

Amsterdam, April 29, 2022

Executive Director

/s/ Matthew Kapusta
Matthew Kapusta, Chief Executive Officer

Non-Executive Directors

/s/ David Meek
David Meek, Chairman

/s/ Madhavan Balachandran
Madhavan Balachandran, Member

/s/ Robert Gut
Robert Gut, Member

/s/ Rachelle Jacques
Rachelle Jacques, Member

/s/ Jack Kaye
Jack Kaye, Member

/s/ Leonard Post
Leonard Post, Member

/s/ Paula Soteropoulos
Paula Soteropoulos, Member

/s/ Jeremy P. Springhorn
Jeremy P. Springhorn, Member

B Consolidated Financial Statements of uniQure N.V. for the year ended December 31, 2021

uniQure N.V.

Consolidated Statements of Financial Position

	Note	December 31, 2021	December 31, 2020
		$ in thousands	
Current assets			
Cash and cash equivalents	4	556,256	244,932
Accounts receivable and contract asset	5	58,768	6,618
Prepaid expenses	5	10,540	4,337
Other current assets and receivables	5	2,675	3,024
Total current assets		**628,239**	**258,911**
Non-current assets			
Property, plant and equipment, net	6	43,505	32,328
Right-of-use assets	17	23,820	25,090
Intangible assets other than goodwill, net	7	62,833	6,562
Goodwill	7	27,633	542
Deferred tax asset	15	16,230	16,806
Other non-current assets	4	5,897	2,748
Total non-current assets		**179,918**	**84,076**
Total assets		**808,157**	**342,987**
Current liabilities			
Accounts payable		2,502	3,772
Accrued expenses and other current liabilities	8	28,487	18,038
Lease liabilities - current	17	6,254	5,995
Total current liabilities		**37,243**	**27,805**
Non-current liabilities			
Borrowings	9	97,787	35,259
Lease liabilities - non-current	17	30,072	31,486
Contingent consideration	3	29,542	—
Deferred tax liability, net	15	12,913	—
Other non-current liabilities	8	1,431	491
Total non-current liabilities		**171,745**	**67,236**
Total liabilities		**208,988**	**95,041**
Shareholders' equity			
Share capital		2,802	2,711
Share premium		950,778	915,459
Other reserves		103,603	113,002
Accumulated deficit		(458,014)	(783,226)
Total shareholders' equity	10	**599,169**	**247,946**
Total liabilities and shareholders' equity		**808,157**	**342,987**

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

uniQure N.V.

Consolidated Statements of Profit or Loss and Other Comprehensive Income or Loss

	Note	Years ended December 31, 2021	2020
		$ in thousands, except for per share data (in $)	
License revenues	5	517,400	37,319
Collaboration revenues	5	6,602	195
Total revenues		**524,002**	**37,514**
Cost of contract revenues	5	(27,807)	—
Gross profit		**496,195**	**37,514**
Operating expenses:			
Research and development expenses	12	(144,594)	(118,519)
Selling, general and administrative expenses	12	(55,983)	(43,954)
Total operating expenses		**(200,577)**	**(162,473)**
Other income	2.19	15,155	3,342
Other expense	2.19	(876)	(1,302)
Profit / (loss) from operations		**309,897**	**(122,919)**
Finance income	14	29,821	4,033
Finance expense	14	(11,485)	(21,401)
Finance income / (expense), net		**18,336**	**(17,368)**
Profit / (loss) before income tax (expense) / benefit		**328,233**	**(140,287)**
Income tax (expense) / benefit	15	(3,021)	16,806
Net profit / (loss)		**325,212**	**(123,481)**
Total other comprehensive (loss) / income, net of income tax:			
Items that may be reclassified subsequently to profit or loss			
Foreign currency translation adjustments		(38,182)	16,857
Total comprehensive profit / (loss)		**287,030**	**(106,624)**
Earnings / (loss) per share			
Basic earnings / (loss) per ordinary share	16	7.07	(2.78)
Diluted earnings / (loss) per ordinary share	16	6.89	(2.78)

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

uniQure N.V.

Consolidated Statements of Changes in Equity

	Note	Share Capital No. of shares	Share Capital Amount	Share Premium	Other Reserves	Accumulated deficit	Total equity
		$ in thousands (except number of shares)					
Balance at January 1, 2020		**43,711,954**	**2,651**	**908,075**	**71,262**	**(659,745)**	**322,243**
Net loss		—	—	—	—	(123,481)	(123,481)
Other comprehensive income		—	—	—	16,857	—	16,857
Total comprehensive loss		—	—	—	16,857	(123,481)	(106,624)
Exercises of share options	10	498,678	29	7,169	—	—	7,198
Restricted and performance share units distributed during the period	10	560,986	31	(31)	—	—	—
Share-based compensation expense	10	—	—	—	24,883	—	24,883
Issuance of ordinary shares relating to employee stock purchase plan	10	6,181	—	246	—	—	246
Balance at December 31, 2020		**44,777,799**	**2,711**	**915,459**	**113,002**	**(783,226)**	**247,946**
Net income		—	—	—	—	325,212	325,212
Other comprehensive loss		—	—	—	(38,182)	—	(38,182)
Total comprehensive income		—	—	—	(38,182)	325,212	287,030
Issuance of ordinary shares	10	921,730	55	29,509	—	—	29,564
Income tax benefit of past share issuance cost	10	—	—	3,047	—	—	3,047
Exercises of share options	10	241,496	15	2,638	—	—	2,653
Restricted and performance share units distributed during the period	10	352,886	21	(21)	—	—	—
Share-based compensation expense	10	—	—	—	28,783	—	28,783
Issuance of ordinary shares relating to employee stock purchase plan	10	4,724	—	146	—	—	146
Balance at December 31, 2021		**46,298,635**	**2,802**	**950,778**	**103,603**	**(458,014)**	**599,169**

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

uniQure N.V.

Consolidated Statements of Cash Flows

	Note	Years ended December 31, 2021	2020
		$ in thousands	
Cash flows from operating activities			
Net income / (loss)		325,212	(123,481)
Adjustments to reconcile net income / (loss) to net cash used in operating activities:			
Depreciation, amortization and loss on disposals of intangible assets and property, plant and equipment, and right-of-use assets	6, 7, 17	13,241	10,256
Share-based compensation expense	11	28,783	24,883
Interest expense on leases	17	3,982	3,898
Changes in fair value of derivative financial instruments and contingent consideration	4	6,683	(3,096)
Unrealized foreign exchange (gains) / losses		(32,496)	15,170
Deferred tax expense / (income)	15	3,014	(16,806)
Deferred revenue	5	—	(33,642)
Other non-cash items		(2,800)	—
Changes in operating assets and liabilities:			
Contract asset related to CSL Behring milestone payments	5	(55,000)	—
Accounts receivable, prepaid expenses and other current assets	5	(4,121)	(7,968)
Accounts payable	8	(727)	(2,701)
Accrued expenses and other liabilities	8	14,017	7,866
Cash generated from / (used in) operating activities		299,788	(125,621)
Interest paid	14	(10,519)	(8,029)
Interest received	14	162	937
Net cash generated from / (used in) operating activities		289,431	(132,713)
Cash flows from investing activities			
Acquisition of Corlieve, net of cash acquired	3	(49,949)	—
Receipt of bank deposit		303	249
Purchase of intangible assets	7	—	(2,213)
Purchase of property, plant and equipment	6	(17,438)	(7,271)
Net cash used in investing activities		(67,084)	(9,235)
Cash flows from financing activities			
Proceeds from loan increment	18	65,000	—
Transaction costs related to loan amendments		(933)	—
Proceeds from issuance of ordinary shares related to employee stock option and purchase plans	10	2,798	7,444
Proceeds from public offering of ordinary shares	10	30,899	—
Share issuance costs from issuance of ordinary shares	10	(1,334)	—
Payments for principal portion of lease liability	17	(2,182)	(2,115)
Repayments of debts acquired through acquisition of Corlieve	3	(1,572)	—
Net cash generated from financing activities		92,676	5,329
Currency effect cash and cash equivalents		(3,699)	3,758
Net increase / (decrease) in cash and cash equivalents		311,324	(132,861)
Cash and cash equivalents at the beginning of the year		244,932	377,793
Cash and cash equivalents at the end of the year		**556,256**	**244,932**

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

Notes to the Consolidated Financial Statements

1. General information

uniQure N.V.

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

The Company is registered in the trade register of the Dutch Chamber of Commerce (Kamer van Koophandel) 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 Nasdaq and trade under the symbol "QURE".

This Annual Report and the Consolidated Financial Statements (this "Annual Report") were authorized for issue by the board of directors on April 29, 2022 and will be filed at the trade register of the Chamber of Commerce in Amsterdam, the Netherlands within eight days after adoption by the 2022 general meeting of shareholders.

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 is advancing a focused pipeline of innovative gene therapies, including product candidates for the treatment of Huntington's disease, Fabry disease and temporal focal epilepsy. The Company believes its validated technology platform and manufacturing capabilities provide it its distinct competitive advantages, including the potential to reduce development risk, cost, and time to market. The Company produces its Adeno-associated virus ("AAV") -based gene therapies in its own facilities with a proprietary, commercial-scale, current good manufacturing practices ("cGMP")-compliant, manufacturing process. The Company believe its Lexington, Massachusetts-based facility is one of the world's most versatile gene therapy manufacturing facilities.

Organizational structure of uniQure

uniQure N.V. is the ultimate parent of the following entities:

Entity name
uniQure biopharma B.V.
uniQure IP B.V.
uniQure Inc.
Corlieve Therapeutics SAS
Corlieve Therapeutics AG

2. Summary of Significant 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.

2.1 Basis of Preparation

The Company prepared its consolidated financial statements in compliance with International Financial Reporting Standards ("IFRS") as adopted by the European Union and effective as of December 31, 2021.

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

The functional currency of the Company and each of its entities (with the exception of uniQure Inc.) 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.

The Company files consolidated financial statements with the SEC in accordance with U.S. generally accepted accounting principles, presented in U.S. dollars ($). To consistently report financial information the Company is also presenting its consolidated financial statements in accordance with IFRS in U.S. dollars ($), except where otherwise indicated. Transactions denominated in currencies other than U.S. dollars are presented in the transaction currency with the U.S. dollar amount included in parenthesis, converted at the foreign exchange rate as of the transaction date.

Foreign currency transactions are translated into 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 remeasurement at exchange rates prevailing at reporting date of monetary assets and liabilities denominated in foreign currencies 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 reporting 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 into the presentation currency U.S. dollar at the exchange rates prevailing at the reporting date; items of income and expense are translated at monthly average exchange rates. Issued capital and share premium are translated at historic rates with differences to the reporting date rate, recorded as translation adjustments in other reserves. The exchange differences arising on translation for consolidation are recognized in other comprehensive income. On disposal of a foreign operation, the component of other comprehensive income relating to the foreign operation is recognized in profit or loss.

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, 2021, and the Company's budgeted cash flows for the twelve months following the issuance date.

The financial information of the Company is included in the consolidated financial statements. For this reason, pursuant to Section 2:402 of the Dutch Civil Code, the Statement of Profit or Loss in the separate financial statements exclusively states the share of the result of participating interests and other income and expenses. For an appropriate interpretation of these statutory financial statements, the consolidated financial statements of the Company should be read in conjunction with the separate financial statements, as included in section C "Company-only Financial Statements".

2.2 Use of judgements and estimates

In preparing these consolidated financial statements, management made judgements, estimates and assumptions that affect the application of the Company's accounting policies and the reported amounts of assets, 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. Actual results may differ from these estimates.

Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to estimates are recognized prospectively.

Estimates and assumptions are primarily made in relation to the treatment of the share and purchase agreement ("SPA") entered into on June 21, 2021 to acquire all of the outstanding ordinary shares of Corlieve Therapeutics SAS ("Corlieve"), a privately held French gene therapy company ("Corlieve Transaction"), the treatment of the commercialization and license agreement entered into ("CSL Behring Agreement") between the Company and CSL Behring LLC ("CSL Behring"), the assessment of a valuation allowance on the Company's deferred tax assets in the Netherlands and the U.S., and the December 1, 2020, amendment ("amended BMS CLA") of the 2015 collaboration and license agreement ("BMS CLA") between the Company and Bristol-Myers Squibb ("BMS"). 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 New standards, amendments and interpretations

New and amended standards adopted by the Company in 2021

There were no new IFRS's adopted by the Company in 2021.

New and amended standards not yet adopted by the Company

There are no other IFRSs or IFRIC interpretations that are not yet effective or that could have been early adopted that would have a material impact on the Company in the current or future reporting periods and on foreseeable future transactions.

2.4 Consolidation

The consolidated financial statements comprise the financial statements of the Company and its subsidiaries. Subsidiaries are entities controlled by the Company that the Company is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. The financial statements of subsidiaries are included in the consolidated financial statements from the date control commences until the date control ceases.

Intra-group transactions, balances, income and expenses on transactions between uniQure entities are eliminated in consolidation. Profits and losses resulting from intra-group 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.

2.5 Current versus non-current classification

The Company classifies assets and liabilities as current when they are expected to be realized or settled within twelve months after the end of the reporting period (except for liabilities for which the Company does not have an unconditional right to defer settlement of that liability for at least twelve months after the end of the reporting period), when they are realized or settled within the Company's normal operating cycle or when they are primarily held for trading purposes. Cash and cash equivalents are presented as current unless it is restricted from being exchanged or used to settle a liability for at least twelve months after the reporting period.

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

2.6 Fair value measurement

The Company measures financial instruments such as derivatives and non-financial assets at fair value at each reporting date using valuation techniques that are appropriate in the circumstances and for which sufficient data are available as disclosed in Note 4.3.

2.7 Segment reporting

The Company's chief operating decision-maker regularly reviews and determines whether a particular component of uniQure's activities constitutes a separate operating segment by identifying and reviewing the allocation of resources to that component of uniQure's activities and/or assessing the performance of that particular component of uniQure's activities. The leadership team is identified as the chief operating decision-maker and reviews the consolidated operating results regularly to make decisions about the resources and to assess overall performance. The leadership team regularly reviews total cash operating expenditures by departmental area. The leadership team has determined that the activities of uniQure are one segment, which comprises the discovery, development and commercialization of innovative gene therapies, and the segmental analysis is the same as the analysis for uniQure as a whole.

2.8 Notes to the Consolidated Statement of Cash Flows

The consolidated statements of cash flows have been prepared using the indirect method. Cash and cash equivalents include bank balances, demand deposits and other short-term highly liquid investments (with maturities of less than three months at 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 are translated at the average exchange rates for the reporting period. Exchange differences, if any, affecting cash and cash equivalents are presented separately in the consolidated statements of cash flows.

2.9 Business Combination

On July 30, 2021 ("Acquisition Date"), the Company acquired Corlieve. The Company evaluated the Corlieve transaction as to whether or not the transaction should be accounted for as a business combination or asset acquisition. Refer to Note 3 "*Corlieve transaction*" for further detail.

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 a reporting unit below its carrying amount. As of December 31, 2021, the Company has not recognized any impairment charges related to goodwill.

Refer to Note 3 "*Corlieve transaction*" for further detail.

b. Acquired research and development

The Company identified various licenses that combined with the results of the research and development activities conducted in relation to Corlieve's gene therapy program for TLE ("AMT-260") since incorporation of Corlieve in 2019 constitute an In-process research and development intangible asset ("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 generally occurs when regulatory approval to market a product 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.

In case of abandonment, the IPR&D Intangible Asset will be written-off. In accordance with IAS 38, Intangibles Assets, 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. As of December 31, 2021, the Company has not recognized any impairment charges related to the IPR&D Intangible Asset.

Refer to Note 3 "*Corlieve transaction*" for further detail.

c. Contingent consideration

Each reporting period, the Company revalues the contingent consideration obligations associated with the Corlieve Transaction to their fair value and records changes in the fair value within research and development expenses. Changes in contingent consideration result from changes in assumptions regarding the probabilities of achieving the relevant milestones, or probability of success ("POS"), the estimated timing of achieving such milestones, and the interest rate to discount the payments.

Contingent consideration related to the Corlieve Transaction is remeasured at fair value at each reporting date and subsequent changes in the fair value of the contingent consideration are recognized in profit or loss.

Refer to Note 3 "*Corlieve transaction*" for further detail.

2.10 Intangible Assets

(a) Licenses

Acquired licenses have a finite useful life and are carried at cost less accumulated amortization and impairment losses. Amortization is calculated using the straight-line method to allocate the cost of licenses over their estimated useful lives (generally 20 years unless a license expires prior to that date). Amortization is included in research and development expenses.

(b) Research and development

Research and development expenditures are expensed as incurred. Development expenses are capitalized prospectively following regulatory approval for commercial production of a target.

(c) Goodwill

In addition to the goodwill recognized as part of the Corlieve Transaction, there is also goodwill originating from the acquisition of InoCard in July 2014, which represents the excess of the consideration transferred over the fair value of the identifiable net assets acquired. The carrying amount of goodwill besides goodwill associated to the Corlieve Transaction for the year ended December 31, 2021, was $0.5 million (2020: $0.5 million).

2.11 Property, plant and equipment

Property, plant and equipment comprise 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.

Subsequent costs are included in the asset's carrying amount or recognized as a separate asset, as appropriate, when it is probable that future economic benefits associated with the item will flow to uniQure and the cost of the item can be measured reliably. All other repairs and maintenance costs 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 Profit or Loss and Other Comprehensive Income or 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

The assets' residual values and useful lives are reviewed, and adjusted if appropriate, at each reporting date. An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is greater than its estimated recoverable amount.

2.12 Leases

At inception of a contract, the Company assesses whether a contract is, or contains, a lease. A contract is, or contains, a lease if the contract conveys the right to control the use of an identified assets for a period of time in exchange for consideration. At commencement, the Company allocates the consideration in the contract to each lease component on the basis of its relative stand-alone prices. The Company recognizes a right-of-use asset and a lease liability at the lease commencement date.

Lease liabilities are initially measured at the present value of minimum lease payments and a right to use asset is recorded for the same amount. Lease liabilities are measured at the present value of the lease payments that are not paid at that date including:

- fixed payments less any lease incentives receivable; and

- variable lease payments that are based on an index or a rate.

The lease payments are discounted using the interest rate implicit in the lease. If that rate cannot be determined, the Company's incremental borrowing rate at the lease commencement date is used, which is based on an assessment of the interest rate the Company would have to pay to borrow funds, including the considerations of factors such as the nature of the asset and location, collateral, market terms and conditions, as applicable. After the commencement date, the amount of lease liabilities is increased to reflect the accretion of interest (presented as finance expense in the Consolidated Statements of Profit or Loss and Other Comprehensive Income or Loss) and reduced for the lease payments made.

The interest element of the finance expense is determined so as to produce a constant periodic rate of interest on the remaining balance of the liability for each period during the lease term. The interest element is presented within cash flows from operating activities and the repayment of the liability is presented within cash flows from financing activities. In addition, the carrying amount of lease liabilities is remeasured if there is a modification, a change in the lease term, a change in the in-substance fixed lease payments, or a change in future lease payments arising from a change in an index. When the lease liability is remeasured, a corresponding adjustment is made to the carrying amount of the right-of-use asset.

Right-of-use assets are measured at cost comprising the following:

- the amount of the initial measurement of lease liability;

- any lease payment made at or before the commencement date less any lease incentives received; and

- any initial direct costs.

The right-of-use assets are subsequently accounted for using principles for property, plant and equipment. Right-of-use assets are depreciated using the straight-line method from the commencement date to the end of the lease term. Depreciation expense related to right-of-use assets are presented within operating expenses.

Payments associated with short-term leases and leases of low value assets are recognized on a straight-line basis as an expense in the Consolidated Statements of Profit or Loss and Other Comprehensive Income or Loss. Short-term leases are leases with a term of 12 months or less. The Company determines the lease term as the non-cancellable term of the lease, together with any periods covered by an option to the extend the lease if it is reasonably certain to be exercised, or any periods covered by an option to terminate the lease, if it is reasonably certain not to be exercised. The Company applies judgement in evaluating whether it is reasonably certain to exercise an option to renew.

2.13 Impairment

Non-financial assets

Goodwill impairment reviews are undertaken annually or more frequently if events or changes in circumstances indicate a potential impairment.

Non-financial assets, other than goodwill, that have been previously impaired are reviewed for possible reversal of the impairment at each subsequent reporting date.

2.14 Financial instruments, equity

Initial recognition and measurement

Financial assets and financial liabilities are initially recognized when the Company becomes a party to the contractual provisions of the instrument.

A financial asset (unless it is accounts receivable without a significant financing component) or a financial liability is initially measured at fair value plus, for an item not at fair value through profit and loss, transaction costs that are directly attributable to its acquisition or issue.

Financial assets

The Company subsequently recognizes an allowance for expected lifetime credit losses, which is presented within “Other expense” in the Consolidated Statements of Profit or Loss and Other Comprehensive Income for its accounts receivables unless material. The Company applies a simplified approach to measurement of expected lifetime credit losses based on the probability of default of its counterparties. The probability of default is derived from applicable external credit ratings. Loss allowances for financial assets measured at amortized cost are deducted from the gross carrying amount of the assets.

All other financial assets are recognized when the Company becomes a party to the contractual provisions of the instrument.

The Company derecognizes a financial asset when the contractual rights to the cash flows from the financial asset expire.

Borrowings

The Company classifies and measures borrowings initially at fair value and subsequently measures borrowings at amortized cost using the effective interest method. The Company recognizes interest expense and foreign exchange gains and losses in the Consolidated Statements of Profit or Loss and Other Comprehensive Income. The Company derecognizes borrowings when its contractual obligations are discharged or cancelled, expire, or its terms are modified and the cash flows of the modified liability are substantially different. The Company also recognizes any gain or loss on derecognition is in the Consolidated Statements of Profit or Loss and Other Comprehensive Income. If the cash flows of the borrowings do not substantially differ before and after modification, then the Company continues to apply the originally effective interest rate and recognizes the difference in net present value as at modification date in the Consolidated Statements of Profit or Loss and Other Comprehensive Income. Any fees incurred are capitalized.

Other financial liabilities

The Company recognizes other financial liabilities on the trade date when the entity becomes a party to the contractual provisions of the instrument and derecognizes the financial liability when its contractual obligations are discharged or cancelled, or expire. Other financial liabilities are initially measured at fair value less any directly attributable transaction costs. Following the initial recognition, these liabilities are measured at amortized cost using the effective interest method.

Derivative financial instruments

Derivatives are initially measured at fair value and subsequently at fair value through profit and loss. The Company does not use derivatives to hedge any risks and does not apply hedge accounting.

Equity

An equity instrument is defined as any contract that evidences a residual interest in the assets of an entity after deducting all of its liabilities. An instrument is an equity instrument only if the issuer has an unconditional right to avoid settlement in cash or another financial asset.

Incremental costs directly attributable to the issue of new ordinary shares or options are shown in equity as a deduction, net of tax, from the proceeds.

Ordinary shares are classified as equity.

Dividend distributions to the Company's shareholders are recognized as a liability in uniQure's Consolidated Statement of Financial Position in the period in which the dividends are approved by its shareholders. To date, uniQure has not paid dividends.

2.15 Income taxes

Income tax comprises current and deferred tax. Income tax is recognized in profit and loss. Tax consequences related to items recognized in other comprehensive income are recognized in other comprehensive income as well.

Current tax comprises the expected tax payable or receivable on the taxable income or loss for the year and any adjustment to the tax payable or receivable in respect of previous years.

Deferred tax is recognized in respect of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. Deferred tax is not recognized for temporary differences on the initial recognition of assets or liabilities in a transaction that is not a business combination and that affects neither accounting nor taxable profit or loss, temporary differences related to investments in subsidiaries to the extent that the Company is able to control the timing of the reversal of the temporary differences and it is probable that they will not reverse in the foreseeable future and taxable temporary differences arising on the initial recognition of goodwill.

Deferred tax assets are recognized for unused tax losses, unused tax credits and deductible temporary differences to the extent that it is probable that future taxable profits will be available against which they can be used at the individual tax filing entity level. Unrecognized deferred tax assets are reassessed at each reporting date and recognized to the extent that it has become probable that future taxable profits will be available against which they can be used at the individual tax filing entity level.

The Company's management periodically evaluates positions taken in tax returns with respect to situations in which applicable tax regulation is subject to interpretation. It establishes provisions where appropriate.

Income tax is measured using tax rates enacted or substantively enacted at the reporting date. Deferred tax is measured at the tax rates that are expected to be applied to temporary differences when they reverse.

Income tax assets and liabilities are offset when there is a legally enforceable right to offset current tax assets against current tax liabilities and when the deferred income taxes assets and liabilities relate to income taxes levied by the same taxation authority on either the taxable entity or different taxable entities where there is an intention to settle the balances on a net basis.

2.16 Employee benefits

uniQure operates a defined contribution pension plan for all employees at its Amsterdam facility in the Netherlands, which is funded by uniQure through payments to an insurance company. uniQure 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 employee service in the current and prior periods. The contributions are recognized as employee benefit expense when they are due. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in the future payments is available.

In 2016, the Company adopted 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.

2.17 Share-based compensation

Employee share-based compensation plans

The fair value of services received in exchange for equity instruments granted is recognized as an expense, with a corresponding adjustment to Other reserves in equity. The total amount to be expensed over the vesting period is determined by reference to the fair value of the instruments granted and based on the share price and vesting conditions. For share-based payments that do not vest until the employees have completed a specified period of service, uniQure recognizes the services received as the employees render services during the service period. For the allocation of the expenses to be recognized, the Company treats each installment of a graded vesting award as a separate share grant.

For PSUs which depend on a performance condition, the Company recognizes an amount for the services received during the vesting period based on the best available estimate of the number of equity instruments expected to vest. The Company will revise that estimate if subsequent information indicates that the number of equity instruments expected to vest differs from previous estimates.

Options

The fair value of options granted is determined at the grant date.

Restricted share units ("RSUs")

The fair value of RSUs granted is determined at the grant date by reference to the share-price.

Performance share units ("PSUs")

Awards of PSUs are subject to the achievement of specified performance objectives. The fair value of PSUs granted in prior years was determined at the date performance was determined and the discretion on the final number of awards to be granted was removed. The fair value of PSUs granted is determined at the grant date by reference to the share-price.

2.18 Provisions

Provisions are recognized when the Company has a present legal or constructive obligation as a result of past events, it is probable that an outflow of resources will be required to settle the obligation, and the amount can be reliably estimated.

Provisions are measured at the present value of amounts expected to be required to settle the obligation using a pre-tax rate that reflects current market assessments of the time value of money and the risks specific to the obligation. The increase in the provision due to the passage of time is recognized as interest expense.

2.19 Revenue recognition

The Company primarily generates revenue from its commercialization and license agreement with CSL Behring and its collaboration, research, and license agreements with BMS for the development and commercialization of product candidates.

CSL Behring collaboration

On June 24, 2021 ("Signing Date"), the Company entered into a commercialization and license agreement pursuant to which CSL Behring received exclusive global rights to etranacogene dezaparvovec ("Product"). The Company concluded that CSL Behring is a customer in accordance with IFRS 15 and identified two material performance obligations related to the CSL Behring Agreement:

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

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

These performance obligations are considered distinct from one another, as CSL Behring can benefit from the identified service either on its own or together with other resources that are readily available to CSL Behring, and as the performance obligations are separately identifiable from other performance obligations in the CSL Behring Agreement.

Refer to Note 5 "*Collaboration arrangements and concentration of credit risk*" for further detail.

Bristol-Myers Squib collaboration

The Company primarily generates revenue from its collaboration and license agreement with its collaboration partner BMS. The Company initially entered into this agreement in 2015 and amended it in 2020.

The Company evaluated the initial BMS CLA and determined that its performance obligations were as follows:

- Providing pre-clinical research activities ("Collaboration Revenue");
- Providing clinical and commercial manufacturing services for products ("Manufacturing Revenue"); and
- Providing access to its technology and know-how in the field of gene therapy as well as actively contributing to the target selection, the collaboration as a whole, the development during the target selection, the pre-clinical and the clinical phase through participating in joint steering committee and other governing bodies ("License Revenue").

As further discussed in Note 5, "*Collaboration arrangements and concentration of credit risk*", as a result of the December 2020 amended BMS CLA, the Company's performance obligation related to License Revenues was materially completed as of the date of the amendment effective date of December 1, 2020. The Company may still be required to provide pre-clinical research activities or clinical and commercial manufacturing services when BMS exercises its options for those services.

License Revenue

Until the December 2020 amendment of the BMS CLA the Company recognized License Revenue over the expected performance period based on its measure of progress towards the completion of certain activities related to its services. Following the December 2020 amendment of the BMS CLA the Company's performance was materially completed and it materially satisfied its performance obligation (see Note 5, *"Collaboration arrangements and concentration of credit risk"*, for a detailed discussion).

Collaboration and Manufacturing Revenue

The Company recognizes Collaboration Revenues associated to optional work orders it receives from BMS to provide analytical development and process development activities that are reimbursable by BMS in accordance with the BMS CLA as well as the amended BMS CLA.

BMS and the Company entered into a Master Clinical Supply Agreement in April 2017 for the Company to supply gene therapy products during the clinical phase as well as into a binding term sheet to supply gene therapy products during the commercial phase to BMS. In December 2020, BMS and the Company also entered into a Research Supply Agreement. Revenues from product sales will be recognized when earned. The Company will provide these services as it receives optional work orders from BMS in relation to such services.

2.20 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.

The Company's other income also consists of employee retention credits received under the U.S. Coronavirus Aid, Relief, and Economic Security Act, income related to a settlement agreement that the Company and VectorY B.V. entered into in April 2021, income derived from a net modification gain resulting from the amendments to the Company's loan agreements under the 2021 Amended Facility and 2021 Restated Facility, as well as income from subleasing part of the Company's Amsterdam facility. Other expense consists of expenses incurred in relation to the subleasing income.

3. Corlieve Transaction

On Acquisition Date, the Company acquired Corlieve. Following Corlieve's formation in November 2019, Corlieve obtained exclusive licenses to certain patents from two French research institutions that continue to collaborate with the Company. Corlieve also obtained an exclusive license from Regenxbio Inc. ("Regenxbio") to use AAV9 to deliver any sequence that affects the expression of the Glutamate inotropic receptor kainate type subunit 2 ("GRIK 2") gene sequence in humans. Corlieve and Regenxbio simultaneously entered into a collaboration plan related to agreed joint preclinical research and development activities. At the Acquisition Date, Corlieve and its Swiss subsidiary, Corlieve Therapeutics AG, employed seven employees. Corlieve's result for the full year 2021 was a $7.6 million loss. The result included in the Company's consolidated results for the year ended December 31, 2021 is a $4.4 million loss.

The Company evaluated the Corlieve transaction as to whether the acquired set of activities and assets is a business (or concentration test). The Company has the option of applying or not applying the concentration test. The concentration test would determine if substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. Based on the fair values of the gross assets acquired, the Company determined the concentration test was not met. The Company further analyzed whether or not the acquired inputs and processes that have the ability to create outputs would meet the definition of a business. Significant judgment was required in the application of this assessment to determine whether an acquired set of activities and assets is not a business.

Identifiable assets and liabilities of Corlieve, including identifiable intangible assets, were recorded at their fair values as of the Acquisition Date, when the Company obtained control. The excess of the fair value of the consideration transferred over the fair value of the net assets acquired was recorded as goodwill.

Consideration

On the Acquisition Date, the Company acquired 97.7% of the outstanding ordinary shares of Corlieve in return for EUR 44.9 million ($53.3 million as of the Acquisition Date). As contractually required the Company acquired the remaining outstanding ordinary shares on February 9, 2022 following the expiration of a minimum holding period ("Mandatorily Redeemable Shares"). The Company recorded a liability related to the obligation to acquire these Mandatorily Redeemable Shares for an amount of EUR 0.7 million ($0.9 million) as of the Acquisition Date. The Company financed the Corlieve Transaction from its cash on hand.

In addition to the payments to acquire 100% of the outstanding ordinary shares, Corlieve's former shareholders are eligible to receive up to EUR 35.8 million ($40.6 million as of December 31, 2021) upon achievement of certain development milestones through Phase I/II and EUR 143.1 million ($162.3 million as of December 31, 2021) upon achievement of certain milestones associated with Phase III development and obtaining approval to commercialize Corlieve's target candidate for the treatment of temporal lobe epilepsy ("AMT-260" or "TLE") in the United States of America and the European Union. The Company may elect to pay up to 25% of such milestone payments through the issuance of the Company's ordinary shares.

As of the Acquisition Date, the Company recorded EUR 20.2 million ($24.0 million) as a contingent liability (presented as "Non-current liability") for the fair value of these milestone payments. The fair value of the contingent liability as of December 31, 2021 amounted to EUR 26.0 million ($29.5 million). The fair market value of the contingent consideration was determined using unobservable initial inputs with respect to (i) the probability of achieving the relevant milestones, or POS, (ii) the estimated timing of achieving such milestones, and (iii) the interest rate used to discount the payments. The Company determined the fair market value of the contingent consideration by calculating the probability-adjusted payments based on each milestone's probability of achievement. The probability-adjusted payments were then discounted to present value using a discount rate representing the Company's credit risk. This discount rate was determined using the effective interest rate of the Company's existing debt facility adjusted for difference in maturity dates based on CCC yield curve. Changes in fair value of the contingent liability are recognized within research and development expenses in the consolidated statements of operations.

The following table summarizes the acquisition-date fair value of each major class of consideration transferred:

	Allocation € in thousands
Consideration	
Cash	€ 44,876
Contingent consideration	20,165
Liability related to Mandatorily Redeemable Shares (see below)	719
Fair value of total consideration	**€ 65,760**

Identifiable assets acquired and liabilities assumed

The following table summarizes the recognized amounts of assets acquired and liabilities assumed at the acquisition date:

	Allocation € in thousands
Recognized amounts of identifiable assets acquired and liabilities assumed	
Current assets including €2.8 million of cash	€ 2,902
Property, plant and equipment	34
Identifiable intangible asset	53,564
Current liabilities	(1,132)
Deferred tax liability, net	(11,915)
Debt	(1,352)
Other non-current liabilities	(260)
Total identifiable net assets acquired	**41,841**

Identified intangible assets

The Company identified various licenses that combined with the results of the research and development activities conducted in relation to AMT-260 since incorporation of Corlieve in 2019 constitute an IPR&D Intangible Asset.

The Company determined the fair value of the IPR&D Intangible Asset using a present value model based on expected cash flows. Estimating the amounts and timing of cash flows required to complete the development of AMT-260 as well as net sales, cost of goods sold, and sales and marketing costs involved considerable judgment and uncertainty. The expected cash flows are materially impacted by the probability of successfully completing the various stages of development (i.e., dosing of first patient in clinical trial, advancing into late-stage clinical development and obtaining approval to commercialize a product candidate) as well as the weighted average cost of capital of 10.4% used to discount the expected cash flows. Based on all such information and its judgment the Company estimated the fair value of the IPR&D Intangible Asset at EUR 53.6 million ($63.6 million) as of the Acquisition Date.

Deferred tax liability, net

Corlieve's deferred tax assets at the time of acquisition amounted to EUR 1.5 million ($1.7 million). Recognition of the IPR&D Intangible Asset gave rise to a deferred tax liability of EUR 13.4 million ($15.9 million) at the enacted French corporate income tax rate of 25.0%. The Company consequently recorded a net deferred tax liability of EUR 11.9 million ($14.2 million as of the Acquisition Date). Changes in the net deferred tax liability after the Acquisition Date will be recorded in income tax expense in the consolidated statements of operations.

Goodwill

Goodwill arising from the acquisition has been determined as follows:

	Allocation	
	€	
	$ in thousands	
Consideration transferred	€	65,760
Fair value of identifiable net assets		41,841
Goodwill	**€**	**23,919**

Goodwill represents the excess of total consideration over the estimated fair value of net assets acquired. The Company recorded EUR 23.9 million ($28.4 million) of goodwill in the consolidated balance sheet as of the Acquisition Date. The goodwill primarily relates to the recognition of a deferred tax liability recognized in association with the IPR&D Intangible asset of EUR 13.4 million ($15.9 million as of Acquisition Date) as well as the fair market value of the experienced workforce and potential synergies from the acquisition. The Company allocated the goodwill to its reporting unit. The Company does not expect any portion of this goodwill to be deductible for income tax purposes.

Debt

As of the Acquisition Date, Corlieve held a loan with outstanding amount equal to EUR 1.0 million ($1.2 million), which loan was repaid in its entirety in September 2021. As of the Acquisition Date, Corlieve also held a loan with outstanding amount equal to EUR 0.4 million ($0.4 million), which was repaid in its entirety in December 2021.

Other

As of the Acquisition Date, the Company also acquired other assets and assumed other liabilities, which included among others, EUR 2.9 million ($3.4 million) of current assets, which consisted of EUR 2.8 million ($3.3 million) of cash, and EUR 1.1 million ($1.3 million) of current liabilities.

4. Financial Risk Management

4.1 Financial Risk Factors

uniQure is exposed to a variety of financial risks, including credit risk, market risk (e.g., currency risk, interest rate risk and other price risk) and liquidity risk. The Company's overall management program focuses on preservation of capital and the unpredictability of financial markets and has sought to minimize potential adverse effects on its financial performance and position.

uniQure's risk management policies are established to identify and analyze the risks faced by the Company and are reviewed regularly to reflect changes in market conditions and its activities. Financial risk management is carried out by the finance department, which identifies and evaluates financial risks and hedges these risks if deemed appropriate.

uniQure does not engage in speculative transactions, nor does it issue or hold financial instruments for trading purposes.

a) 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. The Company currently has no wholesale debtors other than BMS and CSL Behring.

The Company deposited funds as security to landlords related to its facility in Lexington, Massachusetts and its facility in Amsterdam. The Company also deposited funds to the provider of our U.S. corporate credit cards. The deposits are neither impaired nor past due.

The Company's 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. Cash and cash equivalents and restricted cash were placed at the following banks and accounts receivable were receivable from the following trade customers:

	As of December 31,			
	2021		2020	
	Amount	Credit rating	Amount	Credit rating
	$ in thousands		$ in thousands	
Cash, cash equivalents and restricted cash				
Bank of America	103,546	Aa2	73,922	Aa2
Rabobank	454,101	Aa2	173,758	Aa3
BNP Paribas	1,211	Aa3	—	—
Credit Suisse	495	Baa1	—	—
Total	**559,353**		**247,680**	
Accounts receivable and contract assets				
Bristol Myers Squibb	914	A2	4,536	A2
CSL Behring	57,854	A3	2,082	A3
Total	**58,768**		**6,618**	

Ratings are by Moody's. The credit exposure related to accounts receivable from BMS and accounts receivable and contract assets from CSL Behring is not considered material.

b) Market Risk

uniQure's market risks did not substantially change during the twelve months ended December 31, 2021 compared to the twelve months ended December 31, 2020.

(i) Currency risk

uniQure primarily operates from Lexington, MA in the United States of America and Amsterdam, the Netherlands. uniQure is exposed to foreign exchange risk arising from various currencies, primarily to the U.S. dollar and the euro and to a lesser extent to the British pound and the Swiss Franc. As uniQure's U.S. operations are primarily conducted in the U.S. dollar, its exposure to changes in foreign currency is insignificant. Similarly, the exposure to changes in foreign currencies of the Company's Swiss and French entities are insignificant as well.

The Company's Dutch operations hold significant amounts of U.S. dollars in cash and cash equivalents, have debt and interest obligations to Hercules Capital, Inc. ("Hercules") (See note 9 "*Borrowings*") 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 impact earnings and other comprehensive income or loss. On December 31, 2021, if the euro had weakened 10% against the U.S. dollar with all other variables held constant, pre-tax earnings of the Dutch entities for the year would have been $42.9 million higher (2020: $12.8 million higher), and other comprehensive income or loss would have been $24.0 million higher (2020: $5.8 million higher). Conversely, if the euro had strengthened 10% against the US dollar with all other variables held constant, pre-tax earnings for the year would have been $42.9 million lower (2020: $12.8 million lower), and other comprehensive income or loss would have been $32.2 million lower (2020: $8.9 million higher). uniQure strives to mitigate foreign exchange risk through holding sufficient funds in euro and dollars to finance budgeted cash flows for the next year.

The Company strives to mitigate foreign exchange risk through holding sufficient funds in euro and dollars to finance budgeted cash flows for twelve months forward.

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.

(ii) Interest rate risk

The Company's interest rate risk arises from short- and long-term debt. In June 2013, the Company entered into the Hercules Agreement, which was last amended and restated in December 2021, under which the Company's borrowings bear interest at a variable rate with a fixed floor. Long-term debt issued at fixed rates expose the Company to fair value interest rate risk. As of December 31, 2021, the loan bore a nominal interest rate of 7.95%.

On December 31, 2021 if interest rates on borrowings had been 1.0% higher with all other variables held constant, pre-tax results for the year would have been $0.6 million (2020: $0.3 million) lower.

(iii) Other price risk

uniQure is not exposed to significant price risk.

c) Liquidity risk

Management believes uniQure's cash and cash equivalents as of December 31, 2021, plus the $55.0 million of milestone payments subsequently collected from CSL Behring by the date of this Annual Report associated with the global regulatory submissions for etranacogene dezaparvovec, and assuming the receipt of $175.0 million of milestone payments to be received from CSL Behring upon their first commercial sales in certain markets, will fund the Company's operations into the first half of 2025. The Company manages liquidity through a rolling forecast of its liquidity reserve based on expected cash flows and raises cash if needed, either through the issuance of shares or credit facilities.

The table below analyzes the Company's financial liabilities in relevant maturity groupings based on the term until the contractual maturity date (excluding lease liabilities disclosed in Note 17 "*Leases*"). Disclosed in the table below are the contractual undiscounted cash flows. Balances due within 12 months equal their carrying value balances 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, 2020					
Borrowings (including interest payments)	—	3,141	39,271	—	—
Accounts payable, accrued expenses and other current liabilities	—	21,810	—	—	—
Total	**—**	**24,951**	**39,271**	**—**	**—**
At December 31, 2021					
Borrowings (including interest payments)	—	7,984	26,054	101,549	—
Accounts payable, accrued expenses and other current liabilities	—	30,989	—	—	—
Commitments related to Corlieve acquisition (nominal amount)	226,862	2,269	—	—	—
Total	**226,862**	**41,242**	**26,054**	**101,549**	**—**

In relation to the Corlieve Transaction, the Company 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 the Company agreed to as part of the SPA. 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 with the exception of a payment we owe upon acquiring the remaining outstanding shares as well as certain payments for post-acquisition services in 2022. The Company expects these obligations will become payable between 2022 and 2031. If and when due, up to 25% of the milestone payments can be settled with its ordinary shares.

4.2 Capital risk management

The Company's objectives in managing capital are to safeguard the Company's ability to continue as a going concern and to minimize the cost of capital to provide returns for shareholders and benefits for other stakeholders.

uniQure has no firm sources of additional financing. Until such time, if ever, as uniQure can generate substantial cash flows from successfully commercializing its proprietary product candidates, the Company expects to finance its cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution and licensing arrangements.

On December 15, 2021, the Company and Hercules amended and restated the 2021 Amended Facility ("2021 Restated Facility"). The Company is subject to covenants under this facility with Hercules, and may become subject to covenants under any future indebtedness that could limit its ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely impact its ability to conduct its business. In addition, its pledge of assets as collateral to secure its obligations under the 2021 Restated Facility may limit its ability to obtain debt financing.

If financing is not available when needed, including through debt financings or equity offerings, or is available only on unfavorable terms, uniQure may be unable to meet its cash needs. If uniQure raises additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, uniQure may have to relinquish valuable rights to its technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to it. If uniQure is unable to raise additional funds through equity or debt financings when needed, uniQure may be required to delay, limit, reduce or terminate its product development or future commercialization efforts or grant rights to develop and market product candidates that the Company would otherwise prefer to develop and market itself, which could have a material adverse effect on its business, financial conditions, results of operations and cash flows.

The amount of total shareholders' equity as recorded in the Consolidated Statements of Financial Position is managed as capital by the Company.

4.3 Fair value measurement

Financial instruments measured at fair value are categorized as follows:

- Level 1: quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2: inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly (i.e., as prices) or indirectly (i.e., derived from prices).
- Level 3: inputs for the asset or liability that are not based on observable market data (unobservable inputs).

The carrying amounts of financial assets and financial liabilities, measured at amortized cost, are a reasonable approximation of their fair value and therefore information about the fair values of each class is not disclosed.

Liabilities measured at fair value using Level 3 inputs as of December 31, 2021 consisted of contingent consideration, and as of December 31, 2020, liabilities measured at fair value using level 3 input consisted of derivative financial instruments.

The movement in the fair value of these Level 3 instruments during the years ended December 31, 2021, and 2020, is as follows:

	Contingent Consideration	Derivative financial instruments	Total
		$ in thousands	
At January 1, 2020	**—**	**3,075**	**3,075**
Gains recognized in profit or loss	—	(2,300)	(2,300)
Gain from derecognition of warrants	—	(796)	(796)
Currency translation effects	—	21	21
At December 31, 2020	**—**	**—**	**—**
Amount recorded for contingent consideration on Acquisition Date of Corlieve	23,950	—	23,950
Losses recognized in profit or loss	6,683	—	6,683
Currency translation effects	(1,091)	—	(1,091)
At December 31, 2021	**29,542**	**—**	**29,542**

Contingent Consideration

The Company is required to pay up to EUR 178.8 million ($202.8 million at the December 31, 2021 foreign exchange rate) to the former shareholders of Corlieve upon the achievement of contractually defined milestones in connection with the Company's acquisition of Corlieve (refer to Note 3 *"Corlieve transaction"*). The Company recorded a liability for the fair market value of the contingent consideration of EUR 20.2 million ($24.0 million) at the Acquisition Date. The fair market value was determined using unobservable initial inputs with respect to (i) the probability of achieving the relevant milestones, or POS, (ii) the estimated timing of achieving such milestones, and (iii) the interest rate used to discount the payments. The Company determined the fair market value of the contingent consideration by calculating the probability-adjusted payments based on each milestone's probability of achievement. The probability-adjusted payments were then discounted to present value using a discount rate representing the Company's credit risk. This discount rate was determined using the effective interest rate of the Company's existing debt facility adjusted for difference in maturity dates based on CCC yield curve.

The fair value of the contingent consideration as of December 31, 2021 was $29.5 million using discount rates ranging from 10.9% to 11.9% as well as a 55% likelihood of AMT-260 advancing into clinical development by no later than early 2024. The Company increased the likelihood of advancing into clinical development from 40% to 55% following the designation of a lead candidate in late October 2021, which resulted in EUR 5.0 million ($5.8 million) increase of the contingent liability. If as of December 31, 2021 the Company had assumed a 100% likelihood of AMT-260 advancing into clinical development, then the fair value of the contingent consideration would have increased to $47.0 million. If as of December 31, 2021 the Company assumed that it would discontinue development of the AMT-260 program, then the contingent consideration would be released to income. Changes in fair value of the contingent liability are recognized within research and development expenses in the consolidated statements of operations.

Derivative financial instruments

Pursuant to the BMS CLA, the Company in 2015 granted BMS two warrants (together the "BMS Warrants") that were subsequently terminated in connection with the amendment to the BMS CLA on December 1, 2020. The Company granted to BMS:

- A warrant that allowed BMS to purchase a specific number of the Company's ordinary shares such that its ownership would have equaled 14.9% immediately after such purchase ("1st warrant"). The 1st warrant could have been exercised on the later of (i) the date on which the Company received from BMS the Target Designation Fees (as defined in the BMS CLA) associated with the first six new targets (a total of seven Collaboration Targets); and (ii) the date on which BMS designated the sixth new target (the seventh Collaboration Target); and

- A warrant that allowed BMS to purchase a specific number of the Company's ordinary shares such that its ownership would have equaled 19.9% immediately after such purchase ("2nd warrant" and together with 1st warrant, the "warrants"). The warrant could have been exercised on the later of (i) the date on which the Company received from BMS the Target Designation Fees associated with the first nine new targets (a total of ten Collaboration Targets); and (ii) the date on which BMS designated the ninth new target (the tenth Collaboration Target).

On December 1, 2020, the Company derecognized the warrants when these were terminated in accordance with the amended BMS CLA.

Pursuant to the terms of the BMS CLA the exercise price in respect of each warrant was equal to the greater of (i) the product of (A) $33.84, multiplied by (B) a compounded annual growth rate of 10% (or approximately $57.32 as of November 30, 2020) and (ii) the product of (A) 1.10 multiplied by (B) the weighted average volume price ("VWAP") for the 20 trading days ending on the date that is five trading days prior to the date of a notice of exercise delivered by BMS.

The fair value of the warrants as of December 31, 2019 was $3.1 million. During the year ended December 31, 2020, the Company recognized a $3.1 million gain in non-operating (losses) / gains related to fair value changes of the BMS Warrants. The gain recognized in the year ended December 31, 2020 includes $0.8 million from the derecognition of the BMS Warrants on December 1, 2020 (nil for December 31, 2021).

The Company used Monte-Carlo simulations to determine the fair market value of the BMS Warrants. The valuation model incorporated several inputs, the risk-free rate adjusted for the period affected, an expected volatility based on historical Company volatility, the expected yield on any dividends and management's expectations on the timelines of reaching certain defined trigger events for the exercising of the warrants, as well as management's expectations regarding the number of ordinary shares that would be issued upon exercise of the warrants. All of these represent Level 3 inputs. Additionally, the model assumed BMS would exercise the warrants only if it was financially rational to do so.

The warrants could only have been exercised following the occurrence of events contractually defined in the warrant agreements. The probability of the occurrence of these events represented another significant unobservable input used in the calculation of the fair value of the warrants.

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

5. Collaboration arrangements and concentration of credit risk

CSL Behring collaboration

On the Signing Date, uniQure biopharma B.V., a wholly-owned subsidiary of uniQure N.V., entered into the CSL Behring Agreement with CSL Behring, pursuant to which CSL Behring received exclusive global rights to the Product. On May 6, 2021, a day after the expiration of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, the CSL Behring Agreement became fully effective (the "Closing").

Pursuant to the CSL Behring Agreement, the Company received a $450.0 million upfront cash payment and $12.4 million in other payments related to the Closing and the transfer of the license. The Company is eligible to receive up to $1.6 billion in additional payments based on the achievement of regulatory and commercial milestones. The CSL Behring Agreement also provides that the Company will be eligible to receive tiered double-digit royalties in a range of up to a low-twenties percent of net sales of the Product based on sales thresholds.

On the Signing Date, the Company and CSL Behring entered into a development and commercial supply agreement, pursuant to which, among other things, the Company will supply the Product to CSL Behring at an agreed-upon price commensurate with the stand-alone selling price ("SSP"). The Company will be responsible for supplying development and commercial Product until such time that these capabilities may be transferred to CSL Behring or a designated contract manufacturing organization. The Company will be completing the HOPE-B clinical trial and the validation of the manufacturing process on behalf of CSL Behring, as well as provide further development services if requested by CSL Behring. Activities related to on-demand development services as well as activities related to the completing the HOPE-B clinical trial will be reimbursed by CSL Behring at an agreed full-time-employee rate ("FTE-rate") and CSL Behring will also reimburse agreed third-party expenses incurred in relation to performing these activities. The validation of the manufacturing process as well as Manufacturing Development will be reimbursed through a future milestone payment. If completed after certain contractually agreed upon dates, the milestone payment will be reduced in accordance with a pre-specified mechanism.

The Company concluded that CSL Behring is a customer in accordance with IFRS 15.

The Company identified two material performance obligations related to the CSL Behring Agreement:

(i) License Sale; and

(ii) Manufacturing Development.

These performance obligations are considered distinct from one another, as CSL Behring can benefit from the identified service either on its own or together with other resources that are readily available to CSL Behring, and as the performance obligations are separately identifiable from other performance obligations in the CSL Behring Agreement. The Company continued to develop the Product between the Signing Date and the Closing and performed certain reimbursable activities to fulfill the transfer of the global rights ("Additional Covenants" and together with the License the "License Sale"). The Additional Covenants are not considered distinct from the performance obligation to sell the license to CSL Behring as CSL Behring could not benefit from the Additional Covenants on their own, or have these activities be performed with readily available resources.

The Company determined that the fixed upfront payment of $450.0 million and the $12.4 million that the Company received in relation to the Additional Covenants should be allocated to the License Sale. In addition, the Company concluded that variable milestone payments, sales milestone payments and royalties should be allocated to the License Sale performance obligation as well. The Company determined that the License Sale was completed on May 6, 2021, when it transferred the license and CSL Behring assumed full responsibility for the development and commercialization of the Product. At the Closing, the Company evaluated the amounts of potential payments and the likelihood that the payments will be received. The Company utilized the most likely amount method to estimate the variable consideration to be included in the transaction price. Since the Company cannot control the achievement of regulatory and first commercial sales milestones, the Company concluded that the potential payments are constrained as of the Closing. The Company determined that it would recognize revenue related to these payments only to the extent that it becomes highly probable that no significant reversal of recognized cumulative revenue will occur thereafter.

Similarly, the Company will record expenses related to its existing license and other agreements as well as its financial advisor for a high single digit percentage of any such revenue recognized associated to meeting a milestone. The Company will include payments related to sales milestones in the transaction price when their achievement becomes highly probable, and it will include royalties on the sale of Product once these have been earned. At the date of these financial statements, the Company collected $55.0 million of milestone payments related to the global regulatory submissions. The Company recorded these as license revenue in the year ended December 31, 2021. The Company recognized $517.4 million of revenues related to the License Sale in the year ended December 31, 2021.

The Company determined that the variable milestone payment related to Manufacturing Development should be allocated to the Manufacturing Development performance obligation. The Company concluded that this milestone payment represents the SSP of the services based on the estimated cost of providing the services including a reasonable margin. The services related to Manufacturing Development will be provided between the Closing and the completion of an agreed manufacturing development plan. The variable consideration will be reduced if the Company does not complete the development by pre-agreed dates. The Company utilized the most likely amount method to estimate the variable consideration to be included in the transaction price. Completion of Manufacturing Development is partially dependent on the timing of regulatory submissions by CSL Behring as well as regulatory approvals of the developed manufacturing processes. Since the Company cannot control the timing or outcome of any regulatory decisions, the Company concluded that it would recognize revenue related to this payment when it becomes highly probable that the milestone has been achieved. The Company has not recognized any revenue related to Manufacturing Development.

The Company recognized $2.4 million of collaboration revenue in the year ended December 31, 2021, respectively, compared to nil in the same period in 2020. The Company generates such collaboration revenue from services rendered in relation to completing the HOPE-B clinical trial on behalf of CSL Behring. CSL Behring may request additional development services or request the Company to support the transfer of manufacturing to a party designated by CSL Behring. These collaboration services will be reimbursed at the pre-agreed full-time-employee rate ("FTE-rate"). The Company concluded that these rights at the Closing do not represent material rights.

The Company incurred $2.1 million of expenses for obligations related to the CSL Behring Agreement that had not been satisfied as of December 31, 2020. The Company capitalized these expenses as contract fulfillment costs (presented within Other current assets). As of December 31, 2020, the Company also recognized a $2.1 million receivable (presented within Accounts receivable) from CSL Behring for expenses for which it has a right of reimbursement as well as a contract liability (presented within Accrued expenses and other current liabilities) for the same amount. In accordance with IFRS 15 the Company could not recognize any license revenue related to the CSL Behring Agreement in the period ended December 31, 2020. Following the Closing, the Company collected the $2.1 million of accounts receivable related to reimbursable contract fulfillment costs that was outstanding as of December 31, 2020. As of December 31, 2021, the Company recorded accounts receivable of $2.9 million from CSL Behring related to clinical development services as well as a contract asset of $55.0 million related to milestone payments associated with CSL Behring's global regulatory submissions, which were considered highly probable at year end and subsequently occurred by the date of this Annual Report. As of the date of this Annual Report, the Company has collected the $55.0 million from CSL Behring.

BMS collaboration

2015 Agreement

In May 2015, the Company entered into the BMS CLA and various related agreements with BMS, which the Company collectively refers to as the BMS CLA, which provided BMS with exclusive access to the Company's gene therapy technology platform for the research, development and commercialization of therapeutics aimed at multiple Collaboration Targets. The initial four-year research term under the collaboration terminated on May 21, 2019. During the initial research term of the BMS CLA, the Company supported BMS in discovery, non-clinical, analytical and process development efforts in respect of the Collaboration Targets. For any Collaboration Targets that may be advanced, the Company will be responsible for manufacturing of clinical and commercial supplies. BMS reimbursed the Company for all its research and development costs in support of the collaboration, and will lead development, regulatory and commercial activities for any Collaboration Targets that may be advanced. The BMS CLA initially provided that the Company and BMS could potentially have collaborated on up to ten Collaboration Targets in total.

2020 Amendment

On December 1, 2020, the Company and BMS entered into the amended BMS CLA. Under the amended BMS CLA, BMS is limited to four Collaboration Targets. For a period of one-year from the effective date of the amended BMS CLA, BMS was able to replace up to two of the four active Collaboration Targets with two new targets in the field of cardiovascular disease. The Company continues to be eligible to receive research, development, and regulatory milestone payments of up to $217.0 million for each Collaboration Target, if defined milestones are achieved.

Since the December 2020 amendment, BMS is no longer entitled to designate the fifth to tenth Collaboration Targets and as such the Company's remaining obligations under the amended BMS CLA are substantially reduced. The Company is also no longer entitled to receive up to an aggregate $16.5 million in target designation payments for the research, development and regulatory milestone payments associated with the fifth to tenth Collaboration Targets.

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

The amended BMS CLA does not extend the initial four-year research term that expired in May 2019. BMS may place purchase orders to provide limited services primarily related to analytical and development efforts in respect of the four Collaboration Targets. BMS may request such services for a period not to exceed the earlier of (i) the completion of all activities under a Research Plan and (ii) November 30, 2023, if no replacement targets are designated. BMS continues to reimburse the Company for these services.

During the year ended December 31, 2020, the Company evaluated the impact of the amendment of the BMS CLA had in relation to its performance obligation related to License Revenue. The Company did not identify any new distinct performance obligations and determined the amended BMS CLA did not represent a separate contract in accordance with IFRS 15. The Company evaluated the effect the modification had on its measure of progress towards the completion of its performance obligation related to License Revenue and determined that its remaining performance obligation under the amended BMS CLA was immaterial and recognized the remaining balance of unrecognized License Revenue as of November 30, 2020.

Services to BMS are rendered by the Dutch operating entity. Total collaboration and license revenue generated with BMS are as follows:

	Years ended December 31,	
	2021	2020
	$ in thousands	
Bristol Myers Squibb	4,176	37,514
Total	**4,176**	**37,514**

Amounts owed by BMS in relation to the Collaboration and License Revenue are as follows (presented as "Accounts receivables" as of December 31, 2021 and of December 31, 2020):

	December 31, 2021	December 31, 2020
	$ in thousands	
Bristol Myers Squibb	914	4,536
Total	**914**	**4,536**

Collaboration Revenue

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

The Company generated $4.2 million collaboration revenue for the year ended December 31, 2021 (December 31, 2020: $0.2 million).

License Revenue

The Company recognized no License Revenue for the year ended December 31, 2021 (December 31, 2020: $33.0 million).

On May 21, 2015, the Company recorded a $60.1 million upfront payment and in August 2015 it recorded a $15.0 million payment it received from BMS in relation to the designation of the second, third and fourth Collaboration Targets. The Company recognized License Revenue over the expected performance period based on its measure of progress towards the completion of certain activities related to its services. The Company determined such progress by comparing activities performed at the end of each reporting period with total activities expected to be performed. The Company estimated total expected activities using several unobservable inputs, such as the probability of BMS designating additional targets, the probability of successfully completing each phase and estimated time required to provide services during the various development stages. The estimation of total services at the end of each reporting period involves considerable judgment.

The amount of services the Company expects to provide is significantly impacted by the number of Collaboration Targets that it estimates BMS would pursue. As a result of the December 1, 2020 amendment of the BMS CLA the Company no longer is required to potentially provide any services in relation to six additional targets that BMS might have designated. The Company determined its remaining performance obligation is immaterial. The Company adjusted its measure of progress towards the completion of its activities related to its services as of the December 1, 2020 modification date accordingly. The Company recognized the remaining balance of unrecognized License Revenue as of November 30, 2020 of $27.8 million in profit and loss during the year ended December 31, 2020 as License Revenue.

The Company includes variable consideration related to any research, development, and regulatory milestone payments, in the transaction price once it is considered highly probable that including these payments in the transaction price would not result in the reversal of cumulative revenue recognized. Due to the significant uncertainty surrounding the development of gene-therapy product candidates and the dependence on BMS's performance and decisions, the Company does not currently consider this highly probable. However, there was a milestone that was recorded as license revenue in the year ended December 31, 2020 (see below).

On December 17, 2020 BMS designated one of the four Collaboration Targets as a candidate to advance into Investigational New Drug-enabling studies ("IND-enabling studies") entitling the Company to receive a $4.4 million research milestone payment. The Company recorded the $4.4 million as License Revenue in the year ended December 31, 2020.

The Company recognizes License Revenue related to product sales by BMS from any of the Collaboration Targets when the sales occur. The Company is eligible to receive net sales-based milestone payments and tiered mid-single to low double-digit royalties on product sales. The royalty term is determined on a licensed-product-by-licensed-product and country-by-country basis and begins on the first commercial sale of a licensed product in a country and ends on the expiration of the last to expire of specified patents or regulatory exclusivity covering such licensed product in such country or, with a customary royalty reduction, ten years after the first commercial sale if there is no such exclusivity.

6. Property, plant and equipment

	Leasehold improvements	Laboratory equipment	Office equipment	Construction in-progress	Total
			$ in thousands		
Cost	34,611	18,232	4,212	341	57,396
Accumulated depreciation	(12,728)	(13,483)	(2,414)	—	(28,625)
Carrying amount January 1, 2020	**21,883**	**4,749**	**1,798**	**341**	**28,771**
Additions	—	—	—	7,900	7,900
Reclassifications	1,775	3,148	772	(5,695)	—
Disposals - cost	—	—	(132)	—	(132)
Disposals - accumulated depreciation	—	—	114	—	114
Depreciation expense	(2,691)	(2,281)	(721)	—	(5,693)
Currency translation effects	1,000	261	79	28	1,368
Carrying amount December 31, 2020	**21,967**	**5,877**	**1,910**	**2,574**	**32,328**
Cost	37,849	22,106	5,024	2,574	67,553
Accumulated depreciation	(15,881)	(16,229)	(3,115)	—	(35,225)
Carrying amount December 31, 2020	**21,968**	**5,877**	**1,909**	**2,574**	**32,328**
Additions	—	22	25	19,023	19,070
Reclassifications	9,581	6,187	629	(16,397)	—
Disposals - cost	(362)	(2,102)	(1,045)	—	(3,509)
Disposals - accumulated depreciation	143	2,029	1,017	—	3,189
Depreciation expense	(2,841)	(2,473)	(757)	—	(6,071)
Currency translation effects	(1,209)	(81)	(81)	(131)	(1,502)
Carrying amount December 31, 2021	**27,280**	**9,459**	**1,697**	**5,069**	**43,505**
Cost	45,372	25,499	4,465	5,069	80,405
Accumulated depreciation	(18,092)	(16,040)	(2,768)	—	(36,900)
Carrying amount December 31, 2021	**27,280**	**9,459**	**1,697**	**5,069**	**43,505**

Total depreciation expense was $6.1 million for the year ended December 31, 2021 (December 31, 2020: $5.7 million). Depreciation expense is allocated to research and development expenses to the extent it relates to the Company's manufacturing facility and equipment and laboratory equipment. All other depreciation expenses are allocated to selling, general and administrative expense.

The carrying amount of property, plant and equipment by location is set out below:

	December 31, 2021	December 31, 2020
	$ in thousands	
Amsterdam (the Netherlands)	26,160	16,379
Lexington (United States of America)	17,311	15,949
Other	34	—
Carrying amount	**43,505**	**32,328**

7. Intangible assets and goodwill

	Acquired licenses	Acquired IPR&D	Goodwill	Total
	$ in thousands	$ in thousands	$ in thousands	$ in thousands
Cost	8,317	—	496	8,813
Accumulated amortization and impairment	(2,890)	—	—	(2,890)
Carrying amount January 1, 2020	**5,427**	**—**	**496**	**5,923**
Additions	2,333	—	—	2,333
Amortization expense	(1,555)	—	—	(1,555)
Impairment expense	(294)	—	—	(294)
Disposal - cost	1,759	—	—	1,759
Disposal - accumulated amortization and impairment	(1,759)	—	—	(1,759)
Currency translation effects	650	—	46	696
Carrying amount December 31, 2020	**6,561**	**—**	**542**	**7,103**
Cost	9,852	—	542	10,394
Accumulated amortization	(3,291)	—	—	(3,291)
Carrying amount December 31, 2020	**6,561**	**—**	**542**	**7,103**
Corlieve transaction (See note 3, "Corlieve transaction")	-	63,618	28,409	92,027
Amortization expense	(1,407)	—	—	(1,407)
Disposal - cost	(4,165)	—	—	(4,165)
Disposal - accumulated amortization	1,334	—	—	1,334
Currency translation effects	(248)	(2,860)	(1,318)	(4,426)
Carrying amount December 31, 2021	**2,075**	**60,758**	**27,633**	**90,466**
Cost	5,194	60,758	27,633	93,585
Accumulated amortization	(3,119)	—	-	(3,119)
Carrying amount December 31, 2021	**2,075**	**60,758**	**27,633**	**90,466**

a. Acquired licenses

All intangible assets are owned by uniQure biopharma B.V, a subsidiary of the Company.

b. Acquired in-process research and development

As part of its acquisition of Corlieve as of July 30, 2021, the Company identified certain intangible assets related to an IPR&D Intangible Asset. Refer to Note 3 *"Corlieve transaction"*.

c. Goodwill

As part of its acquisition of Corlieve as of July 30, 2021, the Company recorded goodwill. Refer to Note 3 *"Corlieve transaction"*.

8. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities include the following items:

	December 31, 2021	December 31, 2020
	$ in thousands	
Accruals for services provided by vendors-not yet billed	13,012	8,269
Personnel related accruals and liabilities	12,603	7,687
Accrued contract fulfillment costs and costs to obtain a contract	2,872	—
Contract liability (see note 5, "Collaboration arrangements and concentration of credit risk")	—	2,082
Total	**28,487**	**18,038**

9. Borrowings

On June 14, 2013, the Company entered into a venture debt loan facility with Hercules, which was amended and restated on June 26, 2014, and again on May 6, 2016 ("2016 Amended Facility"). On December 6, 2018, the Company signed an amendment that both refinanced the then-existing $20.0 million 2016 Amended Facility and allowed the Company to draw down an additional $15.0 million ("2018 Amended Facility"). The 2018 Amended Facility extended the loan's maturity date from May 1, 2020 until June 1, 2023. The interest rate is adjustable and is the greater of (i) 8.85% and (ii) 8.85% plus the prime rate less 5.50% per annum. Under the 2018 Amended Facility, the Company owes a back-end fee of 4.95% of the outstanding debt. In addition, in May 2020 the Company paid a back-end fee of $1.0 million in relation to the 2016 Amended Facility.

On January 29, 2021, the Company and Hercules amended the 2018 Amended Facility ("2021 Amended Facility"). Pursuant to the 2021 Amended Facility, Hercules agreed to an additional Facility of $100.0 million ("Tranche B") increasing the aggregate principal amount of the term loan facilities from $35.0 million to up to $135.0 million. On January 29, 2021, the Company drew down $35.0 million of the Tranche B. Advances under Tranche B bore interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance of $70.0 million and all accrued but unpaid interest on advances under Tranche B was due on June 1, 2023, which date could had been extended by the Company by up to two twelve-month periods. Advances under the 2021 Amended Facility could have been prepaid without charge after July 29, 2021. The back-end fee in respect of advances under the 2021 Amended Facility ranged from 1.65% to 6.85%, depending on the repayment date. In addition to Tranche B, the 2021 Amended Facility had also extended the interest only payment period of the previously funded $35.0 million term loan ("Tranche A") from January 1, 2022 to June l, 2023. The January 29, 2021 amendment resulted in a non-substantial modification in accordance with IFRS 9. As a result of the modification, a modification loss of $0.1 million was recorded as other income in the statement of profit or loss during the year ended December 31, 2021.

On December 15, 2021, the Company and Hercules amended and restated the 2021 Amended Facility ("2021 Restated Facility"). Pursuant to the 2021 Restated Facility, Tranche A and Tranche B of the 2021 Amended Facility with a total outstanding balance of $70.0 million were consolidated into one tranche with a total commitment of $100.0 million. The Company drew down an additional $30.0 million, resulting in total principal outstanding as of December 31, 2021 of $100.0 million. The 2021 Restated Facility extended the loan's maturity date from June 1, 2023 until December 1, 2025. The interest-only period is extended from January 1, 2023 to December 1, 2024, or December 1, 2025 if, prior to June 30, 2024, either (a) the Biologics License Application ("BLA") for AMT-061 is approved by the U.S. Food and Drug Administration ("FDA") or (b) AMT-130 is advanced into a pivotal trial. The interest rate is adjustable and is the greater of (i) 7.95% and (ii) 7.95% plus the prime rate less 3.25% per annum. Under the 2021 Restated Facility, the Company owes a back-end fee of 4.85% of the outstanding debt. The Company is required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. The Company continues to owe a $2.5 million back-end fee related to the 2021 Amended Facility which is due on June 1, 2023. The December 15, 2021 amendment resulted in a non-substantial modification in accordance with IFRS 9. As a result of the modification, a modification gain of $3.0 million was recorded as other income in the statement of profit or loss during the year ended December 31, 2021.

The amortized cost (including interest due presented as part of accrued expenses and other current liabilities) of the 2021 Restated Facility was $98.4 million as of December 31, 2021, compared to $35.5 million as of December 31, 2020 for the 2018 Amended Facility. The foreign exchange loss on borrowings was $5.3 million in 2021 (2020: gain of $3.1 million). The fair value of the loan approximates its carrying amount. Inputs to the fair value of the loan are considered Level 3 inputs.

The movement in the amortized cost of the borrowings during the years ended December 31, 2021, and 2020, is as follows:

	Borrowings
	$ in thousands
At January 1, 2020	**35,906**
Non-cash changes recognized in profit or loss	(381)
At December 31, 2020	**35,525**
Cash flows (drawdowns on amendments, net of fees paid)	64,067
Non-cash changes recognized in profit or loss	(1,199)
At December 31, 2021	**98,393**

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

Years	Amount
	$ in millions
2021	7.2
2020	3.7

As a covenant in the 2021 Restated Facility the Company has periodic reporting requirements and is required to keep a minimum cash balance deposited in bank accounts in the United States, equivalent to the lesser of (i) 65% of the outstanding balance of principal due or (ii) 100% of worldwide cash and cash equivalents. This restriction on cash and cash equivalents only relates to the location of the cash and cash equivalents, and such cash and cash equivalents can be used at the discretion of the Company. The Company, beginning on April 1, 2023, is also required to keep a minimum of unrestricted cash of at least 50% of the loan amount outstanding. If, prior to June 30, 2024, either (a) the BLA for AMT-061 is approved by the FDA or (b) AMT-130 is advanced into a pivotal trial, the minimum cash covenant will be lowered to at least 30% of the loan amount outstanding and its effectiveness will be deferred to April 1, 2024. In combination with other covenants, the 2021 Restated Facility restricts the Company's ability to, among other things, incur future indebtedness and obtain additional debt financing, to make investments in securities or in other companies, to transfer assets, to perform certain corporate changes, to make loans to employees, officers, and directors, and to make dividend payments and other distributions to its shareholders. The Company secured the facilities by directly or indirectly pledging its total assets of $808.2 million with the exception of $103.2 million of cash and cash equivalents and other current assets held by uniQure N.V.

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

The aggregate maturities of the loan, including $35.6 million of coupon interest payments and financing fees, for each of the 47 months subsequent to December 31, 2021, are as follows:

Years	Amount
	$ in thousands
2022	7,984
2023	10,580
2024	15,474
2025	101,549
Total	**135,587**

10. Total Shareholders' equity

As of December 31, 2021, the Company's reserve for a currency translation adjustment was a loss of $31.3 million (2020: gain of $6.9 million) as a result of $38.2 million presented in the Consolidated Financial Statements of Profit or Loss and Other Comprehensive Income or Loss as other comprehensive loss (2020: $16.9 million other comprehensive income). The reserve for the currency translation adjustment is reflected in the Company's equity, under other comprehensive (loss) / income.

As of December 31, 2021, the Company's authorized share capital is €4.0 million (or $4.5 million when translated at an exchange rate as of December 31, 2021, of $1.13 / €1.00), divided into 80,000,000 ordinary shares, each with a nominal value of €0.05. The Company's shareholders, at the 2021 Annual General Meeting of Shareholders held on June 16, 2021, approved an increase in the number of authorized ordinary shares by 20,000,000 to 80,000,000 million.

All ordinary shares issued by the Company were fully paid. Besides the minimum amount of share capital to be held under Dutch law, there are no distribution restrictions applicable to the equity of the Company.

On March 1, 2021, the Company entered into a Sales Agreement with SVB Leerink LLC ("SVB Leerink") with respect to an at-the-market ("ATM") offering program, under which the Company may, from time to time in its sole discretion, offer and sell through SVB Leerink, acting as agent, its ordinary shares, up to an aggregate offering price of $200.0 million. The Company will pay SVB Leerink a commission equal to 3% of the gross proceeds of the sales price of all ordinary shares sold through it as sales agent under the Sales Agreement. In March and April 2021, the Company issued an aggregate of 921,730 ordinary shares at a weighted average price of $33.52 per ordinary share, with net proceeds of $29.6 million, after deducting underwriting discounts and net of offering expenses. The Company defers direct, incremental costs associated to this offering, except for the commission costs to SVB Leerink, which are a reduction to additional paid-in capital, and will deduct these costs from additional paid-in capital in the consolidated balance sheets proportionately to the amount of proceeds raised. During the year ended December 31, 2021, $1.3 million of direct, incremental costs were deducted from additional paid-in capital.

Following the Closing, the Company consumed its tax net operating loss carryforwards from the years 2011 to 2018. The Company allocated the tax benefit from the release of the valuation allowance related to net operating loss carryforwards generated by share issuance costs incurred in 2014, 2015, 2017 and 2018 to additional paid-in capital. This resulted in an increase of additional paid-in capital of $3.0 million in the year ended December 31, 2021.

11. Share-based compensation

Share-based compensation expense recognized by classification included in the Consolidated Statements of Profit or Loss and Other Comprehensive Profit or Loss was as follows:

	Years ended December 31,	
	2021	2020
	$ in thousands	
Research and development	16,096	13,471
Selling, general and administrative	12,659	11,369
Total	**28,755**	**24,840**

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

	Years ended December 31,	
	2021	2020
Award type	$ in thousands	
Share options	14,088	12,921
Restricted share units	12,971	8,602
Performance share units	1,696	3,317
Total	**28,755**	**24,840**

The Company satisfies the exercise of share options and vesting of Restricted Share Unites ("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 (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 Company previously had a 2012 Equity Incentive Plan (the "2012 Plan") As of December 31, 2021, 14,000 fully vested shares options are outstanding (December 31, 2020: 14,000) under the 2012 Plan.

At the general meeting of shareholders on January 9, 2014, the Company's shareholders approved the adoption of the 2014 Plan. At the annual general meetings of shareholders in June 2015, 2016, 2018 and 2021, uniQure shareholders approved amendments of the 2014 Plan, increasing the shares authorized for issuance by 1,070,000 shares in 2015, 3,000,000 shares in 2016, 3,000,000 shares in 2018 and 4,000,000 shares in 2021 for a total of 12,601,471 shares. The 2014 Plan allows for various awards such as the granting of options, restricted share units and performance share units.

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 Plan

The following table summarizes option activity under the Company's 2014 Plan for the years ended December 31, 2021 and 2020:

	Options		
	Number of ordinary shares	Weighted average exercise price	Weighted average remaining contractual life in years
Outstanding at January 1, 2020	**2,683,104**	**$ 21.29**	**7.46**
Granted	653,852	$ 49.63	
Forfeited	(172,548)	$ 42.03	
Expired	(6,451)	$ 45.76	
Exercised	(498,678)	$ 14.43	
Outstanding at January 1, 2021	**2,659,279**	**$ 21.29**	**7.18**
Granted	1,174,893	$ 35.85	
Forfeited	(258,718)	$ 40.78	
Expired	(25,633)	$ 42.81	
Exercised	(241,496)	$ 10.98	
Outstanding at December 31, 2021	**3,308,325**	**$ 31.02**	**7.05**
Fully vested and exercisable at December 31, 2020	1,542,405	$ 18.05	6.15
Fully vested and exercisable at December 31, 2021	1,786,825	$ 24.47	5.49
Outstanding and expected to vest at December 31, 2021	1,521,500	$ 38.71	8.88
Total weighted average grant date fair value of options issued during 2021 (in $ millions)		$ 24.6	
Granted to directors and officers during 2021 (options, grant date fair value $ in millions)	312,704	$ 6.5	

The weighted-average share price of options exercised during the year ended December 31, 2021 at the date of exercise was $31.88.

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

	Granted during the year	Weighted average grant - date fair value (in $)
2021	1,174,893	20.95
2020	653,852	28.08

Share options outstanding at the end of the year have the following weighted-average remaining contractual life and ranges of exercise prices:

Weighted average remaining contractual life	Range exercise price per share	Number of options
0 to 5 years	$5.31 - $78.01	839,646
6 years	$17.59 - $39.97	501,060
7 years	$31.71- $78.01	459,405
8 years	$38.67- $65.87	452,884
9 years	$28.24- $37.00	1,055,330
At December 31, 2021		**3,308,325**

Weighted average remaining contractual life	Range exercise price per share	Number of options
0 to 5 years	$5.37 - $78.01	528,231
6 years	$5.31- $10.71	469,157
7 years	$17.59- $39.97	551,028
8 years	$31.71- $78.01	535,740
9 years	$38.67- $65.87	575,123
At December 31, 2020		**2,659,279**

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

	Years ended December 31,	
Assumptions	2021	2020
Options with change of control and service-based vesting conditions	3,308,325	2,659,279
Share price [1)]	$5.31- $78.01	$5.31- $78.01
Estimated fair value per option as of grant date	$2.83 - $45.94	$2.83 - $45.94
Expected volatility	70%-80%	70%-80%
Expected term	10 years	10 years
Exercise price	$5.31- $78.01	$5.31- $78.01
Expected dividend yield [2)]	0%	0%
Risk-free rate [3)]	0.16% - 3.18%	0.16% - 3.18%

1) Closing share price on the grant dates.
2) The Company currently does not pay dividends and has no plans to do so.
3) Based on Government bonds with a term that is commensurate with the expected term of each option tranche. Also considered is the risk- free rate over the performance period for each option tranche.

Expected option term

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 included for the full contractual term.

Expected volatility

Volatility was based on a publicly traded peer group with similar years on the market as compared to the Company. The Company's own volatility was weighted against the peer group to arrive at expected volatility.

Restricted share units

The movement in the number of RSUs issued under the 2014 Plan is as follows:

	RSU	
	Number of Ordinary shares	Weighted average grant-date fair value
Non-vested at January 1, 2020	**370,830**	**$ 28.62**
Granted	376,799	$ 48.18
Distributed	(206,881)	$ 24.18
Forfeited	(73,404)	$ 46.41
Non-vested at January 1, 2021	**467,344**	**$ 43.56**
Granted	574,921	$ 36.14
Distributed	(220,518)	$ 40.56
Forfeited	(111,130)	$ 40.98
Non-vested at December 31, 2021	**710,617**	**$ 38.89**
Total weighted average grant date fair value of RSUs granted during 2021 (in $ millions)		$ 20.8
Granted to directors and officers during 2021 (shares, $ in millions)	167,230	$ 6.1

RSUs vest over one to three years. RSUs granted to non-executive directors will vest one year from the date of grant. In determining the fair values no payments of dividends were assumed during the service periods.

Performance share units

The movement in the number of PSUs issued under the 2014 Plan is as follows:

	PSU	
	Number of Ordinary shares	Weighted average grant-date fair value
Non-vested at January 1, 2020	**479,422**	**$ 21.17**
Granted	91,003	$ 57.56
Retired	(354,105)	$ 17.44
Distributed	(3,706)	$ 57.56
Non-vested at January 1, 2021	**212,614**	**$ 42.32**
Granted	555,600	$ 30.19
Retired	(132,368)	$ 33.09
Distributed	(2,916)	$ 57.56
Non-vested at December 31, 2021	**632,930**	**$ 33.54**
Total weighted average grant date fair value of PSUs granted and awarded during 2021 (in $ millions)		$ 16.8

The Company granted shares to certain employees in September and December 2021 that will be earned upon achievement of defined milestones. Earned shares will vest upon the later of a minimum service period of one year or three years, or the achievement of defined milestones, subject to the grantee's continued employment. In addition, portions of the December 2021 granted to executives and other members of senior management are subject to achieving a minimum total shareholder return relative to the Nasdaq biotechnology index. The Company recognizes an amount for the services received during the vesting period based on the best available estimate of the number of equity instruments expected to vest. The Company will revise that estimate if subsequent information indicates that the number of equity instruments expected to vest differs from previous estimates.

In January 2018 and January and February 2019, the Company awarded PSUs to its executives and other members of senior management. These PSUs were earned in January 2019 and January 2020, based on the Board's assessment of the level of achievement of agreed upon performance targets through December 31, 2018, and December 31, 2019, respectively. The PSUs awarded for the year ended December 31, 2018 vested in February 2021 and the PSUs awarded for the year ended December 31, 2019 vested in January 2022.

In determining the fair values no payments of dividends were assumed during the service periods.

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, 2021, 4,724 shares have been issued (December 31, 2020: 6,181). As of December 31, 2021, a total of 127,302 ordinary shares remains available for issuance under the ESPP plan.

12. Expenses by nature

Operating expenses excluding expenses presented in other expenses included the following expenses by nature:

	Years ended December 31,	
	2021	2020
	$ in thousands	
Employee-related expenses	99,309	78,978
Laboratory and development expenses	35,596	35,977
Legal and advisory expenses	24,767	17,370
Other operating expenses	10,528	8,772
Office and housing expenses	9,536	8,220
Depreciation and amortization	7,474	7,564
Fair value loss - Corlieve contingent consideration	6,683	—
Patent and license expenses	3,748	2,899
Expenses related to lease arrangements	2,936	2,692
Total	**200,577**	**162,473**

The Company employed an average 397 employees during the year ended December 31, 2021 (2020: 286) including an average 186 employees outside the Netherlands (2020: 148). The average number of employees by category is summarized as follows:

	2021	2020
Research and development	326	237
Selling, general and administrative	71	49
Total	**397**	**286**

Details of employee-related expenses for the years ended December 31 are as follows:

	Years ended December 31,	
	2021	2020
	$ in thousands, except for employee numbers	
Wages and salaries	53,078	40,919
Share-based compensation expenses	28,783	24,883
Other employee expenses	4,570	2,635
Social security costs	4,496	4,068
Contractor expenses	3,170	2,423
Health insurance	3,161	2,271
Pension costs - defined contribution plans	2,051	1,779
Total	**99,309**	**78,978**
Number of employees at the end of the period	463	332

13. Other income

Other income during the year ended December 31, 2021 was $15.2 million compared to $3.3 million during the same period in 2020.

Other income in 2021 and 2020 includes income from payments received from European authorities to subsidize the Company's research and development efforts in the Netherlands. The amount recognized in the year ended December 31, 2021 was $5.3 million compared to $1.9 million in 2020.

In addition, other income includes $2.6 million of employee retention credits received under the U.S. Coronavirus Aid, Relief, and Economic Security Act, during the year ended December 31, 2021. An additional $3.0 million of other income was recorded in the year ended December 31, 2021, related to the receipt by the Company of 69,899 shares of VectorY B.V. in conjunction with a settlement agreement that the Company and VectorY B.V. entered into in April 2021. A further $2.8 million of other income was recorded in the year ended December 31, 2021, derived from a net modification gain resulting from the amendments to the Company's loan agreements under the 2021 Amended Facility and 2021 Restated Facility. Refer to Note 9 "Borrowings" for further details. No such income was recorded in 2020.

In 2021 and 2020 the Company's other income also consisted of income from the subleasing of a portion of the Amsterdam facility while other expense consists of expenses incurred in relation to the subleasing income.

14. Finance income / (expense), net

	Years ended December 31,	
	2021	2020
	$ in thousands	
Finance income		
Foreign exchange gains, net	29,659	-
Derivative gains (see note 4 "Financial Risk Management")	-	3,095
Interest income on cash and cash equivalents	162	938
Total finance income	**29,821**	**4,033**
Finance expense		
Foreign exchange losses, net	-	(13,613)
Interest expense on leases (see note 17 "Leases")	(3,982)	(3,898)
Interest expense on Hercules borrowing (see note 9 "Borrowings")	(7,245)	(3,722)
Interest expense on cash and cash equivalents	(258)	(169)
Total finance expense	**(11,485)**	**(21,401)**
Finance income / (expense), net	**18,336**	**(17,368)**

Foreign exchange gains / (losses), net include foreign currency gains and losses on cash and cash equivalents, Hercules borrowing as well as loans between entities within the uniQure group and other foreign currency monetary items.

15. Income taxes

No current tax charges or liabilities were recorded in 2021 and 2020 by our Dutch and U.S. entities. The Company has not recognized its net deferred tax assets in the Netherlands as the Company does not consider it probable that taxable profit will be available against which its deductible temporary differences can be utilized. The Company continued to recognize its net deferred tax assets in the United States as December 31, 2021 as the Company determined that utilization became probable as a result of taxable profits during the past four fiscal periods in combination with the projected future taxable profits in the United States.

In connection with the Corlieve acquisition, the Company recognized a deferred tax liability related to acquired identifiable intangible assets and a deferred tax asset for net operating tax loss carryforwards for a net of EUR 11.9 million ($14.2 million) as of the Acquisition Date.

The reconciliation of the Dutch statutory income tax rate to the Company's effective tax rate for the years ended December 31, 2021, and 2020 (1% in 2021 and 12% in 2020) is as follows:

	Years ended December 31,			
	2021		2020	
	%	$ in thousands	%	$ in thousands
Net income / (loss) before tax for the period		328,233		(140,287)
Expected tax (expense) / benefit at the tax rate enacted in the Netherlands (25%)	25%	(82,058)	25%	35,072
Difference in tax rates between the Netherlands and foreign jurisdictions	0%	365	0%	318
Tax effect of:				
Non-deductible expenses	3%	(9,918)	(4)%	(5,850)
Current-year loss for which no deferred tax asset is recognized	5%	(16,266)	(23)%	(31,649)
Current year changes in unrecognized temporary differences, net	(30)%	99,981	5%	6,729
Expiration of net operating loss carryforwards in current year for which no deferred tax asset was recognized	0%	—	(3)%	(4,620)
Recognition of previously unrecognized net operating loss carryforwards	(1)%	4,875	8%	11,560
Recognition of previously unrecognized temporary differences, net	0%	—	4%	5,246
Income tax (expense) / benefit	1%	**(3,021)**	12%	**16,806**
Income tax (expense) / benefit				
Current tax expense		(7)		—
Deferred tax (expense) / benefit		(3,014)		16,806
Income tax (expense) / benefit recorded in the period		**(3,021)**		**16,806**

Non-deductible expenses relate to share-based compensation expenses for an amount of $7.5 million in 2021 (2020: $6.6 million) and fair value loss on derivatives for an amount of $0.8 million in 2020. The fair value loss on contingent consideration affected the effective tax rate by an amount of $2.0 million in 2021 (nil in 2020).

Movement in deferred tax balances:

	Balance at 1 January 2021	Recognized in profit and loss	Directly to equity	Other comprehensive income	Acquisition of subsidiary	Balance at 31 December 2021
			$ in thousands			
Movement in deferred tax balances						
Net operating loss carryforwards	11,560	2,743	(3,047)	(17)	1,750	12,989
Lease liabilities	6,263	(312)	—	—	—	5,951
Accrued expenses and other current liabilities	1,117	194	—	—	—	1,311
Property, plant and equipment	1,072	(101)	—	—	—	971
Intangible assets	902	(100)	—	—	—	802
Inventory	—	148	—	—	—	148
Total deferred tax assets	20,914	2,572	(3,047)	(17)	1,750	22,172
IPR&D asset	—	—	—	716	(15,905)	(15,189)
Right-of-use assets	(4,063)	483	—	—	-	(3,580)
Prepaid expenses	(45)	(41)	—	—	-	(86)
Total deferred tax liabilities	(4,108)	442	—	716	(15,905)	(18,855)
Net deferred tax asset	**16,806**	**3,014**	**(3,047)**	**699**	**(14,155)**	**3,317**

	Balance at 1 January 2020	Recognized in profit and loss	Balance at 31 December 2020
		$ in thousands	
Movement in deferred tax balances			
Net operating loss carryforwards	—	11,560	11,560
Lease liabilities	—	6,263	6,263
Accrued expenses and other current liabilities	—	1,117	1,117
Property, plant and equipment	—	1,072	1,072
Intangible assets	—	902	902
Total deferred tax assets	—	20,914	20,914
Right-of-use assets	—	(4,063)	(4,063)
Prepaid expenses	—	(45)	(45)
Total deferred tax liabilities	—	(4,108)	(4,108)
Net deferred tax asset	**—**	**16,806**	**16,806**

Deferred tax assets and liabilities have not been recognized in respect of the following items, because it is not probable that future taxable profit will be available against which the Company can use the benefits therefrom.

Unrecognized temporary differences:

	Years ended December 31,			
	2021		2020	
	Gross Amount	Tax Effect	Gross Amount	Tax Effect
	$ in thousands			
Unrecognized temporary differences				
Deductible temporary differences	19,660	5,056	22,603	5,651
Net operating loss carryforwards	205,506	53,021	588,217	147,054
Total	225,166	58,077	610,820	152,705
Right-of-use assets	(10,715)	(2,764)	(10,217)	(2,554)
Total	(10,715)	(2,764)	(10,217)	(2,554)
Unrecognized deferred temporary differences, net	**214,451**	**55,313**	**600,603**	**150,151**
Unrecognized deferred temporary differences in relation to equity				
Share issuance costs incurred in relation to public offerings	22,971	4,501	35,030	8,758
Unrecognized deferred tax assets in relation to equity	**22,971**	**4,501**	**35,030**	**8,758**

Netherlands

On May 6, 2021, the CSL Behring Agreement became effective (refer to Note 4 *"Collaboration arrangements and concentration of credit risk"*). The Company recorded $462.4 million of license revenue related to closing the transaction. The Company recorded such revenue in its Dutch tax return related to the 12-month period ended December 31, 2020, which it filed on February 10, 2022. As such, the Company filed a return showing a taxable profit in the Netherlands in 2020, which resulted in the consumption of substantially all of its Dutch net operating losses for the years 2011 to 2018. The Company's remaining Dutch net operating tax losses carried forward relate to 2019 and 2021. The Dutch government on June 4, 2021 enacted legislation, whereby such net operating tax losses can be carried forward indefinitely. The Company expects to continue incurring tax losses for the foreseeable future. As such, the Company concluded that it should not recognize deferred tax assets as of December 31, 2020 in relation to its Dutch net deductible temporary differences in the Netherlands. The Company allocated the tax benefit related to net operating loss carryforwards generated by share issuance cost incurred in 2014, 2015, 2017 and 2018 to share premium. This resulted in an increase of share premium as well as deferred tax expenses of $3.0 million.

A portion of the unrecognized temporary differences in relation to equity relates to share issuance costs incurred in relation to public offerings. Any subsequently recognized tax benefits will be credited directly to share premium. As of December 31, 2021, the tax benefit was $4.5 million ($8.8 million as of December 31, 2020). The change is attributable to recognized tax benefit upon the close of the CSL Behring Agreement and changes in the foreign currency rate.

The Dutch corporate tax rate for fiscal years 2020 and 2021 was 25%. In December 2021, changes were enacted that raised the corporate income tax rate from 25% to 25.8% from 2022 onwards.

A tax reform in December 2018 limited the carryforward of tax losses arising from January 1, 2019, to six years after the end of the respective period. Tax losses incurred prior to this date continue to expire nine years after the end of the respective period.

In June 2021 legislation was enacted allowing for an indefinite carryforward from fiscal year 2022 onwards of existing and future 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.

The Dutch fiscal unity as of December 31, 2021 has an estimated $228.5 million (2020: $588.2 million) of taxable losses that are available for carry forward indefinitely.

The fiscal periods from 2019 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%. In addition, the Company is subject to state income taxes resulting in a combined tax rate of 27.32% for its U.S. operation. As of December 31, 2021, an estimated $39.1 million of net operating losses remain to be carried forward. These losses will expire between 2035 and 2037.

The Company's U.S. operations generated taxable income in the fiscal years 2018 to 2021. Based on the current design of the Company's worldwide operations, 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 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 2018 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 years 2021 was 26.5%, as of January 1, 2022 the tax rate is decreased to 25%.

The Company's French operation has incurred losses since incorporation and is expected to continue incurring tax losses for the foreseeable future.

The French operation as of December 31, 2021 has an estimated $9.1 million of taxable losses that are available for carry forward indefinitely.

16. Basic and diluted earnings per share

Basic earnings per share is calculated by using the weighted average number of ordinary shares outstanding. Diluted earnings per share is 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 for the period ended December 31, 2020, all potentially dilutive ordinary shares would have an anti-dilutive effect, if converted, and thus have been excluded from the computation of loss per share for the year ended December 31, 2020. The antidilutive shares for the period ended December 31, 2020 are presented without giving effect as to whether exercise prices would be above the share price as of December 31, 2020.

Profit / (loss) attributable to ordinary shareholders (diluted):

	Year ended December 31,			
	2021		2020	
	Continuing operations	Total	Continuing operations	Total
	$ in thousands			
Profit / (loss) attributable to ordinary shareholders (basic and diluted)	325,212	325,212	(123,481)	(123,481)

The weighted-average number of ordinary shares (diluted) are summarized below:

	Years ended December 31,	
	2021	2020
	ordinary shares	
Weighted-average number of ordinary shares (basic)	45,986,467	44,466,365
Effect of stock options under 2014 Plan and previous option plans and Nasdaq inducement rules	768,952	—
Effect of non-vested RSUs and earned PSUs	469,092	—
Effect of employee share purchase plan	1,299	—
Weighted-average number of ordinary shares (diluted) at 31 December , 2021	**47,225,810**	**44,466,365**

The following table presents ordinary share equivalents that were excluded from the calculation of diluted net income / (loss) per ordinary share for the years ended December 31, 2021 and 2020 as the effect of their inclusion would have been anti-dilutive:

	Years ended December 31,	
	2021	2020
	ordinary shares	
Anti-dilutive ordinary shares equivalents		
Stock options under 2014 Plans and previous plan	2,553,373	2,673,279
Non-vested RSUs and PSUs	874,455	679,958
Employee share purchase plan	1,842	560
Total anti-dilutive ordinary share equivalents	**3,429,670**	**3,353,797**

17. Leases

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

Lexington, Massachusetts / United States

In July 2013, the Company entered into a lease for a facility in Lexington, Massachusetts, United States. The term of the lease commenced in November 2013, was set for 10 years starting from the 2014 rent commencement date and is non-cancellable. Originally, the lease for this facility had a termination date of 2024. In November 2018, the term was expanded by five years to June 2029. The lease continues to be renewable for two subsequent five-year terms. Additionally, the lease was expanded to include an additional 30,655 square feet within the same facility and for the same term. The lease of the expansion space commenced on June 1, 2019.

The contractually fixed annual increase of lease payments through 2029 for both the extension and expansion lease have been included in the lease payments.

In December 2021, the Company entered into a new lease for an additional facility in Lexington, Massachusetts, United States of approximately 13,501 square feet of space. The lease is expected to commence in the first half of 2022, is set for seven years starting from the rent commencement date and is non-cancellable. 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 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.

On December 1, 2017, the Company entered into an agreement to sub-lease three 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. In February 2020, the Company amended the agreement to sub-lease to take back one of the three floors effective March 1, 2020. The fixed lease payments to be received during the remaining term under the agreement to sub-lease amount to $5.4 million (EUR 4.7 million) as of December 31, 2021.

In May 2021, the Company entered into a sublease agreement to let an additional approximately 1,080 square meters of office space to accommodate the hiring of additional full-time employees. The lease expires in October 2028 and includes an option to break the lease on October 31, 2023.

Other information related to leases is included below for the period ended December 31, 2021:

	Year ended December 31,			
	2021			
	Lexington	Amsterdam	Other	Total
	$ in thousands			
Depreciation charge for right-of-use assets	1,767	959	210	2,936
Interest expense on lease liabilities	2,313	1,584	85	3,982
Variable lease payments not included in the measurement of lease liabilities	591	—	—	591
Total cash outflows	3,455	2,234	476	6,165
Additions to right-of-use assets	—	1,829	284	2,113
Carrying amount of right-of-use assets as of December 31, 2021	13,106	9,385	1,329	23,820

Other information related to leases is included below for the period ended December 31, 2020:

	Year ended December 31, 2020			
	Lexington	Amsterdam	Other	Total
	$ in thousands			
Depreciation charge for right-of-use assets	1,767	762	163	2,692
Interest expense on lease liabilities	2,418	1,455	25	3,898
Variable lease payments not included in the measurement of lease liabilities	526	—	—	526
Total cash outflows	3,360	2,509	144	6,013
Additions to right-of-use assets	—	—	376	376
Carrying amount of right-of-use assets as of December 31, 2020	14,873	9,184	1,033	25,090

Sublease income for the year ended December 31, 2021 was $0.9 million (2020: $0.9 million).

As of December 31, 2021, the lease liability maturity analysis of contractual undiscounted cash flows is as follows:

	Year ended December 31, 2021			
	Lexington	Amsterdam	Other	Total
	$ in thousands			
Not later than 1 year	3,552	2,328	374	6,254
Later than 1 year and not later than 5 years	16,861	9,426	698	26,985
Later than 5 years	11,680	10,252	238	22,170
Total undiscounted lease liabilities at December 31, 2021	**32,093**	**22,006**	**1,310**	**55,409**
Lease liabilities included in the Consolidated Statements of Financial Position as of December 31, 2021	**21,784**	**13,454**	**1,088**	**36,326**
Current	3,552	2,328	374	6,254
Non-current	18,232	11,126	714	30,072

As of December 31, 2020, the lease liability maturity analysis of contractual undiscounted cash flows is as follows:

	Year ended December 31, 2020			
	Lexington	Amsterdam	Other	Total
	$ in thousands			
Not later than 1 year	3,455	2,165	375	5,995
Later than 1 year and not later than 5 years	15,813	8,658	717	25,188
Later than 5 years	16,280	12,807	110	29,197
Total undiscounted lease liabilities at December 31, 2020	**35,548**	**23,630**	**1,202**	**60,380**
Lease liabilities included in the Consolidated Statements of Financial Position as of December 31, 2020	**22,925**	**13,545**	**1,011**	**37,481**
Current	3,455	2,165	375	5,995
Non-current	19,470	11,380	636	31,486

18. 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, such as, Note 3 "*Corlieve transaction*" and Note 5 "*Collaboration arrangements and concentration of credit risk*", amongst others.

19. Related party transactions

In the period ended December 31, 2021, and 2020, executive directors received regular salaries, post-employment benefits and share-based payments. Additionally, non-executive directors received compensation for their services in the form of cash compensation and equity grants.

20. Key management compensation

On October 21, 2021, the Company held an Extraordinary General Meeting of its shareholders and Rachelle Jacques was appointed to the Board of Directors (the "Board") as a non-executive director. Ms. Jacques will also serve as a member of the Audit Committee of the Board effective as of October 21, 2021.

On June 16, 2021, the Company's shareholders voted to approve the reappointment of Mr. David Meek and Ms. Paula Soteropoulos as non-executive directors of the Board. Mr. Meek has been appointed chairman of the Board. Mr. Philip Astley-Sparke did not stand for reappointment and retired from the Board on June 16, 2021.

On June 15, 2021, Christian Klemt was appointed as Chief Financial Officer. Mr. Klemt was the Company's Chief Accounting Officer from August 2017 to June 2021, and he will continue to serve as general manager of the Company's Amsterdam site. Matthew Kapusta, who has been the Company's Chief Executive Officer since December 2016 and had been the Company's Chief Financial Officer from January 2015 to June 2021, will continue to serve as the Company's Chief Executive Officer.

On May 17, 2021, Pierre Caloz was appointed as Chief Operating Officer. Mr. Caloz oversees all manufacturing operations, global CMC development and innovation, supply chain, and facilities.

On September 14, 2020, the Company appointed Ricardo Dolmetsch, Ph.D. as President, Research and Development. Dr. Dolmetsch succeeded Sander van Deventer, M.D., Ph.D., the former Executive Vice President, Research and Product Development. On August 25, 2020, the Company entered into a separation agreement with Robert Gut, M.D., Ph.D., pursuant to which Dr. Gut transitioned from his role as Chief Medical Officer on October 14, 2020, to be appointed a non-executive director of the Board of Directors. On December 1, 2020, at an extraordinary general meeting, the Company's shareholders voted to approve the appointment of Dr. Gut as a non-executive director on the Board of Directors. Dr. Gut had previously been appointed as a non-executive director on the Board of Directors on June 13, 2018 by the Company's shareholders and had resigned as a non-executive director on August 20, 2018, to be appointed as the Company's Chief Medical Officer. On October 24, 2018, at an extraordinary general meeting, the Company's shareholders voted to approve the appointment of Dr. Gut as an executive director on the Board of Directors.

On June 17, 2020, the Company's shareholders voted to approve the appointment of Leonard E. Post, Ph.D., as a non-executive director of the Board of Directors. Dr. Post replaced Dr. David Schaffer, whose term as a non-executive director of the Board of Directors ended on the same date. Dr. Post has also assumed the role of chair of the Company's Research and Development Committee of the Board of Directors.

Board of Directors

The aggregate remuneration of the Board of Directors amounted to $7.7 million for the year ended December 31, 2021 (2020: $9.2 million). Details by director are as follows:

		Year ended December 31, 2021					
		Short-term employee benefits	Share-based payments [1]	Post employment benefits	Board fee	Termination benefits	Total
		$ in thousands					
Matthew Kapusta	Executive	961	4,034	9	—	—	5,004
Total executive director		**961**	**4,034**	**9**	**—**	**—**	**5,004**
David Meek [2]	Non-Executive, Chairman	—	180	—	67	—	247
Philip Astley-Sparke [3]	Non-Executive, former Chairman	—	33	—	40	—	73
Madhavan Balachandran	Non-Executive	—	176	—	49	—	225
Robert Gut	Non-Executive	—	1,142	—	24	—	1,166
Rachelle Jacques [4]	Non-Executive	—	17	—	8	—	25
Jack Kaye	Non-Executive	—	174	—	60	—	234
Leonard Post	Non-Executive	—	257	—	50	—	307
Paula Soteropoulos	Non-Executive	—	174	—	54	—	228
Jeremy P. Springhorn	Non-Executive	—	176	—	63	—	239
Total non-executive directors		**—**	**2,329**	**—**	**415**	**—**	**2,744**

		Year ended December 31, 2020					
		Short-term employee benefits	Share-based payments [1]	Post employment benefits	Board fee	Termination benefits	Total
		$ in thousands					
Matthew Kapusta	Executive	958	3,662	8	—	—	4,628
Total executive director		**958**	**3,662**	**8**	**—**	**—**	**4,628**
Philip Astley-Sparke	Non-Executive, Chairman	—	183	—	90	—	273
Robert Gut [5]	Non-Executive	532	1,607	9	3	639	2,790
Jack Kaye	Non-Executive	—	184	—	60	—	244
Leonard Post [6]	Non-Executive	—	42	—	27	—	69
Paula Soteropoulos	Non-Executive	—	183	—	50	—	233
Madhavan Balachandran	Non-Executive	—	190	—	50	—	240
Jeremy P. Springhorn	Non-Executive	—	190	—	65	—	255
David Meek	Non-Executive	—	221	—	45	—	266
David Schaffer [7]	Non-Executive	—	200	—	—	—	200
Total non-executive directors		**532**	**3,000**	**9**	**390**	**639**	**4,570**

[1] The share-based payment reflects the value of equity settled share options and RSUs expensed during the year, as required by IFRS 2.
[2] Appointed Chairman of the Board of Directors on June 16, 2021.
[3] Term ended on June 16, 2021.
[4] Appointed on October 21, 2021.
[5] No longer executive as from October 14, 2020. Appointed as non-executive on December 1, 2020. Note that the remuneration indicated includes remuneration received as both an executive and non-executive director.
[6] Appointed on June 17, 2020.
[7] Term ended on June 17, 2020.

Management team

The compensation costs of the Management Team (excluding Mr. Kapusta and Dr. Gut) for the years ended December 31, 2021, and 2020 were as follows:

	Short-term employee benefits	Share-based payments	Post employment benefits	Termination benefits	Total
			$ in thousands		
Year ended December 31, 2021	4,765	7,193	167	—	12,125
Year ended December 31, 2020	3,452	7,247	72	673	11,444

Refer to Note 11 "*Share-based compensation*" for further information regarding share-based payment awarded to key management personnel and directors. Expenses resulting from the acceleration of performance share units for executives leaving the Company are presented within share-based payments. Termination benefits include separation pay for the period ended December 31, 2020, that was agreed as part of a termination arrangement.

21. Events after the reporting date

None.

C Company-only Financial Statements uniQure N.V. for the year ended December 31, 2021

uniQure N.V.

Company-Only Statement of Financial Position

	Note	December 31, 2021	December 31, 2020
		$ in thousands	
Non-current assets			
Intangible fixed assets	3	27,132	—
Financial fixed assets	4	508,016	111,656
Total fixed assets		**535,148**	**111,656**
Current assets			
Receivables from affiliated entities		30,879	21,236
Other current assets		324	243
Cash and cash equivalents		102,892	114,928
Total current assets		**134,095**	**136,407**
Total assets		**669,243**	**248,063**
Current liabilities			
Payable to affiliated entity		32,040	—
Accrued expenses and other current liabilities		7,646	117
Total current liabilities		**39,686**	**117**
Non-current liabilities			
Non-current liabilities	5	30,388	—
Total non-current liabilities		**30,388**	**—**
Total liabilities		**70,074**	**117**
Shareholders' equity			
Share capital		2,623	2,508
Share premium		814,013	778,694
Legal reserves		(31,296)	6,885
Other reserves		137,548	108,789
Accumulated deficit		(323,719)	(648,930)
Total shareholders' equity	**6**	**599,169**	**247,946**
Total liabilities and shareholders' equity		**669,243**	**248,063**

The accompanying notes are an integral part of these company-only financial statements.

uniQure N.V.

Company-Only Statement of Profit or Loss

	Years ended December 31,	
	2021	2020
	$ in thousands	
Share in results from participating interests	348,083	(93,257)
Other income and expenses	(22,871)	(30,224)
Net profit / (loss)	**325,212**	**(123,481)**

The accompanying notes are an integral part of these company-only financial statements.

Notes to the Company-only Financial Statements

1. General

uniQure N.V. ("uniQure" or the "Company") was incorporated on January 10, 2012.

The Company-only financial statements are part of the 2021 financial statements of uniQure N.V. On February 10, 2014, the Company converted from a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) incorporated under the laws of the Netherlands 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 the parent company of the uniQure group and is listed on Nasdaq. The Company provides intercompany funding to its operational subsidiaries in the form of loans and equity financing. The Company conducts its business through its Dutch subsidiary uniQure biopharma B.V. ("Biopharma") and its French subsidiary Corlieve Therapeutics SAS. Biopharma owns the U.S. operating entity uniQure Inc. The Company issued a joint and several liability statements per Section 2:403 of the Dutch Civil Code, for the benefit of its Dutch subsidiaries, thereby establishing a contingent liability.

uniQure N.V. forms a fiscal unity with its Dutch subsidiaries for income tax purposes. In accordance with the standard conditions, a company and its subsidiaries that form the fiscal unity are jointly and severally liable for tax payable by the fiscal unity. The allocation of the tax expense will be considered at the time when the Company will be eligible to process tax expenses.

2. Basis of preparation

These Company-only financial statements have been prepared in accordance with Title 9, Book 2 of the Dutch Civil Code. For setting the principles for the recognition and measurement of assets and liabilities and determination of the result for its Company-only financial statements, uniQure makes use of the option provided in Section 2:362 (8) of the Dutch Civil Code. This means that the principles for the recognition and measurement of assets and liabilities and determination of the result are the same as those applied in the consolidated financial statements and are based on International Financial Reporting Standards as adopted by the European Union for the financial year ended December 31, 2021.

Please see the notes to the consolidated financial statements for a description of these recognition and measurement principles, including those for foreign currency transactions and intra-group transactions. For an appropriate interpretation of these separate financial statements, the separate financial statements should be read in conjunction with the consolidated financial statements.

With reference to the Company-only income statement of uniQure, use has been made of the exemption pursuant to Section 2:402 of the Dutch Civil Code.

In the Company-only financial statements, participating interests in group companies and long-term loan receivables are presented at their net asset value, being the equity of the respective participating interest in group companies. If the net asset value of a participating interest in group companies is negative, then the carrying amount of the long-term loan receivable from that participating interest in group companies is reduced with the negative equity amount. The Company adopted a policy whereby a reduction of negative equity will first be recorded as a reversal of a reduction of a long-term loan receivable's carrying amount before reversing reductions of the carrying amount of participating interests in group companies.

The Company-only financial statements have been prepared on a going concern basis based on the Company's cash and cash equivalents as of December 31, 2021, and the Company's budgeted cash flows for the twelve months following the issuance date.

3. Intangible fixed assets

	Goodwill
	$ in thousands
Cost	—
Balance at January 1, 2020	—
Balance at December 31, 2020	**—**
Balance at January 1, 2021	—
Acquisitions through business combination	28,409
Effect of movement in exchange rates	(1,277)
Balance at December 31, 2021	**27,132**
Accumulated amortization and impairment losses	
Balance at January 1, 2020	—
Balance at December 31, 2020	**—**
Balance at January 1, 2021	—
Balance at December 31, 2021	**—**
Carrying amounts	
Balance at January 1, 2020	—
Balance at December 31, 2020	—
Balance at December 31, 2021	27,132

Goodwill has been recognized in connection with the Company's acquisition of Corlieve Therapeutics SAS on July 30, 2021. Further disclosures relating to goodwill can be found in Note 3 "Corlieve Transaction" and Note 7 "Intangible Assets" to the consolidated financial statements.

4. Financial fixed assets

uniQure N.V. holds participating interests in the following group companies:

Name	Percentage of shares	Statutory seat
uniQure biopharma B.V.	100%	Amsterdam
uniQure IP B.V.	100%	Amsterdam
Corlieve Therapeutics SAS	100%	Paris

	Investment in participating interests
	$ in thousands
Cost [1)]	686,477
Accumulated share in results from participating interests, including currency translation effects [1)]	(472,761)
Share in results from participating interests for the period, including currency translation effects [1)]	(102,060)
Carrying amount January 1, 2021	**111,656**
Acquisition of shares of Corlieve Therapeutics, net of goodwill acquired (see Note 3 " Corlieve Transaction" to the consolidated financial statements)	49,654
Investments	22,392
Share in results from participating interests for the period [2)]	348,083
Currency translation effects	(23,769)
Carrying amount December 31, 2021	**508,016**
Cost [1)]	703,811
Accumulated share in results from participating interests, including currency translation effects [1)]	(520,109)
Share in results from participating interests for the period, including currency translation effects [1)]	324,314
Carrying amount December 31, 2021	**508,016**

1) Translated into the presentation currency at the December 31, 2021 and December 31, 2020 exchange rate, respectively.
2) Translated into the presentation currency at monthly average exchange rates for the year ended December 31, 2021.

Services provided by employees of uniQure N.V. group are partially compensated through the issuance of ordinary shares of uniQure N.V. The Company records any share-based compensation incurred by its participating interests as an investment into the respective participating interest together with a corresponding increase of its share premium.

During the year ended December 31, 2021 the Company received $32.8 million (EUR 28.9 million) in cash from uniQure biopharma B.V. As of December 31, 2021, the Company has an outstanding payable of $32.0 million with uniQure biopharma B.V. (December 31, 2020: receivable of $0.8 million), presented in payable to affiliated entity, respectively receivables from affiliated entities in the Company-Only Statement of Financial Position.

During the year ended December 31, 2021 the Company advanced $2.3 million (EUR 2.1 million) in cash to Corlieve Therapeutics SAS. As of December 31, 2021, the Company has an outstanding receivable of $2.3 million with Corlieve Therapeutics SAS. (December 31, 2020: nil), presented in receivables from affiliated entities in the Company-Only Statement of Financial Position.

5. Non-current liabilities

	As of December 31,	
	2021	2020
	$ in thousands	
Contingent consideration	29,542	—
Other non-current liabilities	846	—
Total non-current liabilities	**30,388**	**—**

Contingent consideration has been recognized in connection with the Company's acquisition of Corlieve Therapeutics SAS on July 30, 2021. Further disclosures relating to the contingent consideration can be found in Note 3 "Corlieve Transaction" and Note 4 "Financial Risk Management" to the consolidated financial statements.

6. Shareholders' equity

During the period covered by these Company-only financial statements uniQure had a single class of shares which are denominated as ordinary shares.

	Attributable to equity holders of the Company						
	Share Capital		Legal Reserves				
	No. of shares	Amount	Share Premium	Currency translation differences	Other Reserves	Accumulated deficit	Total equity
	$ in thousands (except number of shares)						
Balance at January 1, 2021	**44,777,799**	**2,742**	**778,694**	**6,886**	**108,555**	**(648,931)**	**247,946**
Net income	—	—	—	—	—	325,212	325,212
Other comprehensive loss	—	—	—	(38,182)	—	—	(38,182)
Total comprehensive income	—	—	—	(38,182)	—	325,212	287,030
Share capital translation result	—	(210)	—	—	210	—	—
Issuance of ordinary shares	921,730	55	29,509	—	—	—	29,564
Income tax benefit of past share issuance cost	—	—	3,047	—	—	—	3,047
Exercises of share options	241,496	15	2,638	—	—	—	2,653
Restricted and performance share units distributed during the period	352,886	21	(21)	—	—	—	—
Share-based compensation expense	—	—	—	—	28,783	—	28,783
Issuance of ordinary shares relating to employee stock purchase plan	4,724	—	146	—	—	—	146
Balance at December 31, 2021	**46,298,635**	**2,623**	**814,013**	**(31,296)**	**137,548**	**(323,719)**	**599,169**

Further disclosures relating to the capital contributions and share-based payment expenses can be found in Notes 10 "*Shareholder's equity*" and 11 "*Share-based compensation*" to the consolidated financial statements.

As of December 31, 2021, a total of 46,298,635 ordinary shares were issued and paid up in full at a nominal value of €0.05 per share (2020: 44,777,799 ordinary shares). Of these, 1,520,836 ordinary shares were issued during the year (2020: 1,065,845 ordinary shares).

The total proceeds for issuance of shares during the period amount to $32.4 million (2020: $7.4 million).

The Company proposes to the General Meeting of Shareholders to allocate the net income for the twelve-month period ended December 31, 2021, of $325.2 million to the accumulated deficit.

7. Compensation of the Board of Directors

The executive director (two executive directors during 2020 through October 14, 2020) of uniQure N.V. is employed by a subsidiary of the Company. As of December 31, 2021, the Company recorded an amount of $0.0 million (December 31, 2020: $0.0 million) for social security and payroll tax obligations, in relation to the Board of Directors. Personal loans or guarantees have not been provided by any member of the uniQure group to any member(s) of the Board of Directors.

Refer to Note 20 "*Key management compensation*" of the consolidated financial statements.

8. Audit fees

The following table sets forth the fees, for each of the years indicated, when the work was performed by the Company's independent auditors and the percentage of each of the fees out of the total fees when the work was performed by the independent auditors.

	Year ended December 31, 2021			
	KPMG Accountants N.V. $ in thousands	%	Other KPMG network $ in thousands	%
Audit of the financial statements	1,212	91%	180	100%
Other audit services	114	9%	—	0%
Total	**1,326**	**100%**	**180**	**100%**

	Year ended December 31, 2020			
	KPMG Accountants N.V. $ in thousands	%	Other KPMG network $ in thousands	%
Audit of the financial statements	849	91%	180	100%
Other audit services	85	9%	—	0%
Total	**934**	**100%**	**180**	**100%**

The fees listed above relate to the procedures applied to the Company and its consolidated group entities by its independent auditor as referred to in Section 1, subsection 1 of the Dutch Accounting Firms Oversight Act (Dutch acronym: Wta), as well as by Dutch and foreign-based accounting firms, including their tax services and advisory groups. Other audit services in 2021 include $0.1 million related to the March and April 2021 at the market trading program and in 2020 include $0.1 million related to the March 2020 at the market trading program.

Signing of the Financial Statements

Amsterdam, April 29, 2022

Executive Director

/s/ Matthew Kapusta
Matthew Kapusta, Chief Executive Officer

Non-Executive Directors

/s/ David Meek
David Meek, Chairman

/s/ Madhavan Balachandran
Madhavan Balachandran, Member

/s/ Robert Gut
Robert Gut, Member

/s/ Rachelle Jacques
Rachelle Jacques, Member

/s/ Jack Kaye
Jack Kaye, Member

/s/ Leonard Post
Leonard Post, Member

/s/ Paula Soteropoulos
Paula Soteropoulos, Member

/s/ Jeremy P. Springhorn
Jeremy P. Springhorn, Member

D Other Information

Statutory Arrangement Concerning the Appropriation of Profit

The statutory arrangements regarding the appropriation of profit are described in article 10.1 of the articles of association:

10.1. **Profit and loss. Distributions on Shares.**

10.1.1. The Board will keep a share premium reserve and profit reserve for the Shares.

10.1.2. The Company may make distributions on Shares only to the extent that its shareholders' equity exceeds the sum of the paid-up and called-up part of the capital and the reserves which must be maintained by law.

10.1.3. Distributions of profit, meaning the net earnings after taxes shown by the adopted Annual Accounts, shall be made after the adoption of the Annual Accounts from which it appears that they are permitted, without prejudice to any of the other provisions of these articles of association.

10.1.4. The Board may determine that any amount out of the profit shall be added to the reserves.

10.1.5. The profit remaining after application of article 10.1.4 shall be at the disposal of the General Meeting, which may resolve to carry it to the reserves or to distribute it among the Shareholders.

10.1.6. On a proposal of the Board the General Meeting may resolve to distribute to the Shareholders a dividend in the form of Shares in the share capital of the Company.

10.1.7. Subject to the other provisions of this article 10.1 the General Meeting may, on a proposal made by the Board resolve to make distributions to the Shareholders to the debit of one (1) or several reserves which the Company is not prohibited from distributing by virtue of the law.

10.1.8. No dividends shall be paid on Shares held by the Company in its own share capital, unless such Shares are encumbered with a right of use and enjoyment (*vruchtgebruik*) or pledge.

Independent auditor's report

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

Report on the audit of the financial statements 2021 included in the Annual Report

Our opinion

In our opinion:

— the accompanying consolidated financial statements give a true and fair view of the financial position of uniQure N.V. as at December 31, 2021 and of its result and its cash flows for the year then ended, in accordance with International Financial Reporting Standards as adopted by the European Union (EU-IFRS) and with Part 9 of Book 2 of the Dutch Civil Code.

— the accompanying company financial statements give a true and fair view of the financial position of uniQure N.V. as at December 31, 2021 and of its result for the year then ended in accordance with Part 9 of Book 2 of the Dutch Civil Code.

What we have audited

We have audited the financial statements 2021 of uniQure N.V. (the 'Company') based in Amsterdam, the Netherlands. The financial statements include the consolidated financial statements and the company financial statements.

The consolidated financial statements comprise:

1 the consolidated statement of financial position as at December 31, 2021;

2 the following consolidated statements for 2021: the statement of profit and loss and other comprehensive income or loss, changes in equity and cash flows; and

3 the notes comprising a summary of the significant accounting policies and other explanatory information.

The company financial statements comprise:

1 the company-only statement of financial position as at December 31, 2021;

2 the company-only statement of profit or loss for 2021; and

3 the notes comprising a summary of the accounting policies and other explanatory information.

Basis for our opinion

We conducted our audit in accordance with Dutch law, including the Dutch Standards on Auditing. Our responsibilities under those standards are further described in the 'Our responsibilities for the audit of the financial statements' section of our report.

We are independent of uniQure N.V. in accordance with the 'Verordening inzake de onafhankelijkheid van accountants bij assurance-opdrachten' (ViO, Code of Ethics for Professional Accountants, a regulation with respect to independence) and other relevant independence regulations in the Netherlands. Furthermore, we have complied with the 'Verordening gedrags- en beroepsregels accountants' (VGBA, Dutch Code of Ethics).

Our audit procedures were determined in the context of our audit of the financial statements as a whole. Our observations in respect of going concern, fraud and non-compliance with laws and regulations, and the key audit matters should be viewed in that context and not as separate opinions or conclusions.

We believe the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Audit approach

Summary

Materiality
— Materiality of USD 5.0 million — 3% of loss before tax

Group audit
— Audit coverage of 100% of total assets — Audit coverage of 100% of total expenses

Going concern and Fraud/Noclar
— Going concern: no significant going concern risks identified — Fraud & Non-compliance with laws and regulations (Noclar): risk of management override of controls

Key audit matters
Evaluation of the acquisition of Corlieve as a business combination

Opinion
Unqualified

Materiality

Based on our professional judgement we determined the materiality for the financial statements as a whole at USD 5.0 million (2020: USD 4.2 million). The materiality is determined with reference to loss before tax (3%). We consider loss before tax as the most appropriate benchmark, based on our analysis of the common information needs of users of the financial statements and

stakeholders of the Company. On this basis, and given the stage of the Company's research & development projects, we believe that loss before tax is the most relevant metric to determine materiality. We have also taken into account misstatements and/or possible misstatements that in our opinion are material for the users of the financial statements for qualitative reasons.

We agreed with the Board of Directors that misstatements identified during our audit in excess of USD 250 thousand would be reported to them, as well as smaller misstatements that in our view must be reported on qualitative grounds.

Scope of the group audit

uniQure N.V. is at the head of a group of components. The financial information of this group is included in the financial statements of uniQure N.V.

Our group audit mainly focused on significant components with identified risk of material misstatement.

We have:

— performed audit procedures ourselves at the holding, uniQure N.V. and group components uniQure biopharma B.V. and Corlieve Therapeutics SAS; and

— made use of the work of a component auditor for the audit of uniQure Inc..

For the residual population not in scope we performed analytical procedures in order to corroborate that our scoping remained appropriate throughout the audit.

In view of restrictions on the movement of people across borders due to Covid-19, we included in our audit approach various virtual meetings and a virtual file review with the component auditor to evaluate the component auditors' communications and the adequacy of its work.

By performing the procedures mentioned above at group components, together with additional procedures at group level, we have been able to obtain sufficient and appropriate audit evidence about the group's financial information to provide an opinion about the financial statements.

The audit coverage as stated in the section summary is 100% on both total assets and total expenses.

Audit response to going concern – no significant going concern risks identified

The Board of Directors has performed its going concern assessment and has not identified any significant going concern risks. To assess the Board of Directors' assessment, we have performed, inter alia, the following procedures :

- we considered whether the Board of Directors' assessment of the going concern risks includes all relevant information of which we are aware as a result of our audit;
- we analyzed the Company's financial position as at year-end and compared it to the previous financial year in terms of indicators that could identify significant going concern risks.

The outcome of our risk assessment procedures did not give reason to perform additional audit procedures on management's going concern assessment.

Audit response to the risk of fraud and non-compliance with laws and regulations

In chapter 3, Risk Factors of the Report of the Board of Directors, the Board of Directors describes its risk assessment in respect of the risk of fraud and non-compliance with laws and regulations.

As part of our audit, we have gained insights into the Company and its business environment, and assessed the design and implementation and, where considered appropriate, tested the operating

effectiveness of the Company's risk management in relation to fraud and non-compliance. Our procedures included, among other things, assessing the Company's code of conduct, whistleblowing procedures, incidents register and its procedures to investigate indications of possible fraud and non-compliance. Furthermore, we performed relevant inquiries with the Board of Directors and other relevant functions, such as the Chief Financial Officer, Chief Legal Officer and the Chief Business Officer. As part of our audit procedures we:

- assessed other positions held by Board of Directors and/or other employees and paid special attention to procedures and governance;
- evaluated investigation reports on indications of possible fraud and non-compliance if any;
- evaluated correspondence with supervisory authorities and regulators if applicable.

In addition, we performed procedures to obtain an understanding of the legal and regulatory frameworks that are applicable to the Company and identified the following areas as those most likely to have a material effect on the financial statements:

- Pharmaceutical regulation (reflecting the Company's involvement in the development of gene therapies);
- Employment legislation (reflecting the Company's activities involving a highly skilled work force); and
- Health and safety regulation (reflecting the nature of the Company's production and distribution processes).

We evaluated the fraud and non-compliance risk factors to consider whether those factors indicate a risk of material misstatement in the financial statements.

Based on the above and on the auditing standards, we identified the following fraud risks that are relevant to our audit, including the relevant presumed risks laid down in the auditing standards, and responded as follows:

— **Management override of controls (a presumed risk)**

Risk:

- Management is in a unique position to manipulate accounting records and prepare fraudulent financial statements by overriding controls that otherwise appear to be operating effectively.

Responses:

- We evaluated the design and the implementation and, where considered appropriate, tested the operating effectiveness of internal controls that mitigate fraud and non-compliance risks, such as processes related to journal entries, estimates and non-routine transactions.
- We performed a data analysis of high-risk journal entries and evaluated key estimates and judgments for bias by the Company's management. Where we identified instances of unexpected journal entries or other risks through our data analytics, we performed additional audit procedures to address each identified risk, including testing of transactions back to source information.
- We incorporated elements of unpredictability in our audit, including detailed testing of certain specific research and development contracts and the related prepaid and accrual position and recognized expenses.

We assessed the presumed fraud risk on revenue recognition as irrelevant, because of the current phase of the Company, being before the launch of a commercial product and therefore product based revenues.

Our procedures to address the identified risks of fraud did not result in a key audit matter.

We communicated our risk assessment, audit responses and results to the Audit Committee of the Board of Directors.

Our audit procedures did not reveal indications and/or reasonable suspicion of fraud and non-compliance that are considered material for our audit.

Our key audit matters

Key audit matters are those matters that, in our professional judgement, were of most significance in our audit of the financial statements. We have communicated the key audit matters to the Board of Directors. The key audit matters are not a comprehensive reflection of all matters discussed.

Compared to last year the key audit matter with respect to the amendment of the collaboration and license agreement is no longer assessed as a key audit matter in the current year as the amendment and the related accounting assessment occurred only in 2020. Furthermore, compared to last year the key audit matter with respect to the business acquisition has been added.

Evaluation of the acquisition of Corlieve as a business combination

Description

As discussed in Notes 2.3.5 and 3 to the consolidated financial statements, the Company acquired 97.7% of the outstanding ordinary shares of Corlieve for a total purchase price of EUR 65.8 million. The Company applied the applicable accounting guidance which requires the acquirer to assess whether the acquisition should be accounted for as an asset acquisition or a business combination.

We identified the evaluation of the acquisition as a business combination to be a key audit matter due to the size of the balances as well as the significant judgement required in assessing if the acquired company meets the definition of a business combination. This evaluation led to a significant risk being identified relating to the Company's process of evaluating the transaction under the two-step framework as defined in IFRS 3. First step involves assessing whether or not substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets as there is judgement involved. Second step involves assessing whether an input, including the workforce and the identification of intangible assets acquired, and a substantive process exists that together significantly contribute to the ability to create outputs.

Our response

The primary procedures we performed to address the key audit matter included the following:

- We evaluated the design and tested the operating effectiveness of certain internal controls related to the business combination process, including controls related to technical accounting review and over the completeness of assets and liabilities acquired.
- We evaluated the calculation prepared by the Company in order to determine whether substantially all of the fair value of the gross assets acquired were concentrated in a single identifiable asset and assessed the qualitative and quantitative factors in determining a business combination as there is no bright line and judgment is involved.

— We read the sale and purchase agreement and performed inquires with management and business development personnel to understand the business rationale for acquiring Corlieve.
— We read the employment terms and inquired of management and business development personnel to challenge management's judgement that the employees acquired represent an organized workforce.
— We involved valuation professionals with specialized skills and knowledge, who assisted us in evaluating the Company's identification of intangible assets acquired.

Our observation

Based on the procedures performed regarding determining whether the Corlieve acquisition should be treated as a business combination or asset acquisition, we consider that management's assessment to treat this as a business combination is reasonable and that the business combination disclosures are adequate.

Report on the other information included in the Annual Report

In addition to the financial statements and our auditor's report thereon, the Annual Report contains other information.

Based on the following procedures performed, we conclude that the other information:

— is consistent with the financial statements and does not contain material misstatements; and
— contains the information as required by Part 9 of Book 2 of the Dutch Civil Code for the management report and other information.

We have read the other information. Based on our knowledge and understanding obtained through our audit of the financial statements or otherwise, we have considered whether the other information contains material misstatements.

By performing these procedures, we comply with the requirements of Part 9 of Book 2 of the Dutch Civil Code and the Dutch Standard 720. The scope of the procedures performed is less than the scope of those performed in our audit of the financial statements.

The Board of Directors of uniQure N.V. is responsible for the preparation of the other information, including the information as required by Part 9 of Book 2 of the Dutch Civil Code.

Report on other legal and regulatory requirements

Engagement

We were engaged by the General Meeting of Shareholders as auditor of uniQure N.V. on May 10, 2019, as of the audit for the year 2019 and have operated as statutory auditor ever since that financial year.

Description of responsibilities regarding the financial statements

Responsibilities of the Board of Directors of uniQure N.V for the financial statements

The Board of Directors of uniQure N.V. is responsible for the preparation and fair presentation of the financial statements in accordance with EU-IFRS and Part 9 of Book 2 of the Dutch Civil Code. Furthermore, Board of Directors of uniQure N.V. is responsible for such internal control as

management determines is necessary to enable the preparation of the financial statements that are free from material misstatement, whether due to fraud or error.

As part of the preparation of the financial statements, Board of Directors is responsible for assessing the uniQure N.V.'s ability to continue as a going concern. Based on the financial reporting frameworks mentioned, Board of Directors should prepare the financial statements using the going concern basis of accounting unless the Board of Directors either intends to liquidate uniQure N.V. or to cease operations, or has no realistic alternative but to do so. Board of Directors should disclose events and circumstances that may cast significant doubt on the Company's ability to continue as a going concern in the financial statements.

The Audit Committee of the Board of Directors is responsible for overseeing the uniQure N.V.'s financial reporting process.

Our responsibilities for the audit of the financial statements

Our objective is to plan and perform the audit engagement in a manner that allows us to obtain sufficient and appropriate audit evidence for our opinion.

Our audit has been performed with a high, but not absolute, level of assurance, which means we may not detect all material errors and fraud during our audit.

Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements. The materiality affects the nature, timing and extent of our audit procedures and the evaluation of the effect of identified misstatements on our opinion.

A further description of our responsibilities for the audit of the financial statements is included in the appendix of this auditor's report. This description forms part of our auditor's report.

Amstelveen, April 29, 2022

KPMG Accountants N.V.

B.S. Geerling

Appendix:
Description of our responsibilities for the audit of the financial statements

Appendix

Description of our responsibilities for the audit of the financial statements

We have exercised professional judgement and have maintained professional skepticism throughout the audit, in accordance with Dutch Standards on Auditing, ethical requirements and independence requirements. Our audit included among others:

— identifying and assessing the risks of material misstatement of the financial statements, whether due to fraud or error, designing and performing audit procedures responsive to those risks, and obtaining audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than the risk resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control;

— obtaining an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the uniQure N.V.'s internal control;

— evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by Board of Directors of uniQure N.V.;

— concluding on the appropriateness of Board of Directors of uniQure N.V.'s use of the going concern basis of accounting, and based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on uniQure N.V.'s ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause a company to cease to continue as a going concern;

— evaluating the overall presentation, structure and content of the financial statements, including the disclosures; and

— evaluating whether the financial statements represent the underlying transactions and events in a manner that achieves fair presentation.

We are solely responsible for the opinion and therefore responsible to obtain sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the group to express an opinion on the financial statements. In this respect we are also responsible for directing, supervising and performing the group audit.

We communicate with the Audit Committee of the Board of Directors regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant findings in internal control that we identify during our audit.

We provide the Audit Committee of the Board of Directors with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, related safeguards.

From the matters communicated with the Audit Committee of the Board of Directors, we determine the key audit matters: those matters that were of most significance in the audit of the financial statements. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter or when, in extremely rare circumstances, not communicating the matter is in the public interest.