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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

OR

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

For the transition period from to

Commission file number: 001-36294

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

The Netherlands
(Jurisdiction of incorporation or organization)

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

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

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

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

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

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K ☐

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

Large accelerated filer ☐	Accelerated filer ☒	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐	Emerging growth company ☒

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

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

The aggregate market value of the voting and non-voting ordinary shares held by non-affiliates of the registrant as of December 31, 2017 was $613.9 million, based on the closing price reported as of December 29, 2017 on the NASDAQ Global Select Market.

As of March 9, 2018, the registrant had 31,683,988 ordinary shares, par value €0.05, outstanding.

The documents incorporated by reference are as follows:

Portions of the registrant's definitive Proxy Statement for its 2018 Annual Meeting of Shareholders to be filed with the Securities and Exchange Commission no later than April 30, 2018 and to be delivered to shareholders in connection with the 2018 Annual Meeting of Shareholders, are herein incorporated by reference in Part III of this Annual Report on Form 10-K.

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SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains “forward-looking statements” as defined under federal securities laws. Forward-looking statements are based on our current expectations of future events and many of these statements can be identified using terminology such as “believes,” “expects,” “anticipates,” “plans,” “may,” “will,” “projects,” “continues,” “estimates,” “potential,” “opportunity” and similar expressions. These forward-looking statements may be found in Part I, Item 1A “Risk Factors,” Part I, Item 1 “Business,”, Part II, Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and other sections of this Annual Report on Form 10-K.

Forward-looking statements involve risks and uncertainties that could cause actual results to differ materially from those projected or implied. The most significant factors known to us that could materially adversely affect our business, operations, industry, financial position or future financial performance include those discussed in Part I, Item 1A “Risk Factors,” as well as those discussed in Part II, Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this report, as well as other factors which may be identified from time to time in our other filings with the Securities and Exchange Commission (“SEC”), or in the documents where such forward-looking statements appear. You should carefully consider that information before you make an investment decision.

You should not place undue reliance on these statements, which speak only as of the date that they were made. Our actual results or experience could differ significantly from those anticipated in the forward-looking statements and from historical results, due to the risks and uncertainties described in our Annual Report on Form 10-K including in “Part I, Item 1A. Risk Factors,” as well as others that we may consider immaterial or do not anticipate at this time. These cautionary statements should be considered in connection with any written or oral forward-looking statements that we may make in the future or may file or furnish with the SEC. We do not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of the filing of this Annual Report on Form 10-K to reflect later events or circumstances or to reflect the occurrence of unanticipated events. All forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements.

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

Part I

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

Item 1. Business.

Overview

We are a leader in the field of gene therapy, seeking to develop single treatments with potentially curative results for patients suffering from genetic and other devastating diseases. We are advancing a focused pipeline of innovative gene therapies that have been developed both internally and through our collaboration, focused on cardiovascular diseases, with Bristol Myers-Squibb ("BMS"). We have established clinical proof-of-concept in our lead indication, hemophilia B, and achieved preclinical proof-of-concept in Huntington's disease. We believe our validated adeno-associated virus ("AAV") technology platform and proprietary insect cell-based manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost and time to market. We produce our AAV-based gene therapies in our own facilities with a proprietary, commercial-scale, manufacturing process, which is compliant with established current Good Manufacturing Practices ("GMP"). We believe our Lexington, Massachusetts-based facility is one of the world's leading, most versatile, gene therapy manufacturing facilities.

AMT-061 is our lead product candidate for the treatment of patients with severe and moderately-severe hemophilia B, a serious and rare inherited disease in males characterized by insufficient blood clotting. In October 2017, we announced plans to advance AMT-061, which includes an AAV5 vector carrying the FIX-Padua transgene, into a pivotal study. AMT-061 and AMT-060, the latter of which we previously investigated in a Phase I/II study, are identical in structure apart from two nucleotide substitutions in the coding sequence for the Factor IX ("FIX") protein. Nonclinical studies of non-human primates have demonstrated the FIX-Padua transgene incorporated in AMT-061 expresses protein with approximately six to eight-fold increase in activity compared to the wild-type FIX transgene used in AMT-060. We believe that recently completed manufacturing comparability studies, conducted in accordance with a protocol generally agreed to by the FDA and EMA, demonstrated material comparability between AMT-060 and AMT-061.

We achieved general agreement with the U.S. Food and Drug Administration ("FDA") and the European Medicines Agency ("EMA") on our proposed development plan for AMT-061. The pivotal study is expected to be an open-label, single-dose, multi-center, multi-national trial investigating the efficacy and safety of AMT-061. The FDA has agreed that AMT-061 will be included under the existing Breakthrough Therapy designation and Investigational New Drug ("IND") for AMT-060. The EMA also has agreed that AMT-061 will be included under the current Priority Medicines ("PRIME") designation. Based on our meetings with the FDA and EMA, we plan to expeditiously advance AMT-061 into a pivotal study in 2018 for patients with severe and moderately severe hemophilia B.

In 2017, we acquired a patent family that broadly covers the FIX-Padua variant and its use in gene therapy for the treatment of coagulopathies, including hemophilia B. This family includes a patent issued in the U.S., as well as pending patent applications in Europe and Canada.

In July 2017, we reacquired development and commercial rights in Europe and other select territories for our gene therapy in hemophilia B from Chiesi, our previous co-development partner. We currently own global commercialization rights to our hemophilia B gene therapy.

AMT-130 is our lead product candidate for the treatment of Huntington's disease. Huntington's disease is a severe genetic neurodegenerative disorder causing loss of muscle coordination, behavioral abnormalities and cognitive decline, resulting in complete physical and mental deterioration. AMT-130 consists of an AAV5 vector carrying an engineered micro-RNA which silences the Huntingtin gene. We received orphan drug designation for AMT-130 for the treatment of Huntington's disease in the United States and the European Union and hold global commercialization rights to the program.

In multiple preclinical studies of AMT-130, we showed widespread AAV5 vector distribution and extensive silencing of the human mutant huntingtin gene ("HTT"). In April 2017, we announced positive data from a preclinical study in mini pigs, among the largest Huntington's disease animal models available for testing, demonstrating that a single administration of AMT-130 resulted in significant and dose-dependent reductions in HTT in all regions of the brain,

including the cortex. We recently completed dosing of a Good Laboratory Practices ("GLP") toxicology study in non-human primates with AMT-130.

In April 2015, we entered into an agreement with BMS that provides exclusive access to our gene therapy technology platform for multiple targets focused on cardiovascular diseases. The collaboration includes our proprietary gene therapy candidate, AMT-126, for congestive heart failure. Congestive heart failure, which affects 26 million people worldwide, is the inability of the heart to supply sufficient blood flow to meet bodily demand for oxygen and nutrition. AMT-126 aims to restore the heart's ability to synthesize S100A1, a calcium sensor and master regulator of heart function, and thereby improve clinical outcomes for patients with congestive heart failure. In July 2015, three additional cardiovascular targets were designated for development by BMS.

On August 2017, we announced that preliminary data from a study of AMT-126 in large animals demonstrated both DNA delivery and human S100A1 expression in the myocardium after treatments with product produced from our proprietary insect cell, baculovirus manufacturing process. Based on this finding and others, a preclinical study of AMT-126 was initiated in January 2018 to assess heart function in a diseased pig model. Pending data from this study, which is expected later this year, we and BMS plan to initiate a safety and toxicology study to enable an Investigational New Drug submission to the U.S. Food and Drug Administration.

Our Mission and Strategy

Our mission is to build a leading, fully-integrated, global gene therapy company that leverages our validated technology and manufacturing platforms to accelerate the delivery of transformative therapies to patients in serious need. Our strategy to achieve this mission is to:

Advance AMT-061, a potentially best-in-class treatment of hemophilia B, to patients. AMT-061 combines the advantages of AAV5 with an enhanced Padua-FIX transgene, and may provide optimized clinical and tolerability benefits to all, or nearly all patients with hemophilia B. We have achieved alignment with the FDA and EMA on what we believe is an expedited clinical development plan. We expect to initiate our pivotal study program in 2018.

Maintain our leadership position in commercial-scale AAV manufacturing. We established current GMP, commercial-scale manufacturing capabilities for AAV-based gene therapies in our state-of-the-art Lexington, MA facility. We successfully produced batches of multiple gene therapy products using the same fundamental manufacturing process, methods and controls. We believe the modularity of our platform provides us with distinct advantages, including the potential for reduced development risk and faster times to market.

Build a pipeline of gene therapy programs focused on rare and orphan diseases targeting liver-directed, central-nervous system ("CNS") and cardiovascular diseases. Beyond our lead clinical program for hemophilia B, we have a pipeline of additional AAV-based gene therapy programs in various stages of preclinical development. We are leveraging our leading technology platform, which includes novel vectors, promoters and manufacturing capabilities, to develop gene therapies primarily focused on rare, monogenic liver-directed, and CNS diseases as well as cardiovascular diseases.

Leverage the favorable immunogenicity profile of AAV5-based gene therapies to develop multiple products. We have demonstrated AAV5-based gene therapies to be generally safe and well-tolerated in three clinical trials conducted in 22 patients. No patient treated with AAV5-based gene therapies experienced a confirmed immune response to the capsid or complications associated with T-cell activation, such as a material loss of efficacy. Clinical trials also demonstrated that AAV5 has the lowest prevalence of preexisting neutralizing antibodies (NAb) compared to other AAV vectors, which may enable all, or nearly all patients to be eligible for treatment with AAV5-based gene therapies.

Invest in next-generation technologies to expand the applicability of gene therapy to patients. We are developing proprietary technologies that have the potential to enhance safety and efficacy of our product candidates, and may broaden the applicability of our gene therapies to a wider range of diseases and patients. These technologies include (i) tailored vectors and promoters; (ii) optimized delivery and administration techniques and (iii) novel transgenes. These

technologies are developed both in-house by our experienced research team in Amsterdam, the Netherlands, as well as via collaborations.

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, including the novel Padua-FIX gene we utilize in AMT-061 for hemophilia B; (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 as of December 31, 2017 is provided below:

					Development Stage				
Product/Product Candidate	**Vector**	**Gene**	**Indication**	**Collaborator**	**Pre-clinical**	**Phase I/II**	**Phase III**	**Approved**	**Comments**
Core Programs									
AMT-061	AAV5	FIX-Padua	Hemophilia B	—	▯	▯			Currently preparing for a Phase III study
AMT-130	AAV5	HTT	Huntington's disease	—	▯				Currently conducting IND-enabling toxicology study
AMT-126	Undisclosed	S100A1	Congestive Heart Failure	BMS	▯				Currently conducting preclinical studies

Hemophilia B

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.

Our Development of AMT-061 for Hemophilia B

We are currently developing AMT-061, a gene therapy for the treatment of hemophilia B. AMT-061, which includes an AAV5 vector carrying the FIX-Padua transgene, is designed to restore Factor IX ("FIX") activity, essential for blood clotting in patients with hemophilia B. AMT-061 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.

AMT-061 and AMT-060, the latter of which we previously tested in 10 patients in an ongoing Phase I/II clinical trial, are identical in structure apart from two nucleotide substitutions in the coding sequence for FIX. The gene variant, referred to as FIX-Padua, expresses a protein with a single amino acid substitution that has been reported in multiple preclinical and nonclinical studies to provide an approximate eight to nine-fold increase in FIX activity compared to the wild-type FIX protein. We expect all other critical quality attributes of AMT-061 to be comparable to those of AMT-060, as AMT-061 utilizes the same AAV5 capsid, promoter and proprietary insect cell-based manufacturing platform.

Our goal for AMT-061 is 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

We believe a differentiating feature of AMT-061 is AAV5's favorable tolerability and immunogenicity results. In contrast to data reported using other AAV capsids delivered systemically via IV infusion, no patient treated in clinical trials with our AAV5 gene therapies has experienced any confirmed, T-cell-mediated immune response to the capsid or material loss of FIX activity. Data from the Phase I/II study of AMT-060 also demonstrated clinical proof-of-concept in the presence of preexisting NAb to AAV5, suggesting that all, or nearly all hemophilia B patients may be eligible for treatment with AMT-061. There can be no assurance that future clinical studies will produce similar results.

On January 30, 2017, we received a Breakthrough Therapy designation by the FDA and on April 25, 2017, we received PRIME designation from EMA, for our AMT-060 program. The FDA and EMA have agreed that AMT-061 will be included under these current designations. The FDA has also agreed that AMT-061 will be included under our current IND for AMT-060. The EMA also has agreed that AMT-061 will be included under the current PRIME designation.

Pivotal Trial Program for AMT-061

We plan to expeditiously advance AMT-061 into a pivotal study in 2018 for patients with severe and moderately severe hemophilia B. Based on our multi-disciplinary meetings with the FDA and EMA, we achieved alignment on the clinical and regulatory pathway for AMT-061, including the proposed pivotal trial plan for AMT-061.

The pivotal study is expected to be an open-label, single-dose, multi-center, multi-national trial investigating the efficacy and safety of AMT-061 administered to adult patients with severe or moderately severe hemophilia B. Patients will serve as their own control, with a baseline established during a six-month observational lead-in phase prior to treatment with AMT-061. A short dose-confirmation study is expected to be completed in parallel to the lead-in phase of the pivotal study. Three patients will receive a single IV- dose of AMT-061 at 2 x 10^{13} gc/kg and will be evaluated for a period of approximately six weeks to assess FIX activity levels and confirm the dose. Each patient will continue to be followed longer term, and no lead-in phase is required for the dose-confirmation study.

We have initiated production of multiple clinical-grade batches of AMT-061 in our state-of-the-art Lexington, Massachusetts manufacturing facility. The material, which will be used in our pivotal study program, is being produced under cGMP conditions at commercial scale. The manufacturing process, controls and methods utilized for AMT-061 are consistent with those previously used for AMT-060. Data reviewed to date support comparability between AMT-061 and AMT-060.

Preclinical and Nonclinical Data for AMT-061

AMT-061 nonclinical data demonstrated tolerability and substantial increases in Factor IX ("FIX") activity. A GLP, nonclinical study of AMT-061 has been performed in non-human primates at four different dose levels up to a dose of 9 x 10^{13} gc/kg. The purpose of this study was to compare AMT-061 to AMT-060 with respect to liver transduction, circulating FIX protein levels, circulating FIX activity levels and toxicity, after a single intravenous dose with 13- or 26-week observation periods. Data from the study demonstrated a strong correlation between dose and human FIX expression levels, as well as biological activity of the expressed hFIX protein. At equal doses, circulating vector DNA plasma levels, liver distribution, liver cell transduction and hFIX protein expression were comparable for both AMT-060 and AMT-061. Additionally, AMT-061 demonstrated substantial increases in hFIX clotting activity compared to AMT-060, consistent with those previously reported for FIX-Padua. Based on a statistical analysis of the AMT-061 and AMT-060 non-human primate data, as well as the clinical data from the Phase I/II trial of AMT-060, we believe that AMT-061 administered at a dose of 2 x 10^{13} gc/kg may lead to mean FIX activity of approximately 30 to 50 percent of normal. The study also examined toxicology of AMT-061, including liver enzyme activity, coagulation biomarkers and other safety parameters. Data from the study demonstrated that AMT-061 was well-tolerated with no evidence of any significant toxicological findings. There was no increased thrombin generation or increased fibrin formation or degradation detected during the six months of follow-up. No increase in immunogenicity is expected with AMT-061, as there are no changes in the AAV5 capsid.

Intellectual Property for AMT-061

We acquired a patent family that broadly covers the FIX-Padua variant and its use in gene therapy for the treatment of coagulopathies, including hemophilia B. This family includes a patent issued in the U.S. in 2016, as well as pending patent applications in Europe and Canada. The patent family was acquired from the inventor, Professor Paolo Simioni, a renowned hemophilia expert at the University of Padua, Italy, who is widely recognized as the first to identify this mutant. We recently filed divisional patent applications that would further strengthen our intellectual property position related to the FIX-Padua variant.

Phase I/II Clinical Trial of AMT-060

In the third quarter of 2015, we initiated a Phase I/II clinical trial of AMT-060 in patients with severe or moderately-severe hemophilia B. AMT-060 consists of an AAV5 vector carrying a codon-optimized, wild-type, human Factor IX gene cassette licensed from St. Jude. The study is a 5-year, open-label, uncontrolled, single-dose, dose-ascending multi-center trial that includes two cohorts, with the low-dose cohort using a treatment of $5x10^{12}$ gc/kg and the second-dose cohort using $2x10^{13}$ gc/kg. We enrolled five patients into the low dose cohort in the third quarter 2015. Another five patients were enrolled into the high dose cohort between March and May 2016.

We presented up to twenty-four-months of follow-up data from the study on December 11, 2017 at the 59th annual meeting of the American Society of Hematology (“ASH”). Clinical benefit was maintained in all ten patients in the study, as measured by reduced FIX replacement therapy and bleeding frequency. Across the clinical trials' two dose cohorts, cumulative annualized consumption of FIX replacement therapy decreased by 84% as of deadline for ASH abstract submission. In the higher-dose cohort of the study, no confirmed bleeds were reported in the last twelve months of follow-up, with a reduction in the annualized spontaneous bleed rate of 89% compared to the one-year period prior to gene transfer.

No patients developed inhibitors to FIX and there were no detectable signs of sustained AAV5 capsid-specific T-cell activation. Mild, temporary elevations in ALT were observed in three patients, none of which were associated with changes in in FIX activity or capsid-specific T-cell responses. We will continue to follow-up the patients enrolled into the Phase I/II clinical trial of AMT-060. We currently intend to enroll all future patients in studies related to Hemophilia in clinical studies of AMT-061.

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, 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 2.71 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

We are developing AMT-130, an AAV5-based gene therapy, for the treatment of Huntington’s disease. AMT-130 delivers a DNA cassette encoding a proprietary, engineered microRNA designed to silence the Huntingtin gene, with the goal of inhibiting the production of the mutant protein. AMT-130 is intended to be administered directly into the brain via a stereotactic, MRI-guided catheter.

Preclinical, proof-of-concept studies with a single dose of AMT-130 have been conducted in multiple small and large animal models. In April 2017, we presented preclinical data on AMT-130 in transgenic mini pigs, which are among the largest Huntington’s disease animal models available for testing. The data demonstrated widespread, dose-dependent distribution of the vector throughout the mini pig brain that corresponded strongly with the mutant HTT expression. Researchers also observed a dose-dependent reduction in mutant HTT protein levels of more than 50% in the brain, as

well as similar trends in cerebral spinal fluid. Both the surgical procedure and AMT-130 treatment were well tolerated with no adverse events.

In October 2017, we presented preclinical data on AMT-130 in a mouse model with a highly aggressive form of Huntington's disease that demonstrated significant improvements in both motor-coordination and survival, as well as a dose-dependent, sustained reduction in huntingtin protein.

In November 2017, we completed dosing of our GLP safety and toxicology study of AMT-130 in non-human primates. We expect to complete this study in mid-2018, which we believe will support the filing of an IND with the FDA in the second half of 2018. AMT-130 has received orphan drug designation from the FDA in October 2017 and Orphan Medicinal Product Designation from EMA in January 2018.

Congestive Heart Failure

Collaboration with Bristol-Myers Squibb

In April 2015, we entered into an agreement with BMS that provides exclusive access to our gene therapy technology platform for multiple targets primarily focused on cardiovascular diseases ("Collaboration and License Agreement"). The collaboration included AMT-126, our proprietary gene therapy program for congestive heart failure, which aims to restore the heart's ability to synthesize S100A1, a calcium sensor and master regulator of heart function, and thereby improve clinical outcomes for patients with reduced ejection fraction. Beyond cardiovascular diseases, the agreement also included the potential for a target exclusive collaboration in other disease areas. In total, the companies may collaborate on ten targets, including AMT-126.

We are supporting BMS in the discovery, non-clinical, analytical and process development efforts and are responsible for manufacturing of clinical and commercial supplies using our vector technologies and industrial, proprietary insect-cell based manufacturing platform. BMS reimburses us for all our research and development costs in support of the collaboration, and will lead development, regulatory and commercial activities across all programs.

Congestive Heart Failure and Market Background

Congestive heart failure ("CHF") is the inability of the heart to supply sufficient blood flow to meet bodily demand for oxygen and nutrition. CHF is a rapidly progressing disease affecting 26 million people worldwide, with patients suffering from severe heart failure facing a 5-year mortality rate of over 50%. According to the American Heart Association, the prevalence of CHF is expected to double or triple by 2030. Maladaptive changes in the molecular composition of the diseased heart muscle contribute to its loss of contractile function, lethal tachyarrhythmia, energetic deficit, and maladaptive growth. Currently, there is no effective long-term or causative treatment for this disease.

Status of Programs

We are developing AMT-126, an AAV-based gene therapy carrying the S100A1 transgene, for the treatment of congestive heart failure. In August 2017, we announced that preliminary data from a study of AMT-126 in large animals successfully demonstrated both DNA delivery and human S100A1 expression, with the potential to restore normal levels of S100A1 in the myocardium after a single administration of AMT-126. The product used in this study was produced from our proprietary insect cell, baculovirus manufacturing process. Based on these findings and others, we and BMS advanced AMT-126 into further preclinical studies, including a therapeutic heart failure study in a diseased mini pig model that was initiated in January 2018.

In July 2015, three additional targets for development in cardiovascular indications were designated by BMS. The development process for two of these new targets commenced in 2016.

Other Early-Stage Research

We are pursuing the research of several other product candidates targeting rare and orphan diseases that can be treated using AAV-based gene therapies through application of either a gene replacement or a gene silencing approach. Our focus is on genetic diseases affecting the liver, such as hemophilia A, as well as various CNS disorders.

A key focus area in our early stage research is AAV5-based gene therapies. We believe AAV5 is emerging as a potential best-in-class vector for systemic administration to the liver because of its favorable immunogenicity profile. As opposed to other AAV vectors that have been systemically administered to humans, we have not observed any sustained immune responses to the AAV5 capsid. Moreover, we believe all, or nearly all patients may be eligible for treatment with AAV5-based gene therapies because of a low prevalence of preexisting antibodies to the AAV5 vector.

New Technology Development

We are seeking to develop next-generation technologies with the goal of broadening the applicability of AAV-based gene therapies to 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 therapeutic gene, or transgene.

We have a significant effort dedicated to designing and screening novel AAV vectors with the potential for (i) higher biological potency; (ii) increased specificity and penetration of specific tissue types; and (iii) enhanced safety. Members of our team have significant expertise in vector engineering and have created promising genetically engineered capsids using our a “rationale design” approach.

We are also utilizing a “directed evolution” approach to identifying next-generation AAV vectors, which involves a vector selection process in which libraries of mutant variants are screened for optimal properties. In January 2014, we entered into a collaboration and license agreement with 4D Molecular Therapeutics (“4D”) for the discovery and optimization of next-generation AAV vectors targeting the liver and the brain. We have identified several promising next-generation AAV vectors and are currently in the process of evaluating them for use in future gene therapy programs.

We have also worked extensively on designing synthetic promoters with the potential of enabling higher levels of protein expression in specific tissue types. Promoters are sequences of DNA that sit beside each gene on and whose function is to activate transcription, the initial process whereby protein is synthesized. Synthetic promoters, which do not exist in nature, are optimally tailored to drive gene expression of a target protein at a desired level and specificity. In January 2015, we entered into an agreement with Synpromics, a United Kingdom-based biotechnology company, to jointly fund research relating to the development of optimized promoters. We have identified several promising liver-directed promoters and are currently in the process of evaluating them for use in future gene therapy programs targeting liver-directed diseases.

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 using our proprietary, insect cell-based, baculovirus AAV production system.

This system has a number of advantages that enable high quality commercial-scale manufacturing, including:

- **High Yield.** A single manufacturing run at 500-liter scale can yield many thousands of doses of an AAV gene therapy.
- **High Purity.** The baculovirus system eliminates the risk of introducing mammalian cell derived impurities.
- **Scalability.** This process is reproducible at volumes ranging from 0.02 liters to 500 liters. We believe achieving higher scale production with our insect-cell, baculovirus system is possible.

Collaborations

Bristol-Myers Squibb Collaboration

In April 2015, we entered into a series of agreements with BMS, a publicly traded pharmaceutical company, regarding a collaboration that provides BMS with exclusive access to our gene therapy technology platform for multiple targets in cardiovascular and potentially other diseases.

Collaboration and License Agreement

With respect to the Collaboration and License Agreement with BMS, we refer to the section above.

We have received a total of $140.5 million to date from BMS, including an upfront payment of $50.0 million at the closing of the collaboration, which occurred in May 2015, a $15.0 million payment for the selection of three collaboration targets, in addition to AMT-126, and approximately $75.5 million in two equity investments. We will be eligible to receive additional payments for further designation of new collaboration targets and upon the achievement of research, development and regulatory milestones, including up to $254.0 million for the lead S100A1 therapeutic and up to $217.0 million for each other gene therapy product developed under the collaboration. We will also be eligible to receive net-sales-based milestone payments and tiered single to double-digit royalty payments on product sales.

Equity Agreements

In June 2015, BMS acquired 1.1 million ordinary shares, or 4.9% of our outstanding ordinary shares following the issuance, at a purchase price of $33.84 per share for aggregate consideration of $37.6 million. In August 2015, BMS acquired an additional 1.3 million ordinary shares at a purchase price of $29.67 per share for aggregate consideration of $37.9 million. Immediately after the second equity investment, BMS held 9.9% of our outstanding ordinary shares.

We have also granted BMS two warrants. Pursuant to each agreement, BMS may at its option acquire, at a premium to the market, an additional number of shares such that BMS owns 14.9%, respectively 19.9%, of our outstanding ordinary shares immediately after such purchase. The exercise of each warrant is conditioned upon the designation of a specified number of additional collaboration targets and payment of related fees by BMS, as well as a minimum number of collaboration programs under development.

We also entered into an Investor Agreement with BMS regarding the rights and restrictions relating to the ordinary shares to be acquired by BMS. We have granted BMS certain registration rights that allow BMS to require us to register our securities beneficially held by BMS under the Exchange Act. BMS may make up to two such demands (or three, in the event that either warrant is exercised) for us to register the shares, provided that we may deny such demand if (i) the market value of the shares to be registered is less than $10 million (provided however, if BMS holds less than $10 million worth of our shares, we must comply with their demand for registration), (ii) we certify to BMS that we plan to effect a registration within 120 days of their demand or we are engaged in a transaction that would be required to be disclosed in a registration statement and that is not reasonably practicable to be disclosed at that time, or (iii) we have already effected one registration statement within the twelve months preceding BMS's demand for registration. In addition, independent of their demand registration rights, upon the occurrence of certain events, we must also provide BMS the opportunity to include their shares in any registration statement that we effect.

We have also granted BMS certain information rights under the Investor Agreement, although these requirements may be satisfied by our public filings required by U.S. securities laws.

Pursuant to the Investor Agreement, without our consent, BMS may not (i) acquire a number of shares such that the number of shares that BMS beneficially holds is greater than the percentage acquired, or which may be acquired, after giving effect to each of the tranches under the Share Subscription Agreement and the two warrants; (ii) propose, offer or participate in any effort to acquire us or one of our subsidiaries; (iii) propose, offer or participate in a tender offer for our shares or any exchange of shares that would effect a change of control of our company; (iv) seek to control or influence our governance or policies; (v) join or participate in any group regarding the voting of our ordinary shares; or (vi) take certain other similar actions. BMS may still, among other things, make a non-public, confidential proposal to enter into a business combination or similar transaction with our company. These stand still restrictions will terminate upon the occurrence of certain events including, but not limited to, the acquisition of a certain material number of shares by a third party, if we enter into a merger agreement or similar transaction with a third party, or upon the passage of a defined period of time subsequent to the acquisition of shares pursuant to the Share Subscription Agreement or the warrants.

BMS is also subject to a lock-up pursuant to the Investor Agreement. Without our prior consent, BMS may not sell or dispose of its shares until the later of (i) the fourth anniversary of the purchase of the first tranche of shares pursuant to the Share Subscription Agreement (or fifth anniversary if the Collaboration Agreement is extended), or (ii), in respect of each ordinary share acquired pursuant to the Share Subscription Agreement and the warrants, the first anniversary of

issuance of each such ordinary shares. However, this lock-up may terminate sooner in the event the Collaboration Agreement is terminated.

The Investor Agreement also requires BMS to vote all of our ordinary shares it beneficially holds in favor of all items on the agenda for the relevant general meeting of shareholders of our company as proposed on behalf of our company, unless, in the context of a change of control or similar transaction, BMS has itself made an offer to our company or our supervisory or management boards in connection with the transaction that is the subject of the vote, in which case it is free to vote its shares at its discretion. This voting provision will terminate upon the later of the date on which BMS no longer beneficially owns at least 4.9% of our outstanding ordinary shares, the closing of a transaction that provides BMS exclusive and absolute discretion to vote our shares it beneficially holds, or the termination of the Collaboration Agreement for breach by us.

Chiesi collaboration

On April 20, 2017, we announced that we would not pursue the renewal of the Glybera marketing authorization in Europe when it expired on October 25, 2017. The marketing authorization was withdrawn and the Glybera Commercialization Agreement was terminated. We will be responsible for terminating the Phase IV post-approval study. We recorded $0.9 million contract termination cost in 2017.

On July 26, 2017, we entered into an agreement with Chiesi to reacquire the rights to co-develop and commercialize hemophilia B gene therapy in Europe and other selected territories and to terminate our co-development and license agreement.

Early-Stage Collaborations

4D Molecular Therapeutics (“4D”)

In January 2014, we entered into a collaboration and license agreement with 4D for the discovery and optimization of next-generation AAV vectors targeting the CNS and liver. We funded a three-year (2014-2016) research collaboration, which was extended for an additional year, under a mutually agreed research plan and ended January 18, 2018. We have selected a specified number of AAV variants from the research collaboration and have exclusive rights to further research, develop, manufacture and commercialize the selected AAV variants and products containing such AAV variant. Our obligations under the agreement include payments for the achievement of specified preclinical, clinical and regulatory milestones for each licensed product that we develop under the collaboration. We have also agreed to pay 4D royalties equal to a single-digit percentage of net sales, if any, of licensed products by us or our affiliates.

Synpromics

In January 2015, we entered into an agreement with Synpromics, a United Kingdom-based biotechnology company, pursuant to which we intend to jointly fund research relating to the development of optimized viral promoters. The research is directed at the discovery of alternative small liver-specific promoters for sustainable and increased expression of larger therapeutic genes fitting the package capacity of AAV vectors. Under the agreement, we have agreed to fund a specific testing program on liver promoters, with payments based on the achievement of specified milestones. Following the conclusion of the non-clinical testing phase, further milestones and payments have been agreed through the clinical phase of development and commercialization of products consisting of promoters developed under this agreement.
From this partnership, we have identified several promising liver-directed promoters and are currently in the process of evaluating them for use in future gene therapy programs targeting liver-directed diseases.

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 and other inventions and related technology that are important to our business, such as those relating to our technology

platform. We also rely on trade secrets 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.

Our 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 behind 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, 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 Patent Cooperation Treaty (“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, 2017, our intellectual property portfolio includes the following rights:

- 16 patent families that we own;
- 4 patent families that we exclusively in-license; and
- 1 patent families that we non-exclusively in-license.

As of December 31, 2017, the geographic breakdown of our owned patent portfolio is as follows:

- 15 issued U.S. patents;
- 10 granted European Patent Office patents;

- 1 pending PCT patent application;
- 11 pending U.S. patent applications;
- 12 pending European Patent Office patent applications; and
- 55 pending and 43 granted patent applications in other jurisdictions.

The patent portfolios for our manufacturing platform and most advanced programs are summarized below.

Owned Manufacturing Patents

We own a patent family directed to large scale production of AAV vectors in insect cells. The family includes issued patents in the United States, Europe, Japan and other jurisdictions and pending applications in the United States and other jurisdictions. The standard 20-year term for patents in this family will expire in 2027. This patent family relates to first-generation technology developed by uniQure for improvement of manufacturing in insect cells.

Furthermore, we own patent families directed to improving AAV vectors and covering AAV vectors manufactured at large scale relating to our second-generation technology. One patent family contains pending applications in the United States, Europe and other jurisdictions, and issued patents in the United States, Europe, Japan, Australia, China and other jurisdictions. The standard 20-year term for patents in this family will expire in 2028. We have another patent family which contains an issued patent in the US and pending patents in the United States and Europe. The standard 20-year term for patents in this family will expire in 2031. We also have a patent family relating to our third-generation technology for improved manufacturing. The patent family contains issued patents in the United States and Europe and other jurisdictions, and has patents pending in Europe and other jurisdictions. The standard 20-year term for patents in this family will expire in 2029.

We own patent families related to improved AAV manufacturing with regard to capsid protein expression. One patent family contains patents issued in the United States, Europe, and other jurisdictions. The standard 20-year term for patents in this family will expire in 2026. A more recent patent family contains pending patent applications in the United States, Europe and other jurisdictions. Those patents in this family that have been issued will have the standard 20-year term which will expire in 2035

In addition, we own a family of patents and patent applications relating to a proprietary baculovirus removal process which contributes to obtain regulatory compliant AAV vector products. This family includes granted patents in the United States, Europe, Japan, China, and other jurisdictions. The standard 20-year term for patents in this family, if issued, will expire in 2032.

We own a patent family related to the analysis of manufactured AAV product. Patents are pending in the United States, Europe and other jurisdictions. The standard 20-year term for patents in this family, if issued, will expire in 2035.

We own a family of patent applications which covers AAV5 administration technology through intrathecally delivery routes. This family includes patent applications in the US, Europe and other jurisdictions. The standard 20-year term of patents, if issued, in this family will expire in 2034.

We own a PCT-application, and a concomitantly filed US patent application, which covers AAV5 administration technology in patients utilizing an immunoadsorption procedure. The standard 20-year term of patents in this family, if issued, will expire in 2037.

Owned Product-related Patents

Hemophilia B

We own a patent family, including patents and patent applications, that relates to the use of the Padua mutation in hFIX for gene therapy in AMT-061. A PCT application was filed on September 15, 2009, and patent applications are pending in the United States, Europe, and Canada. The U.S. Patent and Trademark Office issued U.S. Patent 9,249,405 on February 2, 2016, which includes claims directed to Factor IX protein with a leucine at the R338 position of the protein

sequence, nucleic acid sequences coding for this protein, and therapeutic applications, including gene therapy. Additional fast track divisional patent applications have also been filed in the United States and in Europe that would further strengthen our intellectual property position. The standard 20-year patent term of patents in this family will expire in 2029.

Huntington's disease

We own a patent family that relates to gene therapy treatment of Huntington's disease. This family includes patent applications in the US, Europe and other jurisdictions. The standard 20-year patent term of patents in this family will expire in 2035.

S100A1

We hold patents related to our S100A1 product candidate in heart and skeletal muscle diseases. The patents were granted in Europe, Canada, Japan and the US, the term of which will expire in 2020.

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 the third party sources described below in more than one of our programs.

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 have to 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 an earlier 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 standard 20-year term for the underlying patents will expire in 2019.

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.

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 country or territory, subject to a specified notice period

Protein Sciences

In 2016, we revised our existing license contract with Protein Sciences Corporation for the use of its *expresSF+* (“SF+”) 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.

Technology Used for Specific Development Programs

Hemophilia B (AMT-061)

Padua

On April 17, 2017, we entered into an Assignment and License Agreement with Professor Paolo Simioni (“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 Factor IX gene, carrying an R338L mutation (“Padua IP”). Under the Padua Assignment, we have also licensed certain know-how included in the Padua IP. We will provide Dr. Simioni with an initial license fee and reimbursement of past expenses, as well as payments that may come due upon the achievement of certain milestone events related to the development of the Padua IP and may also include royalties on a percentage of certain revenues. We have granted a license back of the Padua IP 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 payments obligations under the Padua Assignment.

Dr. Simioni is serving as advisor and consultant to us for the development of therapeutic products using his invention of FIX-Padua. He will assist in our discussions with regulators, investigators, and key opinion leaders throughout the clinical development of AMT-061.

St. Jude Children’s Research Hospital

In 2008, we entered into a license agreement with St. Jude, which we amended in 2012. Under the 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. We have also agreed to pay St. Jude one-time milestone fees totaling $6.5 million upon the achievement of specified development and regulatory milestones, and an annual maintenance fee creditable against royalties and milestones in the same year. We

have agreed to use commercially reasonable efforts to diligently develop and commercialize products licensed under this agreement.

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.

Huntington's disease

Cold Spring Harbor Laboratory ("CSHL")

In December 2015, we concluded a license agreement with CSHL. Under the agreement, CSHL granted us an exclusive, sublicensable license to develop and commercialize to certain of CSHL's patented RNAi-related technology for the treatment or prevention of Huntington's disease. The standard 20-year patent term for the patent family which is the subject of this license agreement is about to expire in 2031.

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

Congestive heart failure

Heidelberg University Hospital

In June 2017, we concluded a license agreement with Heidelberg University Hospital for exclusive, worldwide and unlimited rights, with the right to sublicense, to patents directed to S100A1. Under the agreement, development and approval milestone payments, and future sub-single-digit royalties on net sales of a licensed product are payable by uniQure to Heidelberg University Hospital.

This license relates to a medical use patent family relating to the therapeutic window and effective dosages of S100A1 in heart disease, patents are pending in the US, Europe, Canada and Japan. The standard 20-year patent term of patents in this family will expire in 2035.

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

uniQure is a registered trademark in various jurisdictions including the United States and the European Union. We intend to seek trade mark protection for other product candidates 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 are aware of numerous companies focused on developing gene therapies in various indications, including AGTC, Abeona Therapeutics, Adverum Biotechnologies, Allergan, Ally Therapeutics, Audentes Therapeutics, AveXis,

Bayer, BioMarin, bluebird bio, Expression Therapeutics, Freeline Therapeutics, Generation Bio, Genethon, GlaxoSmithKline, Homology Medicines, Lysogene, Megenics, Milo Therapeutics, Nightstar, Pfizer, REGENXBIO, Renova Therapeutics, Rocket, Pharmaceuticals, Sangamo BioSciences, Sanofi, Sarepta, Shire, Solid Biosciences, Spark Therapeutics, Takara, Ultragenyx, and Voyager, as well as several companies addressing other methods for modifying genes and regulating gene expression. Although companies and research institutions in the gene therapy field tend to focus on particular target indications, any advances in gene therapy technology made by a competitor may be used to develop therapies competing against one of our product candidates. We may also face competition with respect to the treatment of some of the diseases that we are seeking to target with our gene therapies from protein pharmaceuticals under development at pharmaceutical and biotechnology companies such as Amgen, Bayer, Biogen, BioMarin, CSL Behring, Ionis, Novartis, Novo Nordisk, Pfizer, Roche, Sangamo, Sanofi, Shire, Sobi, Spark, and numerous other pharmaceutical and biotechnology firms.

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 of 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 of 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 (“FCDA”) and regulations and guidance implementing these laws. 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 of 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 (“cGLP”) regulations;

- submission to the FDA of an Investigational New Drug (“IND”) which allows human clinical trials to begin unless the FDA objects within 30 days;

- approval by an independent institutional review board ("IRB") before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with the FDA's or EMA's good clinical practices ("GCP") to establish the safety, potency, purity and efficacy of the proposed biological product for each indication;
- preparation and submission to the FDA of a Biologics License Application ("BLA");
- payment of substantial product and establishment user fees;
- 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;
- 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 US under an IND

Clinical trials involve the administration of the investigational biologic to human subjects under the supervision of qualified investigators in accordance with cGCP requirements. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of an IND. A clinical trial may not proceed in the US unless and until an IND becomes effective, which is 30 days after its receipt by the FDA unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. The protocol and informed consent documents must also be approved by an IRB. The FDA, an IRB, 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. Information about certain clinical trials, including results, must be submitted within specific timeframes for listing on the ClinicalTrials.gov website.

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 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.

FDA Guidance Governing Gene Therapy Products

The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND application; 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 who have been exposed to investigational gene therapies when the risk of such effects is high.

If a gene therapy trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, a protocol and related documentation must be submitted to, and the study registered with, the NIH Office of Biotechnology Activities ("OBA") pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules As part of the NIH protocol registration process, documentation originating from all oversight bodies involved in the review at an initial site(s) regarding their assessment of whether public Recombinant DNA Advisory Committee ("RAC") review is warranted must accompany the Principal Investigator's submission to the NIH. Public RAC review and discussion of a human gene transfer experiment will be initiated in two exceptional circumstances: (1) Following a request for public RAC review from one or more oversight bodies involved in the review at an initial site(s), the NIH concurs that (a) the individual protocol would significantly benefit from RAC review and (b) that the submission meets one or more of the following NIH RAC review criteria: i) the protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk; ii) the protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value; or iii) the proposed vector, gene construct, or method of delivery is associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies involved in the review at an initial site(s) to evaluate the protocol rigorously. In addition, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. After a human gene transfer experiment is publicly reviewed by the full RAC at a regularly scheduled meeting, the NIH OSP will send a letter summarizing the RAC's comments and recommendations (if any) regarding the protocol to the Principal Investigator(s), oversight bodies involved in the review at an initial site(s), and regulatory authorities as appropriate. Unless the NIH determines that there are exceptional circumstances, the NIH will send this letter to the Principal Investigator within 10 working days after the completion of the RAC meeting at which the experiment was reviewed. Receipt of this letter concludes the protocol registration process. Final IBC approval may then be granted. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public.

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. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Discovery of problems may result in a government entity placing restrictions on a product, manufacturer, or holder of an approved BLA, and may extend to requiring withdrawal of the product from the market. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specification.

FDA Programs to Expedite Product Development

The FDA has several programs to expedite product development, including fast track designation and breakthrough therapy designation. 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. The benefits include greater interactions with the FDA, eligibility for accelerated approval based on a surrogate endpoint, eligibility for priority review of the BLA, and rolling review of sections of the BLA.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act ("FDASIA"), 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 the fast track program features as described above, 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.

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, currently exceeding $2.4 million; products with orphan designation are exempt from the BLA filing fee. The sponsor of an approved BLA is also subject to annual product and establishment user fees, currently exceeding $98,000 per product and $513,000 per establishment. These fees are typically increased annually. 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). The FDA will assign a date for its final decision for the product (the PDUFA date) but can request an extension to complete review of a product application,

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 in order for the FDA to reconsider the application. 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; require that post-approval studies, including Phase IV clinical trials, be conducted to further assess a biologic's safety after approval; require testing and surveillance programs to monitor the product after commercialization; or impose other conditions, including distribution restrictions or other risk management mechanisms, including Risk Evaluation and Mitigation Strategies ("REMS"). The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs.

Following approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and the FDA review and approval. The product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. Other post-approval requirements include reporting of cGMP deviations that could affect the identity, potency, purity and overall safety of a distributed product, reporting of adverse effects, reporting new information regarding safety and efficacy, maintaining adequate record-keeping, and complying with electronic record and signature requirements.

Biosimilars and Exclusivity

The Biologics Price Competition and Innovation Act of 2009 which amended the Public Health Service Act ("PHS") authorized the FDA to approve biosimilars under Section 351(k) of the PHS. Under the Act, 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. In order 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. 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. The twelve-year exclusivity market period in the U.S. for biologics has been controversial and may be shortened in the future.

Orphan Drug Exclusivity

Under the Orphan Drug Act, 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. 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 in a head-to-head trial. 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-061 and AMT-130 for the treatment of Hemophilia B and Huntington's disease respectively; 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 or PREA, 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 regenerative therapeutic product as a regenerative medicine advanced therapy ("RMAT") eligible for accelerated approval. 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 PHS, 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. The FDA has recently interpreted gene therapy vectors administered alone to be included in the definition of RMAT.

FDA Regulation of Companion Diagnostics

We may seek to develop companion diagnostics for use in identifying patients that we believe will respond to our gene therapies. FDA officials have issued draft guidance to address issues critical to developing *in vitro* companion diagnostics, such as biomarker qualification, establishing clinical validity, the use of retrospective data, the appropriate patient population and when the FDA will require that the companion diagnostic and the drug be approved simultaneously. The draft guidance issued in July 2011 states that if safe and effective use of a therapeutic product depends on an *in vitro* diagnostic device, then the FDA generally will require approval or clearance of the diagnostic device by the Center for Devices and Radiological Health at the same time that the FDA approves the therapeutic product.

Anti-Kickback Provisions and Requirements

The federal anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration 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. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating

drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, have also been alleged by government agencies to violate false claims laws. 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.

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, independent non-profit healthcare research organizations (Institute for Clinical and Economic Review ("ICER")) and foreign governments, and the prices of drugs have been a focus in this effort. Third party payers are also increasingly challenging the prices charged for medical products and services and examining the medical necessity 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, the level of payment may not be sufficient to allow a company to sell its products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such 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 fail to provide adequate 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. Coverage policies, third party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act 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 health care programs. 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 Trials Directive 2001/20/EC, as amended (and to be replaced by the Clinical Trial Regulation EU 536/2014 in October 2018), provides a system for the approval of clinical trials in the European Union via implementation through national legislation of the member states. Under this system, approval must be obtained from the competent national authority of an EU member state in which the clinical trial is to be conducted. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the CTA, which must be supported by an investigational medicinal product dossier with supporting information prescribed by the Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents. The sponsor of a clinical trial, or its legal representative, must be based in the European Economic Area. European regulators and ethics committees also require the submission of adverse event reports during a study and a copy of the final study report.

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 are expected to qualify for the centralized procedure.

In the marketing authorization application ("MAA") the applicant has to 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 with them is likely 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.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radio-pharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a regular marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal. A marketing authorization under exception circumstances will normally not lead to the completion of a full dossier and hence is unlikely to become a normal marketing authorization.

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(1) 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. 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 is able to 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.

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 Regulation (EC) No 141/2000, as amended. 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 manufacturers' license

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 & approval.

Other Regulatory Requirements

A holder of a marketing authorization for a medicinal product is legally obliged to fulfill a number of 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 legislator or responsible national authority. The approach taken varies from member state to member state. 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 fix their own prices for medicines, but monitor and control company profits and may limit or restrict reimbursement. 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 in order 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 HTA's for pivotal clinical studies designed to support marketing approval.

Orphan Drug Regulation

We have been granted orphan drug exclusivity for AMT-061 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.

Employees

As of December 31, 2017, we had a total of 202 employees. As of December 31, 2017, 35 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 or other labor organizations. We believe that we have good relations with all of our employees and with the work council in the Netherlands.

Research and Development

For information regarding research and development expenses incurred during 2017, 2016 and 2015, see Item 7, *Management's Discussion and Analysis of Financial Condition and Results of Operations-Research and Development.*

Corporate Information

uniQure B.V. (the "Company") was incorporated on January 9, 2012 as a private company with limited liability (besloten vennootschap met beperkte aansprakelijkheid) under the laws of the Netherlands. We are 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. 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 the initial public offering, the Company converted into a public company with limited liability (naamloze vennootschap) and changed its legal name from uniQure B.V. to uniQure N.V.

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

Our website address is www.uniqure.com. We make available free of charge through our Internet website our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and any amendments to these reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. Also available through our website's "Investor Relations Corporate Governance" page are charters for the Audit, Compensation and Nominations and Corporate Governance committees of our board of directors and our Code of Business Conduct and Ethics. We are not including the information on our website as a part of, nor incorporating it by reference into, this report. You may read and copy any materials we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 on official business days during the hours of 10:00 a.m. to 3:00 p.m. Please call the SEC at 1-800-SEC-0330 for information on the Public Reference Room. Additionally, the SEC maintains a website that contains annual, quarterly, and current reports, proxy statements, and other information that issuers (including us) file electronically with the SEC. The SEC's website address is http://www.sec.gov. Unless the context indicates otherwise, all references to "uniQure" or the "Company" refer to uniQure and its consolidated subsidiaries.

Item 1A. Risk Factors

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

Risks Related to the Development of Our Product Candidates

We may encounter substantial delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates.

Clinical and non-clinical development is expensive, time-consuming and uncertain as to outcome. Our product candidates are in early clinical or preclinical development, and there is a significant risk of failure or delay in each of these programs. We cannot guarantee that any preclinical tests or clinical trials will be completed as planned or completed on schedule, if at all. A failure of one or more preclinical tests or clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include, but are not limited to:

- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations ("CROs") and clinical trial sites;
- delays in receiving regulatory authority to conduct the clinical trials or a regulatory authority decision that the clinical trial should not proceed;
- delays in obtaining required Institutional Review Board ("IRB") approval at each clinical trial site;
- imposition of a clinical hold by regulatory agencies after an inspection of our clinical trial operations or trial sites;
- failure by CROs, other third parties or us to adhere to clinical trial requirements or otherwise properly manage the clinical trial process, including meeting applicable timelines, properly documenting case files, including the retention of proper case files, and properly monitoring and auditing clinical sites;
- failure of sites or clinical investigators to perform in accordance with good clinical practices ("GCP") or applicable regulatory guidelines in other countries;
- difficulty or delays in patient recruiting into clinical trials;
- delays or deviations in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites;
- delays in having patients' complete participation in a study or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a study;
- occurrence of serious adverse events associated with a product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols, undertaking additional new tests or analyses or submitting new types or amounts of clinical data.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Such trials and regulatory review and approval take many years. It is impossible to predict when or if any of our clinical trials will demonstrate that product candidates are effective or safe in humans. If the results of our clinical trials are inconclusive, or fail to meet the level of statistical significance required for approval or if there are safety concerns or adverse events associated with our product candidates, we may:

- be delayed in or altogether prevented from obtaining marketing approval for our product candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes with the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;

- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

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

Our ability to recruit patients for our trials is often reliant on third parties, such as the pharmacies at our clinical trial sites. These third parties may not have the adequate infrastructure established to handle gene therapy products or to support certain gene therapy product formulations, or may not agree to recruit patients on our behalf.

In addition, we or our collaborator may not be able to locate and enroll enough eligible patients to participate in these trials as required by the FDA, the EMA or similar regulatory authorities outside the United States and the European Union. This may result in our failure to initiate or continue clinical trials for our product candidates, or may cause us to abandon one or more clinical trials altogether. Because our programs are focused on the treatment of patients with rare or orphan or ultra-orphan diseases, our ability to enroll eligible patients in these trials may be limited or slower than we anticipate considering the small patient populations involved and the specific age range required for treatment eligibility in some indications. In addition, our potential competitors, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, may seek to develop competing therapies, which would further limit the small patient pool available for our studies.

Any inability to successfully initiate or complete preclinical and clinical development could result in additional costs to us or impair our ability to receive marketing approval, to generate revenues from product sales or obtain regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, including changes in the vector or manufacturing process used, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Our progress in early-stage clinical trials may not be indicative of long-term efficacy in late-stage clinical trials, and our progress in trials for one product candidate may not be indicative of progress in trials for other product candidates.

The product candidates in our pipeline are at early-stages of development. Study designs and results from previous studies are not necessarily predictive of our future clinical study designs or results, and initial results may not be confirmed upon full analysis of the complete study data. Our product candidates may fail to show the required level of safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. In 2017, we announced our plans to advance AMT-061, which includes an AAV5 vector carrying the FIX-Padua transgene, into a pivotal study. While we believe AMT-061 and AMT-060, the latter of which was previously studied in a Phase I/II study, have been demonstrated to be materially comparable in nonclinical studies and manufacturing quality assessments, it is possible that future clinical studies of AMT-061 may show unexpected differences in comparison to AMT-060. Should these differences have an unfavorable impact on clinical outcomes, they may adversely impact our ability to achieve regulatory approval or market acceptance of AMT-061.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage clinical trials. If a larger population of patients does not experience positive results during clinical trials, if these results are not reproducible or if our products show diminishing activity over time, our products may not receive approval from the FDA or EMA. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections because of many factors, including changes in regulatory policy during the period of product development. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our products in late-stage clinical trials with larger patient populations could have a material adverse effect on our business that would cause our share price to decline.

Fast track product, breakthrough therapy, priority review, or Regenerative Medicine Advanced Therapy ("RMAT") designation by the FDA, or access to the PRIME scheme by the EMA, for our product candidates may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek fast track, breakthrough therapy designation, RMAT designation, PRIME scheme access or priority review designation for our product candidates if supported by the results of clinical trials. A fast track product designation is designed to facilitate the clinical development and expedite the review of drugs intended to treat a serious or life-threatening condition which demonstrate the potential to address an unmet medical need. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to speed the FDA marketing application review timeframe for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. PRIME is a scheme provided by the EMA to enhance support for the development of medicines that target an unmet medical need.

For drugs and biologics that have been designated as fast track products or breakthrough therapies, or granted access to the PRIME schema, interaction and communication between the regulatory agency and the sponsor of the trial can help to identify the most efficient path for clinical development. Sponsors of drugs with fast track products or breakthrough therapies may also be able to submit marketing applications on a rolling basis, meaning that the FDA may review portions of a marketing application before the sponsor submits the complete application to the FDA, if the sponsor pays the user fee upon submission of the first portion of the marketing application. For products that receive a priority review designation, the FDA's marketing application review goal is shortened to six months, as opposed to ten months under standard review. This review goal is based on the date the FDA accepts the marketing application for review, this application validation period typically adds approximately two months to the timeline for review and decision from the date of submission. RAT designations will accelerate approval but the exact mechanisms have not yet been announced by FDA.

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

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

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

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

We seek to expand our product pipeline in part by in-licensing the rights to key technologies, including those related to gene delivery, genes and gene cassettes. The future growth of our business will depend in significant part on our ability to in-license or otherwise acquire the rights to additional product candidates or technologies, particularly through our collaborations with academic research institutions. However, we may be unable to in-license or acquire the rights to any such product candidates or technologies from third parties on acceptable terms or at all. The in-licensing and acquisition of these technologies is a competitive area, and many more established companies are also pursuing strategies

to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be competitors may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our areas of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition and prospects could suffer.

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

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

As of December 31, 2017, a total of three patients reported serious adverse events related to the treatment of AMT-060 in our Phase I/II hemophilia B trial, including one patient with a short, self-limiting fever in the first 24 hours after treatment and two patients with mild, asymptomatic elevations in liver transaminases.

Adverse events in our clinical trials or those conducted by other parties (even if not ultimately attributable to our product candidates), and the resulting publicity, could result in increased governmental regulation, unfavorable public perception, failure of the medical community to accept and prescribe gene therapy treatments, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

Risks Related to Our Manufacturing

Our manufacturing facility is subject to significant government regulations and approvals. If we fail to comply with these regulations or maintain these approvals our business will be materially harmed.

Our manufacturing facility in Lexington is subject to ongoing regulation and periodic inspection by the EMA, FDA and other regulatory bodies to ensure compliance with current Good Manufacturing Practices (“cGMP”). Any failure to follow and document our adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical study, may result in the termination of or a hold on a clinical study, or may delay or prevent filing or approval of marketing applications for our products.

Failure to comply with applicable regulations could also result in the EMA, FDA or other applicable authorities taking various actions, including levying fines and other civil penalties; imposing consent decrees or injunctions; requiring us to suspend or put on hold one or more of our clinical trials; suspending or withdrawing regulatory approvals; delaying or refusing to approve pending applications or supplements to approved applications; requiring us to suspend manufacturing activities or product sales, imports or exports; requiring us to communicate with physicians and other customers about concerns related to actual or potential safety, efficacy, and other issues involving our products; mandating product recalls or seizing products; imposing operating restrictions; and seeking criminal prosecutions. Any of the foregoing could materially harm our business.

Gene therapies are complex and difficult to manufacture. We could experience production or technology transfer problems that result in delays in our development or commercialization schedules or otherwise adversely affect our business.

The insect-cell based manufacturing process we use to produce our products and product candidates is highly complex and in the normal course is subject to variation or production difficulties. Issues with the manufacturing process, even minor deviations from the normal process, could result in insufficient yield, product deficiencies or manufacturing failures that result in lot failures, insufficient inventory, product recalls and product liability claims.

Many factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or acts of god beyond our control. We also may encounter problems in hiring and retaining the experienced specialized personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing processes or facilities could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs, result in delays in our clinical development or marketing schedules and harm our business.

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

Our development and manufacturing processes involve the use of viruses, chemicals, other (potentially) hazardous materials and produce waste products. Accordingly, we are subject to national, federal, state and local laws and regulations in the United States and the Netherlands governing the use, manufacture, distribution, storage, handling, treatment and disposal of these materials. In addition to ensuring the safe handling of these materials, applicable requirements require increased safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for damages that result, and any such liability could exceed our assets and resources.

Risks Related to Regulatory Approval of Our Products

We are implementing modifications to our lead product candidate for hemophilia B, which may require additional pre-clinical, non-clinical, or clinical studies, or additional chemistry, manufacturing and control development.

In October 2017 we have modified our lead product candidate for hemophilia B from AMT-060 (an AAV-5 based vector encoding the wild-type factor IX gene) to a product candidate designated AMT-061 (an AAV5 based vector encoding the FIX-Padua mutant). Both product candidates are identical in structure apart from two nucleotide substitutions in the coding sequence for FIX. We believe the FIX-Padua mutant to result in enhanced FIX activity. We have conducted a GLP non-human primate pre-clinical study using AMT-061, which demonstrated a substantial increase in FIX activity over AMT-060. The results of our pre-clinical study using AMT-061 may not be predictive of any future clinical trial results for AMT-061. Our pivotal trial, which will be conducted with AMT-061, may not ultimately provide the desired efficacy results or may reveal adverse events or other safety concerns.

We will be required to conduct a clinical study to confirm the appropriate dose for our Phase III study of AMT-061. If we are unable to confirm the dose, we might be required to modify the design or extend the study, resulting in a delay of the treatment phase of our pivotal trial.

We have conducted our pre-clinical studies with both AMT-060 and AMT-061, as well our Phase I/II clinical study with AMT-060, with drug product manufactured at our Amsterdam facility. We intend to manufacture AMT-061 for our future clinical studies at our Lexington facility using a scaled-up and modified process. We will need to demonstrate comparability between AMT-061, manufactured at our Lexington facility and AMT-060, manufactured at our Amsterdam facility, to support regulatory approval and commence our Phase III clinical trial.

It is possible that the applicable regulatory authorities may ultimately not agree with the design or conduct of our comparability, clinical, pre-clinical or non-clinical studies, or with our chemistry, manufacturing, and control development work. The applicable regulatory authorities may find that our data does not support the submission, acceptance or approval of our IND amendment or marketing applications. During future interactions with FDA and the EMA, we may receive unfavorable comments, guidance, and recommendations that negatively impact our development timelines. The approach required by the applicable regulatory authorities may change in the future due to a variety of reasons, including changes in regulatory policy, the outcome of our studies and continuing development, and how our studies and continuing development efforts are ultimately conducted.

Any of the above could delay the submission of a marketing application, or regulatory authorities may not approve or may require material restrictions on any approvals that are received. Any of the foregoing would materially harm our commercial prospects.

We cannot predict when or if we will obtain marketing approval to commercialize a product candidate.

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

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

If we experience delays in obtaining marketing approval for any of our product candidates in the United States or other countries, the commercial prospects of our other product candidates may be harmed and our ability to generate revenues will be materially impaired.

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

We believe that all our current product candidates will be viewed as gene therapy products by the applicable regulatory authorities. Gene therapies are relatively new treatments for which regulators do not have extensive experience or standard review and approval processes. The FDA, unlike the EMA, does not have an exceptional circumstances approval pathway.

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

Regulatory requirements affecting gene therapy have changed frequently and may continue to change, and agencies at both the U.S. federal and state level, as well as congressional committees and foreign governments, have sometimes expressed interest in further regulating biotechnology. For example, the European Commission conducted a public consultation in early 2013 on the application of EU legislation that governs advanced therapy medicinal products, including gene therapy products, which could result in changes in the data we need to submit to the EMA for our product candidates to gain regulatory approval or change the requirements for tracking, handling and distribution of the products which may be associated with increased costs. In addition, divergent scientific opinions among the various bodies involved in the review process may result in delays, require additional resources and ultimately result in rejection. These regulatory agencies, committees and advisory groups and the new regulations and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenues to maintain our business.

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

Regulatory authorities in some jurisdictions, including the European Union and the United States, may designate drugs for relatively small patient populations as orphan drugs. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the relevant indication, the product is entitled to a period of market exclusivity, which precludes the EMA or FDA from approving another marketing application for the same drug for the same indication for that period. The EMA, however, may subsequently approve a similar drug for the same indication during the first product's market exclusivity if the EMA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Orphan drug exclusivity may be lost if the EMA or FDA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if the incidence and prevalence of patients who are eligible to receive the drug in these markets materially increase.

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

The FDA grants product sponsors certain periods of regulatory exclusivity, during which the agency may not approve, and in certain instances, may not accept, certain marketing applications for competing drugs. For example, biologic product sponsors may be eligible for twelve years of exclusivity from the date of approval, seven years of exclusivity for drugs that are designated to be orphan drugs, and/or a six-month period of exclusivity added to any existing exclusivity period or patent life for the submission of FDA requested pediatric data. While we intend to apply for all periods of market exclusivity that we may be eligible for, there is no guarantee that we will receive all such periods of market exclusivity. Additionally, under certain circumstances, the FDA may revoke the period of market exclusivity. Thus, there is no guarantee that we will be able to maintain a period of market exclusivity, even if granted. In the case of orphan designation, other benefits, such as tax credits and exemption from user fees may be available. If we are not able to obtain or maintain orphan drug designation or any period of market exclusivity to which we may be entitled, we will be materially harmed, as we will potentially be subject to greater market competition and may lose the benefits associated with programs.

Risks Related to Commercialization

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

Our ability to generate product revenues will depend on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on many factors, including:

- successful completion of preclinical studies and clinical trials;
- receipt and maintenance of marketing approvals from applicable regulatory authorities;
- our ability to timely manufacture sufficient quantities according to required quality specifications;
- obtaining and maintaining patent and trade secret protection and non-patent, orphan drug exclusivity for our product candidates;
- obtaining and maintaining regulatory approval for our manufacturing facility in Lexington, Massachusetts;
- launch and commercialization of our products, if approved, whether alone or in collaboration with others;
- identifying and engaging effective distributors or resellers on acceptable terms in jurisdictions where we plan to utilize third parties for the marketing and sales of our product candidates;
- acceptance of our products, if approved, by patients, the medical community and third party payers;
- effectively competing with existing therapies and gene therapies based on safety and efficacy profile;
- achieve value based pricing levels based on durability of expression, safety and efficacy;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- complying with any applicable post-approval requirements and maintaining a continued acceptable overall safety profile; and
- obtain adequate reimbursement for the total patient population and each sub group to sustain a viable commercial business model in US and EU markets.

Failure to achieve or implement any of these elements could result in significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business.

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

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

Prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative. The use of such data involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of the diseases we seek to address. The number of patients with the diseases we are

targeting may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, reimbursement may not be sufficient to sustain a viable business for all sub populations being studied, or new patients may become increasingly difficult to identify or access, any of which would adversely affect our results of operations and our business.

The addressable markets for AAV-based gene therapies are also impacted by the prevalence of neutralizing antibodies to the capsids, which are an integral component of our gene therapy constructs. Patients that have pre-existing antibodies to a particular capsid are generally not eligible for administration of a gene therapy that includes this particular capsid. For example, our AMT-061 gene therapy candidate for hemophilia B patients incorporates an AAV5 capsid. In our Phase I/II clinical study of AMT-060, we screened patients for preexisting anti-AAV5 antibodies to determine their eligibility for the trial. Three of the ten patients screened for the study tested positive for anti-AAV5 antibodies on reanalysis, and none of the three tested positive for certain ill-effects from the AAV-based gene therapy, implying that patients who have neutralizing antibodies may be eligible for AAV5-mediated gene transfer. However, we only have been able to test a limited sample of patients and have limited clinical and pre-clinical data, and it is possible that future clinical studies may not confirm these results. This may limit the addressable market for AMT-061 and any future revenues derived from the sale of the product.

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

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

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

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new biotechnology and biopharmaceutical products, including gene therapies, is highly competitive. We may face competition with respect to our product candidates, as well as with respect to any product candidates that we may seek to develop or commercialize in the future, from large and specialty pharmaceutical companies and biotechnology companies worldwide, who currently market and sell products or are pursuing the development of products for the treatment of many of the disease indications for which we are developing our product candidates. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. In recent years, there has been a significant increase in commercial and scientific interest and financial investment in gene therapy as a therapeutic approach, which has intensified the competition in this area.

We are aware of numerous companies focused on developing gene therapies in various indications, including AGTC, Abeona Therapeutics, Adverum Biotechnologies, Allergan, Ally Therapeutics, Audentes Therapeutics, AveXis, Bayer, BioMarin, bluebird bio, Expression Therapeutics, Freeline Therapeutics, Generation Bio, Genethon, GlaxoSmithKline, Homology Medicines, Lysogene, Megenics, Milo Therapeutics, Nightstar, Pfizer, REGENXBIO, Renova Therapeutics, Rocket, Pharmaceuticals, Sangamo BioSciences, Sanofi, Sarepta, Shire, Solid Biosciences, Spark Therapeutics, Takara, Ultragenyx, and Voyager, as well as several companies addressing other methods for modifying genes and regulating gene expression. We may also face competition with respect to the treatment of some of the diseases that we are seeking to target with our gene therapies from protein pharmaceuticals under development at pharmaceutical

and biotechnology companies such as Amgen, Bayer, Biogen, BioMarin, CSL Behring, Ionis, Novartis, Novo Nordisk, Pfizer, Roche, Sangamo, Sanofi, Shire, Sobi, Spark, and numerous other pharmaceutical and biotechnology firms.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than the products that we develop. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market. Because we expect that gene therapy patients may generally require only a single administration, we believe that the first gene therapy product to enter the market for a particular indication will likely enjoy a significant commercial advantage, and may also obtain market exclusivity under applicable orphan drug regimes.

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

Risks Related to Our Dependence on Third Parties

If our collaboration with BMS is not successful or if BMS designates fewer targets than expected in our collaboration agreement, our development plans, financial position and opportunities for growth may be adversely affected.

To earn all milestone payments and royalties potentially due under our collaboration with BMS, we are dependent on BMS electing to designate and actively pursue target indications covered by the collaboration and our achievement of all development, clinical and regulatory milestones under the collaboration. If BMS designates or actively pursues fewer development targets, utilizes contract research organizations, instead of our organization, to conduct non-clinical and pre-clinical studies, or if we fail to achieve a significant number of the applicable milestones, the total payments we receive under this collaboration may be materially lower than are potentially payable.

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

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

Our existing collaboration, and any future collaborations we enter, may pose several risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- we generally have limited or no control over the design or conduct of clinical trials sponsored by our current collaborators;
- we may be hampered from entering into collaboration arrangements if we are unable to obtain consent form our licensor to enter into sublicensing arrangements of technology we have licensed from such licensors;
- if our collaborators do not conduct the clinical trials they sponsor in accordance with regulatory requirements or stated protocols, we will not be able to rely on the data produced in such trials in our further development efforts;
- collaborators may not perform their obligations as expected;
- collaborators may also have relationships with other entities, some of which may be our competitors;
- collaborators may not pursue development and commercialization of any product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

- collaborators could develop, independently or with third parties, products that compete directly or indirectly with our products or product candidates, if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- our collaboration arrangements may impose restrictions on our ability to undertake other development efforts that may appear to be attractive to us;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights that achieves regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including over proprietary rights, contract interpretation or the preferred course of development, could cause delays or termination of the research, development or commercialization of product candidates, lead to additional responsibilities for us, delay or impede reimbursement of certain expenses or result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our rights or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may in some cases be terminated for the convenience of the collaborator and, if terminated, we could be required to expend additional funds to pursue further development or commercialization of the applicable product or product candidates.

If our collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive future research funding or milestone or royalty payments under the collaboration, and we may lose access to important technologies and capabilities of the collaboration. All the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of our development collaborators.

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

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

We rely upon a combination of in-licensed and owned patents, trade secret protection and confidentiality agreements to protect our intellectual property. Our success depends in a large part on our ability to obtain and maintain this protection in the European Union, the United States and other countries, in part by filing patent applications related to our novel technologies and product candidates. Our patents may not provide us with any meaningful commercial protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Successful challenges to our patents may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products.

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

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

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

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

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may

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

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

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

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

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

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

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

Risks Related to Pricing and Reimbursement

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

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

Government authorities and other third party payers, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Reimbursement systems vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. Government authorities and third party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and procedures. Increasingly, third party payers require drug companies to provide them with predetermined discounts from list prices, are exerting influence on decisions regarding the use of particular treatments and are limiting covered indications. Additionally, in the United States and some foreign jurisdictions, legislative and regulatory changes regarding the healthcare system and insurance coverage, particularly considering the new U.S. presidential administration, could result in more rigorous coverage criteria and downward pressure on drug prices, and may affect our ability to profitably sell any products for which we obtain marketing approval.

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

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

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

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

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses to date, expect to incur losses over the next several years and may never achieve or maintain profitability.

We had a net loss of $79.3 million in the year ended December 31, 2017, $73.4 million in 2016 and $82.1 million in 2015. As of December 31, 2017, we had an accumulated deficit of $475.3 million. To date, we have financed our operations primarily through the sale of equity securities and convertible debt, venture loans, through upfront payments from our collaboration partners and, to a lesser extent, subsidies and grants from governmental agencies and fees for services. We have devoted substantially all our financial resources and efforts to research and development, including preclinical studies and clinical trials. A significant portion of potential consideration under our agreement with BMS is contingent on achieving research, development, regulatory and sales milestones. We expect to continue to incur significant expenses and losses over the next several years, and our net losses may fluctuate significantly from quarter to quarter and year to year.

We anticipate that our expenses will increase substantially as we:

- prepare for a pivotal study for AMT-061, our gene therapy candidate in hemophilia B;
- advance the preclinical development and initiate a clinical study for AMT-130, our product candidate in Huntington's disease;
- progress research programs of additional product candidates targeting liver-directed, CNS and cardiovascular disorders;
- conduct any additional trials or tests beyond those originally anticipated to confirm the safety or efficacy of our product candidates;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- acquire or in-license rights to new therapeutic targets or product candidates;
- build clinical, medical, regulatory affairs, development and commercial infrastructure in the United States; and
- maintain, expand and protect our intellectual property portfolio, including in-licensing in license additional intellectual property rights from third parties.

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

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

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

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

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

The issuance of additional sales of our ordinary shares, or the perception that such issuances may occur, including through our "at the market" offering, could cause the market price of our ordinary shares to fall.

On September 15, 2017, we entered into a sales agreement (the "Sales Agreement") with Leerink Partners LLC ("Leerink") to establish an "at the market" ("ATM") program pursuant to which they are able, with our authorization, to offer and sell up to 5 million ordinary shares at prevailing market prices from time to time. We have not currently sold any shares pursuant to the Sales Agreement and do not have any immediate plans to do so. Under the Sales Agreement, Leerink is not required to sell any specific number or dollar amount of our ordinary shares, but will use its reasonable efforts, as our agent and subject to the terms of the Sales Agreement, to sell that number of shares upon our request. Sales of the ordinary shares, if any, may be made by any means permitted by law and deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act, and will generally be made by means of brokers' transactions on the NASDAQ Global Select Market or otherwise at market prices prevailing at the time of sale, or as otherwise agreed with Leerink.

We may terminate the Sales Agreement at any time. For the year ended December 31, 2017, we did not sell any ordinary shares under our at the market program. Whether we choose to terminate the Sales Agreement or affect future sales under our ATM program will depend upon a variety of factors, including, among others, market conditions and the trading price of our ordinary shares relative to other sources of capital. The issuance from time to time of these new ordinary shares through our ATM program or in any other equity offering, or the perception that such sales may occur, could have the effect of depressing the market price of our ordinary shares.

Should we decided to sell shares under our ATM program, there may be a dilutive effect on our estimated earnings per share and funds from operations per share in years during which an offering is ongoing. The actual amount of potential dilution cannot be determined at this time and will be based on numerous factors. The market price of our ordinary shares could decline because of issuances of a large number of shares of our ordinary shares after this offering or the perception that such issuances could occur.

Our management has significant flexibility in applying the net proceeds we would receive from the issuance of ordinary shares should we decided to sell shares under our ATM program. In the event we decide to sell shares under our ATM program, we currently intend to use the net proceeds from such sale for general corporate purposes, which may include capital expenditures, working capital and general and administrative expenses. However, because the net proceeds are not required to be allocated to any specific investment or transaction, investors cannot determine at the time of issuance the value or propriety of our application of the net proceeds, and investors may not agree with our decisions. In addition, our use of the net proceeds from the offering may not yield a significant return or any return at all. The failure by our management to apply these funds effectively could have an adverse effect on our financial condition, results of operations or the trading price of our ordinary shares.

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

As of December 31, 2017, we had $20.0 million of outstanding principal of borrowings under our Loan and Security Agreement with Hercules, which we are required to repay in monthly principal installments from December 2018 through May 2020. We could in the future incur additional debt obligations beyond our borrowings from Hercules. Our existing loan obligations, together with other similar obligations that we may incur in the future, could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, research and development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a disadvantage compared to our competitors that have less debt or better debt servicing options.

We may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under our existing loan obligations. Failure to make payments or comply with other covenants under our existing debt could result in an event of default and acceleration of amounts due. Under our agreement with Hercules, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets or

condition is an event of default. If an event of default occurs and the lender accelerates the amounts due, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all our assets.

Risks Related to Other Legal Compliance Matters

Our relationships with customers and third-party payers will be subject to applicable anti-kickback, anti-bribery, fraud and abuse and other laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

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

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

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain employer's liability insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

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

- decreased demand for any product candidates or products that we develop or sell;
- injury to our reputation and significant negative media attention;
- negative publicity or public opinion surrounding gene therapy;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to further develop or commercialize any products that we develop.

Dependent upon the country where the clinical trial is conducted, we currently hold a maximum of €6,000,000 and minimum of €2,000,000 in clinical trial insurance coverage in the aggregate, with a per incident limit of €450,000 to €1,000,000 with respect to the clinical studies we conduct. Such coverage may not be adequate to cover all liabilities that

we may incur. We may need to increase our insurance coverage as we expand our clinical trials. In addition, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on hiring, training, retaining and motivating key personnel to lead our research and development, clinical operations and manufacturing efforts. Although we have entered into employment agreements with our key personnel, each of them may terminate their employment on short notice. We do not maintain key person insurance for any of our senior management or employees.

The loss of the services of our key employees could impede the achievement of our research and development objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing senior management and key employees may be difficult and may take an extended period because of the limited number of individuals in our industry with the breadth and depth of skills and experience required to successfully develop gene therapy products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms.

If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks Related to Our Ordinary Shares

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

Our share price has been and may in the future be volatile. From the start of trading of our ordinary shares on the NASDAQ Global Select Market on February 4, 2014 through March 9, 2018, the sale price of our ordinary shares ranged from a high of $36.38 to a low of $4.72. The closing price on March 9, 2018, was $25.51 per ordinary share. The stock market in general and the market for smaller biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our ordinary shares may be influenced by many factors, including:

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

An active trading market for our ordinary shares may not be sustained.

Although our ordinary shares are listed on The NASDAQ Global Select Market, an active trading market for our shares may not be sustained. If an active market for our ordinary shares does not continue, it may be difficult for our shareholders to sell their shares without depressing the market price for the shares or sell their shares at all. Any inactive trading market for our ordinary shares may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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

Our directors, executive officers and major shareholders holding more than 5% of our outstanding ordinary shares, in the aggregate, beneficially own approximately 46.9% of our issued shares (including such shares to be issued in relation to exercisable options to purchase ordinary shares) as at December 31, 2017. As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to control many matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could control the election of the board directors and the approval of any merger, consolidation or sale of all or substantially all our assets.

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

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

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

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

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

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our ordinary shares less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (“JOBS Act”) and may remain an emerging growth company for up to five years from our initial public offering. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the independent auditor attestation requirements in the assessment of our internal control over financial reporting; and
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the independent auditor's report providing additional information about the audit and the financial statements.

If some investors find our ordinary shares less attractive because of our reliance on these exemptions, trading market for our ordinary shares may be less active and our share price may be more volatile.

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

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

Risks for U.S. Holders

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

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

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

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

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

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

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

Although we now report as a U.S. domestic filer for SEC purposes, our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in the Netherlands. The rights of our shareholders and the responsibilities of members of our board under Dutch law are different than under the laws of some U.S. jurisdictions. In the performance of their duties, our board members are required by Dutch law to consider the interests of uniQure, its shareholders, its employees and other stakeholders and not only those of our shareholders.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Lexington, Massachusetts / United States

We completed the GMP qualification of our approximately 53,343 square feet manufacturing facility that we lease in Lexington, Massachusetts in 2017. The lease for this facility terminates in 2024, and subject to the provisions of the lease, may be renewed for two subsequent five-year terms.

Amsterdam / The Netherlands

In March 2016, we entered into a lease for an approximately 100,000 square feet facility in Amsterdam, and we amended this agreement in June 2016 in order to lease an additional 11,000 square feet. We consolidated our current three Amsterdam sites into the new site at the end of May 2017. The lease for this facility terminates in 2032, with an option to extend in increments of five-year periods.

In December 2017, we entered into an agreement to sub-lease three of the seven floors of our 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 as well as an option to break the lease prior to December 31, 2020 subject to paying a penalty and breaking certain financial covenants.

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

Item 3. Legal Proceedings.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Part II

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

Our ordinary shares are listed on the NASDAQ Global Select Market under the symbol "QURE". The following table sets forth the range of high and low quarterly sales prices for our ordinary shares for the periods noted, as reported by NASDAQ.

Year	Period	High	Low
2017	Fourth Quarter	$ 21.35	$ 9.47
2017	Third Quarter	$ 9.81	$ 6.00
2017	Second Quarter	$ 6.28	$ 4.72
2017	First Quarter	$ 7.09	$ 5.25
2016	Fourth Quarter	$ 8.32	$ 5.45
2016	Third Quarter	$ 9.72	$ 6.68
2016	Second Quarter	$ 15.00	$ 6.75
2016	First Quarter	$ 19.40	$ 10.61

On March 9, 2018, the last reported sale price on the NASDAQ Global Select Market was $25.51. We have never paid any cash dividends on our ordinary shares, and we do not anticipate paying cash dividends in the foreseeable future. We anticipate that we will retain all earnings, if any, to support operations and to finance the growth and development of our business for the foreseeable future.

Unregistered Sales of Equity Securities

During the period covered by this Annual Report on Form 10-K, we have issued the following securities that were not registered under the Securities Act:

1. On October 2, 2017, we issued 64,648 ordinary shares to the sellers of the Inocard business in connection with the amended purchase agreement by which we acquired the Inocard business. No cash consideration was paid for the shares, as such shares were issued as amended consideration for our previous acquisition of the Inocard business. We deemed the offer and issuance of these shares to be exempt from registration under the Securities Act in reliance on Regulation S of the Securities Act, as an offshore offering of securities and such shares were issued as restricted shares. The sellers of the Inocard business represented to us that they were in compliance with the requirements of Regulation S.

2. In December 2017 we issued 114,172 ordinary shares to certain of the shareholders of the Company pursuant to exercised warrants for $2.0 million in aggregate cash consideration. The warrants that were exercised were issued prior to the Company's initial public offering. We deemed the sale and issuance of these shares to be exempt from registration under the Securities Act in reliance on Regulation S of the Securities Act, as an offshore offering of securities and such shares were issued as restricted shares. The warrant holders represented to us that they were in compliance with the requirements of Regulation S.

Use of Proceeds from Registered Securities

On October 27, 2017, we completed a follow-on public offering of ordinary shares. We issued and sold 5,000,000 ordinary shares at $18.25 per ordinary share, resulting in gross proceeds of approximately $91.3 million. The net proceeds to us from this offering were approximately $85.3 million, after deducting underwriting discounts and commissions and other offering expenses payable by us of approximately $6 million. The offer and sale of the shares in our follow-on offering were registered under the Securities Act pursuant to a registration statement on Form S-3 (File No. 333-216701) which was declared effective by the SEC on May 26, 2017. Following the sale of the shares in connection with the closing of our follow-on offering, the offering terminated. Leerink Partners LLC and Evercore Group L.L.C. acted as joint book-running managers, Chardan Capital Markets, LLC acted as lead manager and H.C. Wainwright & Co., LLC acted as co-manager.

The net proceeds of our follow-on offering were held in a diversified portfolio of bank deposits, government money market funds, government securities (U.S. Treasury and U.S. government agency securities), and high-grade short-

term corporate bonds. All investments were in compliance with our Investment Policy and are highly liquid, with liquidity and capital preservation being the primary investment objectives. Information related to use of proceeds from registered securities is incorporated herein by reference to the “Use of Proceeds” section of the Company’s Form 424B4, which was filed with the Securities and Exchange Commission on October 26, 2017. There has been no material change in the planned use of proceeds from our follow-on offering as described in our final prospectus.

Issuer Stock Repurchases

We did not make any purchases of our ordinary shares during the year ended December 31, 2017. Our affiliates made purchases of our ordinary shares as described in “Unregistered Sales of Equity Securities” above.

Holders

As of March 9, 2018, there were approximately twelve holders of record of our ordinary shares. The actual number of shareholders is greater than this number of record holders, and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include shareholders whose shares may be held in trust by other entities.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Note 10 of Part IV of this Annual Report on Form 10-K.

Item 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations", the consolidated financial statements and related notes, and other financial information included in this Annual Report on Form 10-K.

We derived the selected consolidated statements of operations and comprehensive loss for the years ended December 31, 2017, 2016, and 2015 and the selected consolidated balance sheet data as of December 31, 2017 and 2016 from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K.

We derived the selected consolidated statements of operations and comprehensive loss for the year ended December 31, 2014 and the selected consolidated balance sheet as of December 31, 2015 from our audited consolidated financial statements not included in this Annual Report on Form 10-K. We derived the selected consolidated statements of operations and comprehensive loss for the year ended December 31, 2013 and the selected consolidated balance sheet as of December 31, 2014 and 2013 from our unaudited consolidated financial statements, not included in this Annual Report on Form 10-K. Historical results are not necessarily indicative of the results to be expected in future periods.

We qualified as a U.S. domestic filer for SEC reporting purposes on January 1, 2017, and accordingly have prepared our financial statements in accordance with U.S. GAAP and report our financials in U.S. dollars. Previously we qualified as a foreign private issuer for SEC reporting purposes, and our financial statements were historically prepared in accordance with International Financial Reporting Standards and presented in euro. In this Annual Report on Form 10-K, we have presented all historical financial information in accordance with U.S. GAAP.

	Years ended December 31,				
	2017	2016	2015	2014	2013
	in thousands, except per share data				
License revenues	$ 8	$ 975	$ —	$ —	$ —
License revenues from related parties	4,121	3,940	3,335	1,173	593
Collaboration revenues	4,638	7,164	—	—	—
Collaboration revenues from related parties	4,340	13,019	7,243	4,968	3,339
Total revenues	**13,107**	**25,098**	**10,578**	**6,141**	**3,932**
Operating expenses:					
Research and development expenses	(72,172)	(72,510)	(59,125)	(43,772)	(22,438)
Selling, general and administrative expenses	(24,635)	(25,999)	(23,383)	(17,073)	(14,449)
Total operating expenses	**(96,807)**	**(98,509)**	**(82,508)**	**(60,845)**	**(36,887)**
Other income	15,430	1,465	779	1,022	763
Other expense	(3,073)	—	—	—	—
Loss from operations	**(71,343)**	**(71,946)**	**(71,151)**	**(53,682)**	**(32,192)**
Interest income	117	70	121	220	79
Interest expense	(2,232)	(2,172)	(2,572)	(2,019)	(2,764)
Foreign currency (losses) / gains, net	(3,566)	1,034	(2,496)	5,148	(55)
Other non-operating (expense) / income, net	(2,435)	785	(7,164)	21	(3,543)
Loss before income tax expense	**(79,459)**	**(72,229)**	**(83,262)**	**(50,312)**	**(38,475)**
Income tax benefit / (expense)	199	(1,145)	1,179	535	—
Net loss	**$(79,260)**	**$(73,374)**	**$(82,083)**	**$(49,777)**	**$(38,475)**
Other comprehensive income / (loss), net of income tax:					
Foreign currency translation adjustments net of tax impact of $0.2 million for the year ended December 31, 2017 (2016: $(1.1) million, 2015: $0.7 million, 2014: $0.5 million and 2013:nil)	2,757	271	(1,556)	(5,387)	475
Total comprehensive loss	**$(76,503)**	**$(73,103)**	**$(83,639)**	**$(55,164)**	**$(38,000)**
Basic and diluted net loss per common share	$ (2.94)	(2.93)	(3.72)	(2.91)	(3.56)

	As of December 31,				
	2017	2016	2015	2014	2013
	in thousands				
Cash and cash equivalents	$ 159,371	$ 132,496	$ 221,626	$ 64,688	$ 32,777
Total assets	209,644	190,265	262,663	104,683	47,281
Total debt	20,791	20,236	20,356	20,189	10,160
Accumulated deficit	(475,318)	(396,058)	(322,684)	(240,601)	(190,824)
Total shareholders' equity	$ 89,359	$ 63,631	$ 127,927	$ 42,634	$ 2,295

Quarterly results

You should read the following tables presenting our unaudited quarterly results of operations in conjunction with the consolidated financial statements and related notes contained elsewhere in this Annual Report on Form 10-K. We have prepared this unaudited information on the same basis as our audited consolidated financial statements. Our quarterly operating results have fluctuated in the past and may continue to do so in the future as a result of a number of factors, including, but not limited to, the timing and nature of research and development activities.

Summarized quarterly information for the two fiscal years ended December 31, 2017 and 2016, respectively, is as follows:

	For the Quarter Ended (unaudited)			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	in thousands, except per share data			
Revenue	$ 3,321	$ 4,942	$ 2,260	$ 2,584
Net loss	(20,272)	(21,269)	(10,245)	(27,474)
Basic and diluted net loss per ordinary share	$ (0.80)	$ (0.83)	$ (0.40)	$ (0.88)

Note: Basic and diluted net loss per ordinary share for the four quarters in 2017 do not equal the annual reported amount due to rounding.

	For the Quarter Ended (unaudited)			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	in thousands, except per share data			
Revenue	$ 4,295	$ 4,451	$ 7,221	$ 9,131
Net loss	(22,299)	(21,080)	(15,273)	(14,722)
Basic and diluted net loss per ordinary share	$ (0.90)	$ (0.84)	$ (0.61)	$ (0.58)

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

The following Management's Discussion and Analysis of Financial Condition and Results of Operations ("the MD&A") is intended to help the reader understand our results of operations and financial condition. This MD&A is provided as a supplement to, and should be read in conjunction with, our audited consolidated financial statements and the accompanying notes and other disclosures included in this Annual Report on Form 10-K, including the disclosures under "Risk Factors". Our consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the US ("U.S. GAAP") and unless otherwise indicated are presented in U.S. dollars.

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

Our actual results and the timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this MD&A. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this MD&A, they may not be predictive of results or developments in future periods.

We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a leader in the field of gene therapy, seeking to develop single treatments with potentially curative results for patients suffering from genetic and other devastating diseases. We are advancing a focused pipeline of innovative gene therapies that have been developed both internally and through partnerships, such as our collaboration with Bristol Myers-Squibb focused on cardiovascular diseases. We have established clinical proof-of-concept in our lead indication, hemophilia B, and achieved preclinical proof-of-concept in Huntington's disease. We believe our validated technology platform and manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost and time to market. We produce our AAV-based gene therapies in our own facilities with a proprietary, commercial-scale, GMP-compliant, manufacturing process. We believe our Lexington, Massachusetts-based facility is one of the world's leading, most versatile, gene therapy manufacturing facilities.

Business developments

Below is a summary of our recent significant business developments:

Hemophilia B program

On October 19, 2017, we announced that following multi-disciplinary meetings with the FDA and the EMA, we plan to expeditiously advance AMT-061, which combines an AAV5 vector with the FIX-Padua mutant, into a pivotal study in mid 2018 for patients with severe and moderately severe hemophilia B.

The study is expected to be an open-label, single-dose, multi-center, multi-national trial investigating the efficacy and safety of AMT-061 administered to adult patients with severe or moderately severe hemophilia B.

We have initiated production of multiple clinical-grade batches of AMT-061 in our state-of-the-art Lexington, MA manufacturing facility. Material is being produced at commercial scale and utilizing current Good Manufacturing Practices ("cGMP").

We also announced on October 19, 2017, that we have acquired a patent family that broadly covers the FIX-

Padua variant and our use in gene therapy for the treatment of coagulopathies, including hemophilia B. This family includes a patent issued in the U.S., as well as pending patent applications in Europe and Canada.

Huntington program (AMT-130)

On April 26, 2017, we presented new preclinical data on AMT-130 AMT-130 comprises an AAV5 vector carrying a DNA cassette encoding an engineered microRNA that silences the human huntingtin protein. at the 12th Annual CHDI Huntington's Disease Therapeutics Conference in Malta. Data from the study showed widespread and distribution of the AAV5 vector throughout the brain and extensive silencing of the human mutant huntingtin gene ("HTT") in mini pigs, which are among the largest Huntington's disease animal models available for testing.

The study demonstrated that a single administration of AAV5-miHTT resulted in significant reductions in HTT mRNA in all regions of the brain transduced by AMT-130, as well as in the cortex. Consistent with the reduction in HTT mRNA, a clear dose-dependent reduction in mutant huntingtin protein levels in the brain was observed, with similar trends in the cerebral spinal fluid.

In September 2017, AMT-130 received orphan drug designation from the U.S. Food and Drug Administration.

Also in September 2017, we initiated our GLP toxicology study in non-human primates with AMT-130. We expect to complete this study and file an IND with the FDA by the end of 2018.

On October 18, 2017, we presented new preclinical data on AMT-130 at the European Society of Gene and Cell Therapy ("ESGCT") 25th Anniversary Congress in Berlin, Germany.

Data from the study demonstrated that following administration of AMT-130 in Huntington's disease mouse models, significant improvements in both motor-coordination and survival were observed, as well as a dose-dependent, sustained reduction in huntingtin protein.

Manufacturing intellectual property

In July 2017, we were granted a patent from the United States Patent and Trademark Office. The newly issued Hermens '627 patent significantly expands our leading intellectual property portfolio related to large-scale, highly reproducible manufacturing of AAV in insect cells. This patent, which broadens earlier claims granted in this patent family, is based on research focused on enhancing the genetic stability of the Rep78/52 encoding sequences used to produce AAV vectors in insect cells. The technology covered in the Hermens '627 patent family is currently widely applied in insect cell-based AAV manufacturing.

AAV 5 safety and immunogenicity data

On May 12, 2017, we presented at the American Society of Gene & Cell Therapy's ("ASGCT") Annual Meeting in Washington, D.C., new preclinical data demonstrating successful and effective transduction of AAV5 in non-human primates with pre-existing anti-AAV5 neutralizing antibodies ("NABs"). At all observed levels, pre-existing neutralizing antibodies for AAV5 did not have a negative impact on the transduction effectiveness of the AAV5 vector.

This data suggests that patients with pre-existing anti-AAV5 NABs may be able to be successfully treated with AAV5 gene therapies, such as our product candidates in hemophilia B and in Huntington's disease. This development has the potential to significantly expand the applicability of AAV5 gene therapies to nearly all patients, regardless of pre-existing antibodies. In addition, AAV5 also appears to have a more favorable immunogenicity profile, with no immune responses detected across three clinical studies involving intravenous administration to 22 patients. We believe these factors make AAV5 a highly differentiated, best-in-class vector with the potential to more effectively and safely deliver gene therapies to a greater group of patients in need of treatment.

BMS collaboration

We have made continued progress on our research collaboration with Bristol-Myers Squibb ("BMS") in congestive heart failure. On August 8, 2017, we announced that preliminary data from a study in large animals demonstrated both DNA delivery and human S100A1 expression in the myocardium after treatments with product produced from our proprietary insect cell, baculovirus manufacturing process. Based on this finding and others, we and BMS have advanced the AMT-126, the gene therapy candidate for the treatment of congestive heart failure into further preclinical studies, including a preclinical heart function study in a diseased mini pig model in early 2018.

Chiesi collaboration

On April 20, 2017, we announced that we would not pursue the renewal of the Glybera marketing authorization in Europe when it is expired on October 25, 2017. We will be responsible for terminating the Phase IV post-approval study. We recorded $0.9 million contract termination cost in 2017.

On July 26, 2017, we entered into an agreement with Chiesi to reacquire the rights to co-develop and commercialize hemophilia B gene therapy in Europe and other selected territories and to terminate our co-development and license agreement.

Restructuring

Following the completion of our strategic review in November 2016, we announced a strategic restructuring plan aimed at refocusing our pipeline, consolidating our manufacturing operations and enhancing overall execution to drive shareholder value. Between October 31, 2016, and December 31, 2017, we reduced the number of employees with indefinite contracts from 244 to 202. We plan to complete our restructuring efforts in early 2018. In 2016, we accrued $1.1 million related to termination benefits offered to executive employees. Throughout 2017 we entered into termination agreements with employees, for which we recognized aggregate termination benefits of $2.0 million during 2017.

At the market program

On September 15, 2017, we filed a prospectus supplement to the prospectus dated May 15, 2017, and entered into the Sales Agreement with Leerink to establish an ATM program pursuant to which they are able, with our authorization, to offer and sell up to 5 million ordinary shares at prevailing market prices from time to time. We will pay Leerink a commission equal to 3% of the gross proceeds of the sales price of all shares sold through it as sales agent under the Sales Agreement. We have not yet sold any ordinary shares under the Sales Agreement and have not received any gross proceeds.

Follow-on offering

On October 27, 2017, we completed a follow-on public offering of ordinary shares. We issued and sold 5,000,000 ordinary shares at $18.25 per ordinary share, resulting in gross proceeds to us of approximately $91.3 million. The net proceeds to us from this offering were approximately $85.3 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us. We capitalized $0.5 million of expenses (presented as a reduction of additional paid in capital) related to this offering.

2017 Financial Highlights

Key components of our results of operations include the following:

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Total revenues	$ 13,107	$ 25,098	$ 10,578
Research and development expenses	(72,172)	(72,510)	(59,125)
Selling, general and administrative expenses	(24,635)	(25,999)	(23,383)
Net loss	(79,260)	(73,374)	(82,083)

As of December 31, 2017, we had cash and cash equivalents of $159.4 million (December 31, 2016: $132.5 million). We had a net loss of $79.3 million in 2017, $73.4 million in 2016 and $82.1 million in 2015. As of December 31, 2017, we had an accumulated deficit of $475.3 million (December 31, 2016: $396.1 million). We anticipate that our loss from operations will increase in the future as we:

- advance AMT-061 into late-stage clinical development. In July 2017, we agreed with Chiesi to terminate our Hemophilia Collaboration Agreement. Accordingly, all future development expenses will be borne by us (previously, Chiesi was reimbursing 50% of such costs);
- complete our IND-enabling studies for our proprietary Huntington's disease gene therapy program and initiate clinical studies;
- advance multiple research programs related to gene therapy candidates targeting liver-directed, and central nervous system ("CNS") diseases;
- continue to enhance and optimize our technology platform, including our manufacturing capabilities, next-generation viral vectors and promoters, and other enabling technologies;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- acquire or in-license rights to new therapeutic targets or product candidates;
- maintain, expand and protect our intellectual property portfolio, including in-licensing additional intellectual property rights from third parties; and
- build-out our clinical, medical and regulatory capabilities in the U.S.

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

Critical Accounting Policies and Estimates

In preparing our consolidated financial statements in accordance with U.S. GAAP and pursuant to the rules and regulations promulgated by the Securities and Exchange Commission ("SEC") we make assumptions, judgments and estimates that can have a significant impact on our net income/loss and affect the reported amounts of certain assets, liabilities, revenue and expenses, and related disclosures. We base our assumptions, judgments and estimates on historical experience and various other factors that we believe to be reasonable under the circumstances. Actual results could differ materially from these estimates under different assumptions or conditions. On a regular basis, we evaluate our assumptions, judgments and estimates. We also discuss our critical accounting policies and estimates with the Audit Committee of our Board of Directors.

We believe that the assumptions, judgments and estimates involved in the accounting for the BMS collaboration agreement, share-based payments, contingent consideration, valuation of derivative financial instruments, and research and development expenses, to be our critical accounting policies. Historically, our assumptions, judgments and estimates relative to our critical accounting policies have not differed materially from actual results.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

BMS collaboration agreement

We evaluated our collaboration agreement with BMS and determined that it is a revenue arrangement with multiple components. Our substantive deliverables under the collaboration agreement include an exclusive license to our technology in the field of cardiovascular disease, research and development services, and clinical and commercial manufacturing. In accordance with ASC 605, we analyzed the BMS agreements in order to determine whether the deliverables within the agreement can be separated or whether they must be accounted for as a single unit of accounting.

We concluded that the collaboration agreement consists of three units of accounting, (i) technology (license and target selections), know-how and manufacturing in the field of gene therapy and development and active contribution to the development through the joint steering committee participations, (ii) provision of employees, goods and services for research activities and for specific targets, and (iii) clinical and commercial manufacturing.

Under the terms of the agreements, we received an upfront cash payment from BMS of $50 million in June 2015. In addition, in June 2015, BMS purchased 1.1 million of our ordinary shares at a price of $33.84 per share, resulting in net proceeds of $37.6 million. In August 2015, BMS made a second equity investment of $37.9 million in 1.3 million of our ordinary shares at a price of $29.67 per share. We evaluated the share purchase agreement and the collaboration agreement as one arrangement and determined that the share purchase agreement included four derivative financial instruments, for which the fair value at initial recognition should be part of the total consideration. The total fair value of the derivative financial instruments amounted to $10.1 million at issuance. We deferred the recognition of the upfront cash payment and the fair value of the derivative financial instruments as of the signing date as the agreements were assessed together as a single arrangement. These amounts are being recognized as revenue over the period of performance. We estimate the performance period to be nineteen years, commencing on the effective date of May 21, 2015. The amortization of deferred revenue will be presented as license revenues in the consolidated statements of operations and comprehensive loss on a straight-line basis.

Additionally, BMS was granted two warrants:

- a warrant allowing BMS to purchase a specific number of our ordinary shares such that BMS's ownership will equal 14.9% immediately after such purchase. The warrant can be exercised on the later of (i) the date on which we receive from BMS the Target Designation Fees (as defined in the collaboration agreements) associated with the first six New Targets (as defined in the collaboration agreements); and (ii) the date on which BMS designates the sixth New Target; and
- a warrant allowing BMS to purchase a specific number of our ordinary shares such that BMS's ownership will equal 19.9% immediately after such purchase. The warrant can be exercised on the later of (i) the date on which we receive from BMS the Target Designation Fees associated with the first nine New Targets; and (ii) the date on which BMS designates the ninth New Target.

The exercise price in respect of each warrant will be equal to the greater of (i) the product of (A) $33.84, multiplied by (B) a compounded annual growth rate of 10%; and (ii) the product of (A) 1.10 multiplied by (B) the 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.

For fair value measurement, we applied a Monte-Carlo simulation. The valuation model incorporates several inputs, including the underlying share price the reporting date, the risk free rate adjusted for the period affected, an expected volatility based on a peer group analysis, 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 our expectations regarding the number of ordinary shares that would be issued upon exercise of the warrants. Additionally, the model assumes BMS will exercise the warrants only if it is financially rational to do so. Given the nature of these input parameters, we have classified the analysis as a level 3 valuation.

The estimated annualized volatility for fair value measurement is 75% as of December 31, 2017 (December 31, 2016: 75%) for the warrants.

We conducted a sensitivity analysis to assess the impact on changes in assumptions on the fair value. Specifically, we examined the impact on the fair market of the warrants by increasing the volatility by 10% to 85%. A further sensitivity analysis was performed assuming the exercise date of the warrants would occur one year later than what was assumed in the initial valuation. The table below illustrates the impact on the fair market valuation associated with these changes in assumptions as of December 31, 2017.

	Total warrants in thousands
Base case	$ 1,298
Increase volatility by 10% to 85%	457
Extend exercise dates by one year	161

Share-based payments

We issue share-based compensation awards, in the form of options to purchase ordinary shares, restricted share units and performance share units, to certain of our employees, executive and non-executive board members, and consultants. We measure share-based compensation expense related to these awards by reference to the estimated fair value of the award at the date of grant. The awards are subject to service and/or performance-based vesting conditions. The total amount of the awards is expensed on a straight-line basis over the requisite vesting period.

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

At each balance sheet date, we revise our estimate of the number of options that are expected to become exercisable. We recognize the impact of the revision of original estimates, if any, in the statements of operations and comprehensive loss and a corresponding adjustment to equity. We expect all vested options to be exercised over the remainder of their contractual life. We consider the expected life of the options to be in line with the average remaining term of the options post vesting.

We account for share options as an expense in the statements of operations and comprehensive loss over the estimated vesting period, with a corresponding contribution to equity, as they are all equity-classified.

Business combinations including contingent consideration

We allocate the purchase price of acquired businesses to the tangible and intangible assets acquired and liabilities assumed based upon their estimated fair values on the acquisition date. The purchase price allocation process requires management to make significant estimates and assumptions, especially at the acquisition date with respect to R&D and contingent consideration.

In 2014, following the acquisition of InoCard (later renamed uniQure GmbH), we recorded a contingent consideration obligation at the July 31, 2014 acquisition date of $1.7 million. The amount payable is contingent upon realization of the following milestones as amended in August 2017:

- early candidate nomination of product by a related party;
- acceptance of investigational new drug application by the United States Food and Drug Administration or an equivalent filing in defined Western European countries or Japan;
- completion of dosing of all patients in the first clinical study; and
- full proof of concept of the product in humans after finalization of the first clinical study.

The valuation of the contingent liability is based on significant inputs not observable in the market such as the probability of success (“POS”) of achieving the above research milestones (estimated as likely for the first three milestones as of the balance sheet date), the time at which the research milestones are expected to be achieved (ranging from 2018 to 2021), as well as the discount rate applied. The POS as well as the discount rate both reflect the probability of achieving a milestone as of a specific date. In June 2017, we replaced the risk-adjusted discount rate of 30.0% with our weighted

average rate of capital of 14.5% to reflect the full integration of the acquired business into our operation. All of the above resulted in a $0.3 million increase of the liability. We applied a WACC of 12.0% as of December 31, 2017.

The fair value of the contingent liability as of December 31, 2017 amounted to $4.0 million (December 31, 2016: $1.8 million). Varying the timing of the milestones, the discount rate and the POS of unobservable inputs results in the following fair value changes:

	December 31, 2017
	in thousands
Change in fair value	
Moving out of all milestones by 6 months	$ (212)
Increasing the POS for the first milestone by 20%	1,207
Decreasing the POS for the first milestone by 20%	(1,207)
Reducing the discount rate from 12.0% to 2.0%	1,239
Increasing the discount rate from 12.0% to 22.0%	(617)

Research and development expenses

We recognize research and development expenses as incurred. As of each reporting date, we estimate the level of service performed by our vendors or other counterparties and the associated costs incurred for the services performed. As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the service when it has not yet been invoiced or we have not otherwise been notified of the actual costs. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. The significant estimates in our accrued research and development expenses are related to fees paid to CROs in connection with research and development activities for which we have not yet been invoiced. We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct research and development on our behalf.

The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to vendors and other counterparties will exceed the level of services provided and result in a prepayment of the research and development expenses. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepayment expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in reporting amounts that are too high or too low in any particular period.

Recent Accounting Pronouncements

ASU 2014-09: ASC 606 Revenue from Contracts with Customers

In July 2015, the FASB issued ASU 2015-14, Revenue from Contracts with Customers: Deferral of the Effective Date (“ASU 2015-14”), which deferred the effective date for ASU 2014-09, Revenue from Contracts with Customers (“ASU 2014-09”), by one year. ASU 2014-09 will supersede the revenue recognition requirements in ASC 605, Revenue Recognition, and requires entities to recognize revenue in a way that depicts the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. In 2016, the FASB issued ASU 2016-08, 2016-10 and 2016-12, which provided further clarification on ASU 2014-09. ASU 2014-09 is effective for annual reporting periods beginning after December 15, 2017, including interim periods within that reporting period, which for the Company is January 1, 2018.

ASU 2014-09 provides for two implementation methods to us, (i) full retrospective application to all periods from January 1, 2015 onwards for revenue recognized in relation to collaborations; or (ii) application of the standard from January 1, 2018, onwards to active collaborations with an adjustment to retained earnings as of December 31, 2017, to include the cumulative adjustment to revenue recognized in prior periods in relation to active collaborations. We selected

the cumulative effect method to adopt the standard and will not use practical expedients at initial application. We have one active collaboration arrangement with Bristol Myers Squibb ("BMS"). As a result of the cumulative effect method we will not apply the requirements of ASU 2014-09 to any comparative periods presented and therefore the impact assessment applies to BMS collaboration agreement only.

We are finalizing our evaluation of the impact of adopting this standard. We have considered the new standard and preliminarily expect that the revenue recognition for the existing license will not be materially impacted based on the transfer of the services over the performance obligation. Sales-based milestone payments and royalties will continue to be recognized in the statement of comprehensive income when earned. Collaboration revenues, which are typically related to reimbursements from collaborators for our performance and costs incurred of research and development services under the respective agreements, are recognized in the statement of comprehensive income on the basis of labor hours valued at a contractually agreed rate and as costs incurred.

ASU 2016-02: Leases

In February 2016, the FASB issued ASU 2016-02, Leases ("ASU 2016-02"). The standard amends the existing accounting standards for lease accounting, including requiring lessees to recognize most leases on their balance sheets and making targeted changes to lessor accounting. ASU 2016-02 is effective for annual periods in fiscal years beginning after December 15, 2019. Early adoption is permitted. The new leases standard requires a modified retrospective transition approach for all leases existing at, or entered into after, the date of initial application with an option to use certain transition relief. We expect ASU 2016-02 to have a material impact on our consolidated financial statements, primarily from recognition of a right-of-use asset and lease liability in the consolidated balance sheets and a shift of cash outflows from operating activities to financing activities.

See Note 2 to our consolidate financial statements included in Part IV, Item 15, Exhibits and Financial Statement Schedules of this Annual Report on Form 10-K for a detailed description of recent accounting pronouncements applicable to our business.

Results of Operations

The following table presents a comparison of the twelve months ended December 31, 2017, 2016 and 2015.

	Years ended December 31,				
	2017	2016	2015	2017 vs 2016	2016 vs 2015
	in thousands				
Total revenues	$ 13,107	$ 25,098	$ 10,578	$ (11,991)	$ 14,520
Operating expenses:					
Research and development expenses	(72,172)	(72,510)	(59,125)	338	(13,385)
Selling, general and administrative expenses	(24,635)	(25,999)	(23,383)	1,364	(2,616)
Total operating expenses	**(96,807)**	**(98,509)**	**(82,508)**	**1,702**	**(16,001)**
Other income	15,430	1,465	779	13,965	686
Other expense	(3,073)	—	—	(3,073)	—
Loss from operations	**(71,343)**	**(71,946)**	**(71,151)**	**603**	**(795)**
Non-operating items, net	(8,116)	(283)	(12,111)	(7,833)	11,828
Loss before income tax expense	**(79,459)**	**(72,229)**	**(83,262)**	**(7,230)**	**11,033**
Income tax benefit / (expense)	199	(1,145)	1,179	1,344	(2,324)
Net loss	**$ (79,260)**	**$ (73,374)**	**$ (82,083)**	**$ (5,886)**	**$ 8,709**

Revenue

We recognize total collaboration revenues associated with development activities that are reimbursable by Chiesi (up to the July 2017 termination of the collaboration) and BMS under our respective collaboration agreements.

We recognize license revenues associated with the amortization of the non-refundable upfront payment, target designation fees and research and development milestone payments we have received or might receive from BMS. The timing of these cash payments may differ from the recognition of revenue, as revenue is deferred and recognized over the duration of the performance period. We treat other revenue, such as sales milestone payments or service fees, as earned when receivable.

Our revenue for the years ended December 31, 2017, 2016 and 2015 was as follows:

	Year ended December 31,				
	2017	2016	2015	2017 vs 2016	2016 vs 2015
	in thousands				
License revenue	$ 4,129	$ 4,915	$ 3,335	$ (786)	$ 1,580
Collaboration revenue BMS	4,340	13,019	2,321	(8,679)	10,698
Collaboration revenue Chiesi	4,638	7,164	4,922	(2,526)	2,242
Total revenues	**$ 13,107**	**$ 25,098**	**$ 10,578**	**$ (11,991)**	**$ 14,520**

In association with the upfront payments and target designation fees received from BMS in the second and third quarters of 2015, we recognized $4.1 million in license revenue during the year ended December 31, 2017, compared to $3.9 million and $2.4 million for the years ended December 31, 2016 and December 31, 2015. Following the termination of our collaboration with Chiesi in July 2017, we no longer recognize license revenue in association with the upfront fees received in 2013. We recognized $0.0 million license revenue during the year ended December 31, 2017, compared to $1.0 million and $1.0 million for the years ended December 31, 2016 and December 31, 2015. We recognized our license revenue during the year ended December 31, 2017, net of a $0.5 million reduction for amounts previously amortized in relation to the $2.3 million up-front payments that we were required to repay in accordance with the Glybera Termination Agreement.

Collaboration revenue generated during year ended December 31, 2017, from research activities associated with AMT-126, our BMS-partnered S100A1 heart failure program, was $4.3 million compared to $13.0 million and $2.3 million for the years ended December 31, 2016 and December 31, 2015. We are providing research services to BMS since the May 2015 effective date of our collaboration. In addition to these research services, we sold preclinical materials for $5.7 million to BMS in 2016.

Following the termination of our collaboration with Chiesi in July 2017, we no longer recognize collaboration revenue from our co-development of hemophilia B with Chiesi. We recognized $4.6 million collaboration revenue for the year ended December 31, 2017, compared to $7.2 million and $4.9 million for the years ended December 31, 2016 and December 31, 2015, respectively.

Research and development expenses

We expense research and development costs (“R&D”) as incurred. Our R&D expenses generally consist of costs incurred for the development of our target candidates, which include:

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense;
- costs incurred for laboratory research, preclinical and nonclinical studies, clinical trials, statistical analysis and report writing, and regulatory compliance costs incurred with clinical research organizations and other third-party vendors;
- costs incurred to conduct consistency and comparability studies;
- costs incurred for the start-up and validation of our Lexington facility;
- costs incurred for the development and improvement of our manufacturing processes and methods;
- costs associated with our research activities for our next-generation vector and promoter platform;

- costs incurred, including share-based compensation expense, under our collaboration and license agreement with 4D Molecular Therapeutics;
- changes in the fair value of the contingent consideration related to our acquisition of InoCard;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies; and
- amortization of intangible assets.

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

- *AMT-060/061 (hemophilia B).* We initiated a Phase I/II clinical trial of AMT-060 for the treatment of hemophilia B in the first quarter of 2015. In October 2017, we announced our intention to initiate a pivotal study in 2018 with AMT-061, a gene therapy including an AAV5 vector containing the Padua-FIX gene variant. We incurred costs related to the research, development and production of AMT-061. In July 2017, we and Chiesi terminated our Hemophilia Collaboration Agreement. Accordingly, all future development expenses will be borne by us (previously, Chiesi was reimbursing 50% of such costs);
- *AMT-130 (Huntington's disease).* We have incurred costs related to preclinical and nonclinical studies of AMT-130;
- *AMT-126 (congestive heart failure).* In the third quarter of 2014, we started to incur costs related to the preclinical development of product candidates targeting the S100A1 gene. Since May 2015, all costs related to the program are reimbursed by BMS under the collaboration agreement;
- *Preclinical research programs*. We incur costs related to the research of multiple preclinical gene therapy product candidates with the potential to treat certain rare and other serious medical conditions;
- *Technology platform development and other related research*. We incur significant research and development costs related to vector design, manufacturing and other aspects of our modular gene therapy technology platform that are applicable across all our programs; and
- AMT-110 (*Sanfilippo B*). We incurred costs related to the development and manufacture of clinical supplies of AMT-110 for the Phase I/II clinical trial. We suspended development of this product candidate in late 2016.

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

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

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

Research and development expenses for the year ended December 31, 2017 were $72.2 million, compared to $72.5 million and $59.1 million for the years ended December 31, 2016 and 2015, respectively.

- We incurred $31.4 million in personnel and consulting expenses in 2017 compared to $34.9 million in 2016 and $25.3 million in 2015. Our costs decreased in 2017 by $3.5 million following our November 2016 strategic decision to consolidate our manufacturing in Lexington and focus our product pipeline. Compared to our research and development expenses in 2015, our costs in 2016 increased by $9.6 million a result of the build out of our development clinical and Lexington-based manufacturing organization;
- We incurred $3.9 million in share-based compensation expenses in 2017 compared to $3.3 million in 2016 and $2.2 million in 2015. The increase in 2017 of $0.6 million and the increase of $1.1 million in 2016 were

driven by the recruitment of personnel to support the expansion of our proprietary and collaborator sponsored programs, as well as certain settlement agreements the Company entered into with executives;

- We recorded $1.8 million in termination benefits in 2017 compared to $0.9 million in 2016 related to our restructuring announced in November 2016;
- We incurred $17.3 million in external services and costs related to the development of our product candidates in 2017 compared to $19.2 million in 2016 and $11.5 million in 2015. The reduction in 2017 was a result of the strategic reprioritization of certain product candidates. In 2016 our costs increased compared to 2015 as result of the Phase I/II study of AMT-060, which was initiated in 2015 as well as increased activities to support the research of AMT-126 following the commencement of our collaboration with BMS May 2015;
- We incurred $14.4 million in operating expenses and depreciation expenses related to our rented facilities in in 2017, compared to $13.7 million in 2016 and $9.3 million in 2015. Our costs during 2016 and 2017 increased compared to 2015 due to the rental of temporary research space in Amsterdam (beginning in October 2015) and the build out of our new facility in Amsterdam, which commenced in March 2016 and was completed in April 2017;
- We recorded $3.0 million in expenses related to an increase in the fair value of the contingent consideration owed to the sellers of InoCard business in 2017 compared to a decrease of $1.1 million in 2016 and an increase of $1.3 million in 2015;
- We incurred no share-based compensation expenses related to our collaboration with 4D Molecular Therapeutics in 2017 compared to $0.7 million in 2016 and $6.5 million in 2015;
- We incurred no operating expenses related to the development of Glybera in 2017 and 2016 and $1.0 million in 2015; and
- We recorded a loss of $1.3 million related to the impairment of Glybera-related license assets in 2015.

Selling, general and administrative expenses

Our general and administrative expenses consist principally of employee, office, consultancy, legal and other professional and administrative expenses. We incur 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. We began the commercialization of Glybera in September 2015 and decided to cease commercialization in April 2017. During this period, we incurred selling and marketing costs related to maintaining a patient registry and conducting a post-approval, Phase IV study for Glybera.

Selling, general and administrative expenses for the year ended December 31, 2017 were $24.6 million, compared to $26.0 million and $23.4 million for the years ended December 31, 2016 and 2015, respectively.

- We incurred $8.4 million in personnel and consulting expenses in 2017 compared to $8.8 million in 2016 and $8.4 million in 2015. In 2016, we made investments in our finance, information technology infrastructure, including the recruitment of employees to replace consultants engaged during 2015;
- We incurred $6.3 million of share-based compensation expenses in 2017 compared to $2.2 million in 2016 and $3.0 million in 2015. Our share-based compensation in 2017 increased compared to 2016 as a result of equity grants offered to executives appointed the year prior, including our CEO. In addition, our 2016 share-based compensation expenses were reduced by $0.7 million to record the forfeiture of options upon the resignation of our former CEO;
- We incurred $4.8 million in professional fees in 2017 compared to $5.9 million in 2016 and $6.4 million in 2015. We regularly incur accounting, audit and legal fees associated with operating as a public company. In addition, we incurred significant fees in 2016 related to the conversion of our financial reporting from IFRS to U.S. GAAP, as well as fees associated with the Extera arbitration proceedings and the refinancing of our loan facility in May 2016. In 2015, we incurred legal fees related to the Extera arbitration proceedings, the completion of our follow-on offering in April 2015, the completion of the BMS transaction in May 2015 as well as advisory fees to enhance our internal controls over financial reporting;
- We incurred settlement costs of $1.5 million in 2016 in connection with our arbitration proceeding with Extera, compared to $1.4 million in 2015. No such costs were incurred in 2017; and
- We incurred $0.3 million of costs associated with the Glybera global registry and Phase IV study during the year ended December 31, 2017, compared to $3.2 million in 2016 and $0.7 million for the four month period from September to December 2015. These costs were presented as selling, general and administrative costs prior to May 2017, after which time they are presented as other expense.

Other items, net

Following the termination of our collaboration with Chiesi in July 2017, we recognized $13.8 million income in the year ended December 31, 2017, related to the full recognition of the outstanding deferred revenue. We recognized no such income in 2016 and 2015.

We recognized $1.2 million in income in the year ended December 31, 2017, from payments received from European authorities to subsidize our research and development efforts in the Netherlands compared to $1.5 million in 2016 and $0.8 million in 2015.

We recognized other expense in the year ended December 31, 2017, of $1.7 million related to our decision to not seek renewal of the marketing authorization for Glybera program, as well as the termination of collaborations with Chiesi. We did not recognize any such expenses in 2016 or 2015.

We accrued $0.6 million in contract termination costs in the year ended December 31, 2017, related to vacated facilities at our Amsterdam site. We did not recognize any such expenses in 2016 or 2015.

In addition, we accrued $0.8 million related to various exit activities conducted during year ended December 31, 2017. We did not recognize any such expenses in 2016 or 2015.

Non-operating items, net

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

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

We issued warrants to Hercules and lenders of a convertible loan in 2013 and to BMS in 2015. We recognize changes in the fair value of these warrants within other non-operating income / (expense).

Our non-operating items, net, for the years ended December 31, 2017, 2016 and 2015 were as follows:

	Years ended December 31,				
	2017	2016	2015	2017 vs 2016	2016 vs 2015
	in thousands				
Interest income	$ 117	$ 70	$ 121	$ 47	$ (51)
Interest expense - Hercules long term debt	(2,232)	(2,172)	(2,572)	(60)	400
Foreign currency (losses) / gains, net	(3,566)	1,034	(2,496)	(4,600)	3,530
Other non-operating (expense) / income	(2,435)	785	(7,164)	(3,220)	7,949
Total non-operating (expense) / income, net	**$ (8,116)**	**$ (283)**	**$ (12,111)**	**$ (7,833)**	**$ 11,828**

We recognized a net foreign currency loss related to our borrowings from Hercules and our cash and cash equivalents of $3.6 million in the year ended December 31, 2017, compared to a net gain of $1.0 million in 2016 and a net loss of $2.5 million in 2015.

In the year ended December 31, 2017, we recognized a $2.2 million loss related to fair value changes of warrants compared to a gain of $0.8 million in 2016 and a gain of $0.4 million in 2015.

In the year ended December 31, 2015, we recorded other non-operating expenses of $7.6 million resulting from changes in the fair value of the derivative financial asset recorded in relation to the issuance of shares to BMS. We recorded no such expenses in 2017 or 2016.

Financial Position, Liquidity and Capital Resources

As of December 31, 2017, we had cash, cash equivalents and restricted cash of $161.9 million. We currently expect that our cash and cash equivalents will be sufficient to fund operations into early 2020. The table below summarizes our consolidated cash flow data for years ended December 31:

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Cash and cash equivalents at the beginning of the period	$ 134,324	$ 222,869	$ 65,930
Net cash (used in)/ provided by operating activities	(64,270)	(72,189)	7,468
Net cash used in investing activities	(5,583)	(17,172)	(8,022)
Net cash generated from financing activities	90,074	2,445	160,691
Foreign exchange impact	7,306	(1,629)	(3,198)
Cash, cash equivalents and restricted cash at the end of period	**$ 161,851**	$ **134,324**	$ **222,869**

We have incurred losses and cumulative negative cash flows from operations since our business was founded by our predecessor entity AMT Therapeutics ("AMT") Holding N.V. in 1998. We had a net loss of $79.3 million in 2017, $73.4 million in 2016, and $82.1 million in 2015. As of December 31, 2017, we had an accumulated deficit of $475.3 million.

Sources of liquidity

From our first institutional venture capital financing in 2006 through 2017, we funded our operations primarily through private placements and public offerings of equity securities, convertible and other debt securities and to a lesser extent upfront, target designation or similar payments from our collaboration partners as well as collaboration revenues.

On October 27, 2017, we completed a follow-on public offering of ordinary shares. We issued and sold 5,000,000 ordinary shares at $18.25 per ordinary share, resulting in gross proceeds of approximately $91.3 million. The net proceeds to us from this offering were approximately $85.3 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

In September 2017, we established an "at the market" equity offering program pursuant to which we can sell up to 5 million ordinary shares at prevailing market prices from time to time. No ordinary shares were issued in accordance with this program during 2017.

In April 2015, we completed our follow-on public offering raising total gross proceeds of $88.5 million and net proceeds of $82.5 million after commissions and after deducting share issuance expenses.

Also in April 2015, we entered into collaboration agreements with BMS, the financial terms of which consist of:

- an upfront payment of $50.0 million made at the closing of the transaction on May 2015;
- a $15.0 million payment made in July 2015, following the designation of three additional collaboration targets;
- an initial equity investment of $37.6 million for the purchase of 1.1 million ordinary shares, representing 4.9% of our outstanding shares following such issuance, made in June 2015 at a price of $33.84 per share;
- a second equity investment of $37.9 million for the purchase of an additional 1.3 million ordinary shares, representing 5.0% of our outstanding shares following such issuance, made in August 2015 at a price of $29.67 per share;
- two warrants to acquire additional equity interests, at a premium to market, to own 14.9%, respectively 19.9%, immediately after the purchase based on additional targets being introduced into the collaboration;
- research, development and regulatory milestone payments, including up to $254.0 million for the lead S100A1 therapeutic and up to $217.0 million for each other gene therapy product potentially developed under the collaboration;
- reimbursement for all research costs associated with the collaboration;
- payments for the manufacturing and supply of product to BMS; and
- net sales-based milestone payments and tiered single to double-digit royalties on product sales.

We expect to continue to incur losses and to generate negative cash flows. We have no firm sources of additional financing other than our collaboration agreement with BMS. Until such time, if ever, as we can generate substantial cash flows from successfully commercializing our 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.

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. As at December 31, 2017, $20.0 million was outstanding. The interest rate is adjustable and is the greater of (i) 8.25% or (ii) 8.25% plus the prime rate less 5.25%. The interest-only payment period was extended by 12 months to November 2018 as a result of raising more than $50.0 million in equity financing in October 2017.

We are subject to covenants under our Loan Agreement with Hercules, and may become subject to covenants under any future indebtedness that could limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely impact our ability to conduct our business. In addition, our pledge of assets as collateral to secure our obligations under the Hercules loan agreement may limit our ability to obtain debt financing. To the extent we need to finance our cash needs through equity offerings or debt financings, such financing may be subject to unfavorable terms including without limitation, the negotiation and execution of definitive documentation, as well as credit and debt market conditions, and we may not be able to obtain such financing on terms acceptable to us or at all. If financing is not available when needed, including through debt or equity financings, or is available only on unfavorable terms, we may be unable to meet our cash needs. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, which could have a material adverse effect on our business, financial conditions, results of operations and cash flows.

Net Cash (used in)/generated by operating activities

Net cash used in operating activities was $64.3 million for the year ended December 31, 2017, compared to $72.2 million of cash used for the year ended December 31, 2016 and $7.5 million of cash generated for the year ended December 31, 2015, respectively.

Our cash generated in the year ended December 31, 2015 included a $50.0 million upfront payment, received from BMS following the inception of our collaboration in May 2015 and a $15.0 million payment in August 2015 associated with the designation of the second, third and fourth collaboration targets. Excluding these payments, our cash used in operating activities was $57.5 million in 2015.

The reduction in cash used for the year ended December 31, 2017, compared to the year ended December 31, 2016, is primarily due to a $6.4 million favorable change in our net working capital for the year ended December 31, 2017, compared to a $4.6 million unfavorable change in our net working capital in 2016. These changes in net working capital are driven by a $11.2 million reduction in collaboration revenue in 2017 compared to 2016. In addition, in 2017 we collected $1.1 million in lease incentive payments related to our new Amsterdam facility and decreased our operating expenses during the year ended December 31, 2017 by $6.5 million.

Excluding the payments we received from BMS in 2015, our cash used in operating activities in 2016 increased by $14.7 million. The increase is mainly due to a $3.2 million unfavorable change in our net working capital for the year ended December 31, 2016, compared to a $2.2 million favorable change in our net working capital in 2015. These changes in net working capital are driven by an increase in collaboration revenue of $12.9 million in 2016 compared to 2015 In addition, our operating expenses increased by $20.2 million in 2016 compared to 2015. We also made a $2.9 million payment in December 2016 related to the settlement of the Extera arbitration.

Net cash used in investing activities

In 2017, we used $5.6 million in our investing activities compared to $17.2 million in 2016 and $8.0 million in 2015.

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Build out of Lexington site	$ (1,426)	$ (1,837)	$ (4,772)
Build out of Amsterdam sites	(3,035)	(13,451)	(2,835)
Acquisition of licenses and patents	(1,122)	(1,884)	(415)
Total investments	**$ (5,583)**	**$ (17,172)**	**$ (8,022)**

In 2017, we invested $3.0 million in our new facility in Amsterdam compared to $13.0 million (including a $0.6 million deposit) in 2016.

In 2016, we invested $1.9 million related to an exclusive license from Protein Science Corporation.

In 2015, we invested $2.8 million to upgrade our Amsterdam manufacturing facility and our temporary research facility in Amsterdam.

Net cash generated from financing activities

We received net proceeds of $85.3 million associated with our follow-on offering in October 2017.

In addition, during the year ended December 31, 2017, we received $4.0 million from the exercise of options to purchase ordinary shares in relation to our share incentive plans compared to $2.6 million and $2.9 million in the years ended December 31, 2016 and 2015, respectively.

In 2017, we paid $0.6 million contingent consideration in relation to our 2014 acquisition of the InoCard business.

We received net proceeds associated with the issuance of shares to BMS of $37.6 million in June 2015 and $37.9 million in August 2015.

We received net proceeds of $82.5 million associated with our follow-on offering in April 2015.

Funding requirements

We believe our cash and cash equivalents as of December 31, 2017, will enable us to fund our operating expenses including our debt repayment obligations as they become due and capital expenditure requirements, for at least the next twelve months. Our future capital requirements will depend on many factors, including but not limited to:

- the potential to receive future consideration pursuant to our collaboration with BMS, which is largely contingent on achieving certain research, development, regulatory and sales milestones;
- our ability to enter into collaboration arrangements in the future;
- the scope, timing, results and costs of our current and planned clinical trials, including those for AMT-061 in hemophilia B and AMT-130 in Huntington's disease;
- the scope, timing, results and costs of preclinical development and laboratory testing of our additional product candidates;
- the need for any additional tests, studies, or trials beyond those originally anticipated to confirm the safety or efficacy of our product candidates and technologies;
- the cost, timing and outcome of regulatory reviews associated with our product candidates;
- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution of any of our product candidates for which we receive marketing approval in the future;
- the amount and timing of revenue, if any, we receive from commercial sales of any product candidates for which we, or our collaboration partner, receives marketing approval in the future;

- the costs and timing of preparing, filing, expanding, acquiring, licensing, maintaining, enforcing and prosecuting patents and patent applications, as well as defending any intellectual property-related claims;
- the repayments of the principal amount of our venture debt loan with Hercules, which will contractually start in December 2018 and will run through May 2020;
- the extent to which we acquire or in-license other businesses, products, product candidates or technologies;
- the costs associated with maintaining quality compliance and optimizing our manufacturing processes, including the operating costs associated with our Lexington, Massachusetts manufacturing facility;
- the costs associated with recent and future hiring of senior management and other personnel,
- the timing, costs, savings and operational implications of the corporate restructuring we are implementing following the completion of our strategic review last year.

Contractual obligations and commitments

The table below sets forth our contractual obligations and commercial commitments as of December 31, 2017, that are expected to have an impact on liquidity and cash flows in future periods.

	Undefined	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years	Total
			in thousands			
Debt obligations (including $4.0 million interest payments)	$ —	$ 2,890	$ 14,188	$ 6,882	$ —	$23,960
Operating lease obligations	—	3,872	3,927	12,097	21,030	40,926
Contingent consideration (nominal amount)	16,188	—	—	—	—	16,188
Total	**$ 16,188**	**$ 6,762**	**$ 18,115**	**$ 18,979**	**$ 21,030**	**$81,074**

Due to uncertainty of the timing of achieving milestones, the contingent consideration of $16.2 million (€13.5 million) related to our acquisition of InoCard GmbH (“InoCard”), later renamed uniQure GmbH, is considered to have an undefined contractual maturity. As of December 31, 2017, we expect the milestone obligations will become payable between 2018 and 2021. When due, 50% of the obligations can be settled either in cash or in a variable number of our shares. As of December 31, 2017, we recorded this obligation at its fair value of $4.0 million including $1.1 million we expect to be payable in 2018.

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones (such as the start of a clinical trial, filing of a Biologics License Application, approval by the FDA or product launch). We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these milestones is not fixed and determinable.

We enter into contracts in the normal course of business with clinical research organizations (“CROs”) for preclinical research studies and clinical trials, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

The Company’s predecessor entity received a technical development loan from the Dutch government in relation to the development of our now abandoned product, Glybera. The Company needs to repay the grant through a percentage of revenue derived from product sales of Glybera up to December 31, 2019. Any grant balance remaining at this date will be forgiven. We have decided not to renew our marketing authorization for Glybera in the European Union, which expired in October 2017. We do not expect to derive any revenue from Glybera or to be required to make any repayments under this loan.

Off-Balance Sheet Arrangements

As of December 31, 2017, we did not have any off-balance sheet arrangement as defined in in Item 303(a) (4) of Regulation S-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

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

Market Risk

Currency risk

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

Our Dutch operating entities hold significant amounts of U.S. dollars in cash and cash equivalents, borrowed U.S. dollar from Hercules, generate collaboration revenue in U.S. dollars and receive services from vendors denominated U.S. dollar and occasionally British Pounds. Foreign currency denominated account receivables and account payables are short-term in nature (generally 30 to 45 days).

Variations in exchange rates will impact earnings and other comprehensive income. At December 31, 2017, if the euro had weakened 10% against the U.S. dollar with all other variables held constant, pre-tax earnings for the year would have been $1.8 million lower (December 31, 2016: $4.7 million higher; December 31, 2015: $5.8 million higher), and other comprehensive income would have been $9.0 million higher (December 31, 2016: $3.5 million lower, December 31, 2015: $8.3 million lower). Conversely, if the euro had strengthened 10% against the U.S. dollar with all other variables held constant, pre-tax earnings for the year would have been $1.7 million higher (December 31, 2016: $4.7 million lower, December 31, 2015: $5.8 million lower), and other comprehensive income / (loss) would have been $9.0 million lower (December 31, 2016: $4.5 million higher, December 31, 2015: $10.5 million higher). We have not established any formal practice to manage the foreign exchange risk against our functional currency.

The sensitivity in other comprehensive income to fluctuations in exchange rates is related to the funding by our Dutch holding company of the investing and operating activities of our U.S. based entity and the reporting currency.

Price risk

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

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

We are not exposed to commodity price risk.

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

Interest rate risk

Our interest rate risk arises from short and long-term debt. In June 2013, we entered into the Hercules Agreement under which our borrowings bear interest at a variable rate with a fixed floor. Long-term debt issued at fixed rates expose us to fair value interest rate risk. As of December 31, 2017, the loan bore interest at the rate of the greater of 8.25% and a rate equal to 8.25% plus the prime rate of interest minus 5.25%.

As of December 31, 2017, if interest rates on borrowings had been 1.0% higher/lower with all other variables held constant, pre-tax results for the year would have been $0.2 million (2016: $0.2 million; 2015: $0.2 million) lower/ higher as a result of changes in the fair value of the borrowings. The effect of a change in interest rates of 1.0% on borrowings would have had an insignificant effect on pretax results for the year as a result of changes in the fair value of the borrowings.

Credit Risk

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

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

uniQure'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, cash equivalents and restricted cash were placed at the following banks:

	As of December 31,			
	2017		2016	
	Amount	Credit rating	Amount	Credit rating
	in thousands			
Bank				
Rabobank	$ 76,745	Aa2	$ 134,159	Aa2
Bank of America	84,986	Aa3	—	—
Commerzbank	120	A2	165	Baa3
Total	**$ 161,851**		**$ 134,324**	

Ratings are by Moody's.

Liquidity Risk

We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We manage liquidity through a rolling forecast of our liquidity reserve on the basis of expected cash flow and raise cash if and when needed, either through the issuance of shares or credit facilities.

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

	Undefined	Less than 1 year	Between 1 - 2 years	Between 3 - 5 years	Over 5 years
	in thousands				
At December 31, 2016					
Long-term debt	$ —	$ 2,195	$ 9,098	$ 13,505	$ —
Accounts payable, accrued expenses and other current liabilities	—	15,279	—	—	—
Contingent consideration (nominal amount)	15,255	—	—	—	—
Derivative financial instruments	62	—	—	—	—
Total	**$ 15,317**	**$ 17,474**	**$ 9,098**	**$ 13,505**	**$ —**
At December 31, 2017					
Long-term debt	$ —	$ 2,890	$ 14,188	$ 6,882	$ —
Accounts payable, accrued expenses and other current liabilities	—	11,409	—	—	—
Contingent consideration (nominal amount)	16,188	—	—	—	—
Derivative financial instruments	1,635	—	—	—	—
Total	**$ 17,823**	**$ 14,299**	**$ 14,188**	**$ 6,882**	**$ —**

Due to uncertainty of timing of achieving milestones, the amount for contingent consideration in respect of InoCard is classified as undefined in time. As of December 31, 2017, we expect the milestone obligations will become payable between 2018 and 2021. When due, 50% of the obligations can be settled either in cash or in a variable number of our shares.

Due to uncertainty of timing of exercise of warrants by BMS and Hercules, the amount owed to derivative financial instruments is classified as undefined in time. As of December 31, 2017, we expect the Hercules warrants to be exercised in 2018 and the BMS warrants in 2020.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements and the notes thereto, included in Part IV, Item 15, beginning on pages F 1 incorporated by reference into this Item 8.

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

None.

Item 9A. Controls Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive and financial officer ("CEO"), evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) as of December 31, 2017. Based on such evaluation, our CEO has concluded that as of December 31, 2017, our disclosure controls and procedures were effective.

Management's Annual Report on Internal Control Over Financial Reporting

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

We assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. This assessment was performed under the direction and supervision of our CEO, 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, 2017, based on criteria established in the COSO 2013 framework.

Inherent Limitations of Internal Controls

Our management, including our CEO, does not expect that our disclosure controls and procedures or our internal controls will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a simple error or mistake.

Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements due to error or fraud.

Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting during our most recently completed quarter that have materially affected or are reasonably likely to materially affect our internal control over financial reporting, as defined in Rule 13a-15(f) under the Exchange Act. We continue to enhance the design and documentation of our internal control over financial reporting processes to maintain effective controls over our financial reporting.

Item 9B. Other Information

None.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item regarding our directors, executive directors and corporate governance is incorporated into this section by reference to our Proxy Statement for our 2018 Annual Meeting of Shareholders or will be included in an amendment to this Annual Report on Form 10-K.

Item 11. Executive Compensation

The information required by this Item regarding executive compensation is incorporated into this section by reference to our Proxy Statement for our 2018 Annual Meeting of Shareholders or will be included in an amendment to this Annual Report on Form 10-K.

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

The information required by this Item regarding security ownership of certain beneficial owners, management and related stockholder matters, our equity compensation plans and securities under our equity compensation plans, is incorporated into this section by reference to our Proxy Statement for our 2018 Annual Meeting of Shareholders or will be included in an amendment to this Annual Report on Form 10-K.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required by this Item regarding certain relationships and related transactions and director independence is incorporated into this section by reference to our Proxy Statement for our 2018 Annual Meeting of Shareholders or will be included in an amendment to this Annual Report on Form 10-K.

Item 14. Principal Accounting Fees and Services

The information required by this Item regarding our principal accountant fees and services is incorporated into this section by reference to our Proxy Statement for our 2018 Annual Meeting of Shareholders or will be included in an amendment to this Annual Report on Form 10-K.

Part IV

Item 15. Exhibits, Financial Statement, Financial Statements Schedules, Signatures

Financial Statements and Schedules

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

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

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

Item 16. Form 10-K Summary

Not applicable.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS
FOR THE YEARS ENDED DECEMBER 31, 2017, 2016 AND 2015

Report of Independent Registered Public Accounting Firm

To the Management Board and shareholders of uniQure N.V.:

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of uniQure N.V. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations and comprehensive loss, of shareholders' equity, and of cash flows for each of the three years in the period ended December 31, 2017, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers Accountants N.V.

Amsterdam, The Netherlands
March 14, 2018
R.M.N. Admiraal RA

We have served as the Company's auditor since 2006, which includes periods before the Company became subject to SEC reporting requirements.

uniQure N.V.

CONSOLIDATED BALANCE SHEETS

	December 31, 2017	December 31, 2016
	in thousands, except share and per share amounts	
Current assets		
Cash and cash equivalents	$ 159,371	$ 132,496
Accounts receivable and accrued income	—	3,680
Accounts receivable and accrued income from related party	1,586	5,500
Prepaid expenses	1,139	996
Other current assets	687	1,274
Total current assets	**162,783**	**143,946**
Non-current assets		
Property, plant and equipment, net	34,281	35,702
Intangible assets, net	9,570	8,324
Goodwill	530	465
Other non-current assets	2,480	1,828
Total non-current assets	**46,861**	**46,319**
Total assets	**$ 209,644**	**$ 190,265**
Current liabilities		
Accounts payable	$ 2,908	$ 5,524
Accrued expenses and other current liabilities	8,838	9,766
Current portion of long-term debt	1,050	605
Current portion of deferred rent	737	684
Current portion of deferred revenue	4,613	6,142
Current portion of contingent consideration	1,084	—
Total current liabilities	**19,230**	**22,721**
Non-current liabilities		
Long-term debt, net of current portion	19,741	19,631
Deferred rent, net of current portion	9,114	6,781
Deferred revenue, net of current portion	67,408	75,612
Contingent consideration, net of current portion	2,880	1,838
Derivative financial instruments related party	1,298	51
Other non-current liabilities	614	—
Total non-current liabilities	**101,055**	**103,913**
Total liabilities	**120,285**	**126,634**
Commitments and contingencies (see note 16)		
Shareholders' equity		
Ordinary shares, €0.05 par value: 60,000,000 shares authorized at December 31, 2017 and December 31, 2016 and 31,339,040 and 25,257,420 shares issued and outstanding at December 31, 2017 and December 31, 2016, respectively.	1,947	1,593
Additional paid-in-capital	566,530	464,653
Accumulated other comprehensive loss	(3,800)	(6,557)
Accumulated deficit	(475,318)	(396,058)
Total shareholders' equity	**89,359**	**63,631**
Total liabilities and shareholders' equity	**$ 209,644**	**$ 190,265**

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

uniQure N.V.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Years ended December 31,		
	2017	2016	2015
	in thousands, except share and per share amounts		
License revenues	$ 8	$ 975	$ —
License revenues from related party	4,121	3,940	3,335
Collaboration revenues	4,638	7,164	—
Collaboration revenues from related party	4,340	13,019	7,243
Total revenues	**13,107**	**25,098**	**10,578**
Operating expenses:			
Research and development expenses	(72,172)	(72,510)	(59,125)
Selling, general and administrative expenses	(24,635)	(25,999)	(23,383)
Total operating expenses	**(96,807)**	**(98,509)**	**(82,508)**
Other income	15,430	1,465	779
Other expense	(3,073)	—	—
Loss from operations	**(71,343)**	**(71,946)**	**(71,151)**
Interest income	117	70	121
Interest expense	(2,232)	(2,172)	(2,572)
Foreign currency (losses) / gains, net	(3,566)	1,034	(2,496)
Other non-operating (expense) / income, net	(2,435)	785	(7,164)
Loss before income tax expense	**(79,459)**	**(72,229)**	**(83,262)**
Income tax benefit / (expense)	199	(1,145)	1,179
Net loss	**$ (79,260)**	**$ (73,374)**	**$ (82,083)**
Other comprehensive income / (loss), net of income tax:			
Foreign currency translation adjustments net of tax impact of $0.2 million for the year ended December 31, 2017 (2016: $(1.1) million and 2015: $0.7 million)	2,757	271	(1,556)
Total comprehensive loss	**$ (76,503)**	**$ (73,103)**	**$ (83,639)**
Basic and diluted net loss per ordinary share	$ (2.94)	$ (2.93)	$ (3.72)
Weighted average shares used in computing basic and diluted net loss per ordinary share	26,984,183	25,036,465	22,082,345

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

uniQure N.V.

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY

	Ordinary shares		Additional paid-in capital	Accumulated other comprehensive income/(loss)	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
	in thousands, except share and per share amounts					
Balance at December 31, 2014	**18,092,194**	**$ 1,198**	**$ 287,309**	**$ (5,272)**	**$ (240,601)**	**$ 42,634**
Loss for the period	—	—	—	—	(82,083)	(82,083)
Other comprehensive loss	—	—	—	(1,556)	—	(1,556)
Follow-on public offering	3,000,000	165	82,354	—	—	82,519
Issuance of shares to collaboration partner Bristol-Myers Squibb	2,388,108	132	71,799	—	—	71,931
Exercises of share options	847,642	47	2,818	—	—	2,865
Share-based compensation expense	—	—	11,617	—	—	11,617
Balance at December 31, 2015	**24,327,944**	**$ 1,542**	**$ 455,897**	**$ (6,828)**	**$ (322,684)**	**$ 127,927**
Loss for the period	—	—	—	—	(73,374)	(73,374)
Other comprehensive income	—	—	—	271	—	271
Exercises of share options	750,408	41	2,542	—	—	2,583
Shares distributed during the period	179,068	10	—	—	—	10
Share-based compensation expense	—	—	6,214	—	—	6,214
Balance at December 31, 2016	**25,257,420**	**$ 1,593**	**$ 464,653**	**$ (6,557)**	**$ (396,058)**	**$ 63,631**
Loss for the period	—	—	—	—	(79,260)	(79,260)
Other comprehensive income	—	—	—	2,757	—	2,757
Follow-on public offering	5,000,000	294	84,996	—	—	85,290
Shares issued as consideration in a business combination	64,648	4	584	—	—	588
Exercises of share options	603,740	32	4,088	—	—	4,120
Exercises of convertible loan warrants	114,172	7	1,946	—	—	1,953
Restricted and performance share units distributed during the period	299,060	17	(17)	—	—	—
Share-based compensation expense	—	—	10,280	—	—	10,280
Balance at December 31, 2017	**31,339,040**	**$ 1,947**	**$ 566,530**	**$ (3,800)**	**$ (475,318)**	**$ 89,359**

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

uniQure N.V.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Cash flows from operating activities			
Net loss	$ (79,260)	$ (73,374)	$ (82,083)
Adjustments to reconcile net loss to net cash (used in) / provided by operating activities:			
Depreciation, amortization and impairments	7,543	6,089	6,324
Share-based compensation expense	10,280	6,214	11,617
Change in fair value of derivative financial instruments and contingent consideration	5,194	(1,865)	8,508
Unrealized foreign exchange losses / (gains)	4,222	(755)	(526)
Change in deferred taxes	209	1,145	(1,179)
Change in lease incentives	2,215	649	(577)
Changes in operating assets and liabilities:			
Accounts receivable and accrued income, prepaid expenses and other current assets	9,715	(5,917)	(1,680)
Inventories	-	480	(260)
Accounts payable	(1,670)	344	(774)
Accrued expenses and other liabilities	(1,640)	499	4,929
Deferred revenue	(21,078)	(5,698)	63,169
Net cash (used in) / provided by operating activities	(64,270)	(72,189)	7,468
Cash flows from investing activities			
Purchase of intangible assets	(1,122)	(1,884)	(415)
Purchase of property, plant and equipment	(4,461)	(15,288)	(7,607)
Net cash used in investing activities	(5,583)	(17,172)	(8,022)
Cash flows from financing activities			
Proceeds from issuance of shares related to employee stock option plans	4,044	2,593	2,865
Proceeds from exercises of convertible loan warrants	1,322	-	-
Proceeds from public offering of shares, net of issuance costs	85,290	-	82,519
Contingent consideration payment	(582)	-	-
Proceeds from issuance of shares to collaboration partner	-	-	75,493
Repayment of capital lease obligations	-	(148)	(186)
Net cash generated from financing activities	90,074	2,445	160,691
Currency effect cash, cash equivalents and restricted cash	7,306	(1,629)	(3,198)
Net increase / (decrease) in cash, cash equivalents and restricted cash	27,527	(88,545)	156,939
Cash, cash equivalents and restricted cash at beginning of period	134,324	222,869	65,930
Cash, cash equivalents and restricted cash at the end of period	**$ 161,851**	**$ 134,324**	**$ 222,869**
Supplemental cash flow disclosures:			
Cash paid for interest	**$** 1,624	$ 2,345	$ 2,082
Non-cash (decreases) / increases in accounts payables related to purchases of intangible assets and property, plant and equipment	**$** (1,557)	$ 1,174	$ (792)

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

uniQure N.V.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

FOR THE YEARS ENDED DECEMBER 31, 2017, 2016 AND 2015

1. General business information

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

The Company is registered in the trade register of the 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 25a, Amsterdam 1105 BP, the Netherlands and its telephone number is +31 20 240 6000. The Company's website address is www.uniqure.com.

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

2. Summary of significant accounting policies

2.1 Basis of preparation

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

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

The consolidated financial statements are presented in U.S. dollars, except where otherwise indicated. Transactions denominated in currencies other than U.S. dollars are presented in the transaction currency with the U.S. dollar amount included in parenthesis, converted at the foreign exchange rate as of the transaction date.

The consolidated financial statements presented have been prepared on a going concern basis based on the Company's cash and cash equivalents as of December 31, 2017 and the Company's budgeted cash flows for the twelve months following the signature date.

2.2 Use of estimates

The preparation of consolidated financial statements, in conformity with U.S. GAAP and SEC rules and regulations, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of revenues and expenses during the reporting period. Estimates and assumptions are primarily made in relation to revenue recognition in the determination and measurement of multiple elements and assessment of the performance period over which collaboration revenue is recognized, income taxes, including the realization of deferred tax assets, fair value of derivative financial instruments, share-based compensation, measurement of accrued expenses which have not yet been invoiced as of the balance sheet date and business combinations including contingent consideration payable. If

actual results differ from the Company's estimates, or to the extent these estimates are adjusted in future periods, the Company's results of operations could either benefit from, or be adversely affected by, any such change in estimate.

2.3 Accounting policies

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

2.3.1 Consolidation

The consolidated financial statements comprise the financial statements of the Company and its subsidiaries. Subsidiaries are all entities over which the Company has a controlling financial interest either through variable interest or through voting interest. Currently, the Company has no involvement with variable interest entities.

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

2.3.2 Current versus non-current classification

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

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

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

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

2.3.3 Foreign currency translation

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 consolidated financial statements are presented in U.S. dollars.

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

Upon consolidation, the assets and liabilities of foreign operations are translated into the functional currency of the shareholding entity at the exchange rates prevailing at the balance sheet date; items of income and expense are translated at monthly average exchange rates. The consolidated assets and liabilities are translated from uniQure N.V.'s functional currency, euro, into the reporting currency U.S. dollar at the exchange rates prevailing at the balance sheet date; items of income and expense are translated at monthly average exchange rates. Issued capital and additional paid-in capital are translated at historical rates with differences to the balance sheet date rate recorded as translation adjustments in other comprehensive income / loss. The exchange differences arising on translation for consolidation are recognized in "accumulated other comprehensive income / loss". On disposal of a foreign operation, the component of other comprehensive income / loss relating to that particular foreign operation is recognized in profit or loss. As the intercompany funding of the Company's Lexington operations is neither planned nor likely to be settled in the foreseeable future, the associated foreign exchange effect is presented as accumulated other comprehensive income / loss.

2.3.4 Fair value measurement

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

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

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

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

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

Items measured at fair value on a recurring basis include financial instruments and contingent consideration (note 3, "Fair value measurement"). The carrying amount of cash and cash equivalents, accounts receivable from collaborators, prepaid expenses, other assets, accounts payable, accrued expenses and other current liabilities reflected in the consolidated balance sheets approximate their fair values due to their short-term maturities.

2.3.5 Business combination

On July 31, 2014, the Company closed its acquisition of InoCard GmbH ("InoCard"). This transaction was accounted for as a business combination under the acquisition method of accounting. Accordingly, the tangible and intangible assets acquired and liabilities assumed were recorded at fair value as of the date of acquisition, with the excess purchase price recorded as goodwill. The estimated fair values of the assets acquired and liabilities assumed were determined using the methods discussed in the following paragraphs and required significant judgment and estimates, which could materially differ from actual values and fair values determined using different methods or assumptions.

a. Goodwill

Goodwill represents the excess of the purchase price over the fair value of the net assets acquired when accounted for using the acquisition method of accounting for business combinations. Goodwill is not amortized but is evaluated for impairment within the Company's single reporting unit on an annual basis in the fourth quarter, or more frequently if an event occurs or circumstances change that would more-likely-than-not reduce the fair value of the Company's reporting unit below its carrying amount. The Company has not recognized any impairment charges related to goodwill.

b. Acquired research and development

Acquired research and development ("Acquired R&D") represents the fair value assigned to intangible assets in incomplete research projects that the Company acquires through business combinations. The amounts are capitalized and are accounted for as indefinite-lived intangible assets, subject to impairment testing until completion, abandonment of the projects or when the research findings are commercialized through a revenue-generating project. Upon successful completion or commercialization of a project, uniQure will make a determination as to the then useful life of the intangible asset, generally determined by the period in which the substantial majority of the cash flows are expected to be generated, and begin amortization. In case of abandonment, the asset will be written-off.

c. Contingent consideration

Each reporting period, the Company revalues the contingent consideration obligations associated with this business combination 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 successful achievement of related milestones, the estimated timing in which milestones are achieved and the discount rate used to estimate the fair value of the liability. Changes in the development timeline and the results from development of the AMT-126 program impact the Company's assumptions and judgments, which could result in materially different estimates of the fair value of contingent consideration. Payments made soon after the acquisition date are recorded as cash flows from financing activities, and payments, or the portion of the payments, not made soon after the acquisition date are recorded as cash flows from operating activities. See note 3, "Fair value measurement", for additional information.

2.3.6 Notes to the consolidated statements of cash flows

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

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

2.3.7 Segment information

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

2.3.8 Net loss per share

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

Diluted net loss per share reflects the dilution that would occur if share options or warrants to issue common stock were exercised, or performance or restricted share units were distributed. However, potential common shares are excluded if their effect is anti-dilutive. The Company currently has no dilutive securities due to the net loss position and as such, basic and diluted net loss per share are the same for the periods presented.

2.3.9 Impairment of long-lived assets

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

Goodwill is not amortized but is evaluated for impairment within the Company's single reporting unit on an annual basis, during the fourth quarter, or more frequently if an event occurs or circumstances change that would more-likely-than-not reduce the fair value of the Company's reporting unit below its carrying amount. Based on a quantitative analysis comparing the Company's market capitalization to the carrying amount of the net assets, the Company determines whether further impairment testing is required.

2.3.10 Intangible assets

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).

2.3.11 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.

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

Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which are as follows:

- Leasehold improvements 10years
- Laboratory equipment between 5 - 10years
- Office equipment 5 years

2.3.12 Other (non) current assets

Deposit paid are either presented as other current assets or as other non-current assets based on duration of the underlying contractual arrangement. Deposits are classified as restricted cash. The following table provides a reconciliation of cash, cash equivalents and restricted cash reported in the consolidated balance sheets with amounts presented in the consolidated statements of cash flows:

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Cash and cash equivalents	$ 159,371	$ 132,496	$ 221,626
Restricted cash	2,480	1,828	1,243
Total cash, cash equivalents and restricted cash	**$ 161,851**	**$ 134,324**	**$ 222,869**

2.3.13 Accounts receivables

Accounts receivables are amounts due from services provided to the Company's collaboration partner and are purely trade receivables.

2.3.14 Prepaid expenses

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

2.3.15 Accounts payable and accrued expenses

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

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

2.3.16 Long-term debt

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

2.3.17 Pensions and other post-retirement benefit plans

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

Starting in 2016, the Company adopted a qualified 401(k) Plan for all employees at its Lexington facility in the USA, which offers both a pre-tax and post-tax (Roth) component. Employees may contribute up to 50% of their pre-tax compensation, which is subject to IRS statutory limits for 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.

2.3.18 Share-based compensation

The Company accounts for its share-based compensation awards in accordance with *ASC 718, Compensation-Stock Compensation* and *ASC Subtopic 505-50, Equity-Based Payments to Non-Employees*.

All of the Company's share-based compensation plans for employees are equity-classified.

ASC 718 requires all share-based compensation to employees, including grants of employee options, restricted share units, performance share units and modifications to existing instruments, to be recognized in the consolidated statements of operations and comprehensive loss based on their grant-date fair values, net of an estimated forfeiture rate, over the requisite service period. Forfeitures of employee options are recognized as they occur. ASC 505-50 requires all share-based compensation to non-employees to be recognized in the consolidated statements of operations and comprehensive loss based on their fair values, with the fair values being re-measured until completion of performance.

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

2.3.19 Revenue recognition

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

The Company recognizes revenue when earned and realized or realizable in accordance with *ASC 605, Revenue Recognition*. Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller´s price to the buyer is fixed or determinable; and

- collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as the current portion of deferred revenue and amounts expected to be recognized as revenue after the 12 months following the balance sheet date are classified as the non-current portion of deferred revenue.

Multiple element arrangements are analyzed to determine whether the deliverables within the agreement can be separated or whether they must be accounted for as a single unit of accounting. Deliverables under an agreement are required to be accounted for as separate units of accounting provided that (i) a delivered item has value to the customer on a stand-alone basis; and (ii) if the agreement includes a general right of return relative to the delivered item, the delivery or performance of the undelivered item is considered probable and substantially in the control of the vendor. The allocation of consideration amongst the deliverables under the agreement is derived using a "best estimate of selling price" if vendor specific objective evidence and third-party evidence of fair value are not available. If the delivered element does not have stand-alone value or if the fair value of any of the undelivered elements cannot be determined, the arrangement is accounted for as a single unit of accounting.

a. License revenues

License revenues consist of up-front payments, target selection payments, milestone payments and royalties.

Up-front and target selection payments

Up-front payments, target selection payments or similar non-refundable payments are initially reported as deferred revenue on the consolidated balance sheets and are recognized as revenue on a straight-line basis over the period of the performance obligation. The estimated period of the performance obligation is re-assessed at each balance sheet date.

Milestone payments and royalties

Research-based milestone payments are recognized as revenues either on achievement of such milestones if the milestones are considered substantive or over the period the Company has continuing performance obligations, if the milestones are not considered substantive. When determining if a milestone is substantive, the Company considers the following factors:

- the degree of certainty in achieving the milestone;
- the frequency of milestone payments;
- the Company's efforts, which result in achievement of the milestone;
- the amount of the milestone payment relative to the other deliverables and payment terms; and
- whether the milestone payment is related to future performance or deliverables.

Sales-based milestone payments and royalties are recognized in earnings when earned.

b. Collaboration revenue

Collaboration revenue consists of revenue generated from collaborative research and development arrangements. Services may include the provision of Company staff, consultants or other third-party vendors engaged by the Company in relation to a collaboration program and the manufacturing of gene therapeutic products to the extent these are reimbursed through the respective collaborative research and development program.

Collaboration revenues, which are typically related to reimbursements from collaborators for the Company's performance of research and development services under the respective agreements, are recognized on the basis of labor hours valued at a contractually agreed rate. Collaboration revenues include reimbursements for related out-of-pocket expenses. Cost reimbursements to which the Company is entitled under agreements are recognized as collaboration revenues in the same quarter of the recorded cost they are intended to compensate.

2.3.20 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.

Income from releasing outstanding deferred revenue in relation to the termination of the collaboration with Chiesi is presented as other income.

Cost incurred in 2017 in relation to terminating the marketing of its Glybera program, as well as costs associated with exiting its prior Amsterdam facilities and its Heidelberg site are presented as other expenses.

2.3.21 Research and development expenses

Research and development costs are expensed as incurred. Research and development expenses generally consist of laboratory research, clinical trials, statistical analysis and report writing, regulatory compliance costs incurred with clinical research organizations and other third-party vendors (including post-approval commitments to conduct consistency and comparability studies). In addition, research and development expenses consist of start-up and validation costs related to the Company's Lexington facility and the development and improvement of the Company's manufacturing processes and methods.

2.3.22 Income taxes

Income taxes are recorded in accordance with *ASC 740, Income Taxes*, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

Valuation allowances are provided, if based upon the weight of available evidence, it is more-likely-than-not that some or all of the deferred tax assets will not be realized. The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more-likely-than-not be realized. The determination as to whether the tax benefit will more-likely-than-not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2017, and 2016, the Company did not have any significant uncertain tax positions.

2.3.23 Recent accounting pronouncements

Recently Adopted Accounting Pronouncements

In July 2015, the FASB issued ASU 2015-11, Inventory ("ASU 2015-11"), which requires an entity to measure inventory within the scope at the lower of cost and net realizable value. Net realizable value is the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal, and transportation. Adoption of this guidance, effective January 1, 2017, did not have a material effect on its consolidated financial statements.

In January 2017, the FASB issued ASU 2017-04, simplifying the Test for Goodwill Impairment ("ASU 2017-04"), which simplifies the measurement of goodwill impairment. An entity will no longer perform a hypothetical purchase price allocation to measure goodwill impairment. Instead, impairment will be measured using the difference between the carrying amount and the fair value of the reporting unit. The Company's early adoption as of January 1, 2017, did not have a material effect on its consolidated financial statements.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments ("ASU 2016-15"). This ASU makes targeted amendments to classification of certain

cash flows. The Company's early adoption as of January 1, 2017, did not have a material effect on its consolidated financial statements.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows: Restricted Cash ("ASU 2016-18"). The ASU introduces specific requirements on the presentation of restricted cash and restricted cash equivalents. The Company's early adoption as of January 1, 2017, effected the presentation of restricted cash in relation to leasehold deposit in the Consolidated Balance Sheets and Consolidated Statements of Cash Flows.

Recent Accounting Pronouncements Not Yet Effective

ASU 2014-09: ASC 606 Revenue from Contracts with Customers

In July 2015, the FASB issued ASU 2015-14, Revenue from Contracts with Customers: Deferral of the Effective Date ("ASU 2015-14"), which deferred the effective date for ASU 2014-09, Revenue from Contracts with Customers ("ASU 2014-09"), by one year. ASU 2014-09 will supersede the revenue recognition requirements in ASC 605, Revenue Recognition, and requires entities to recognize revenue in a way that depicts the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. In 2016, the FASB issued ASU 2016-08, 2016-10 and 2016-12, which provided further clarification on ASU 2014-09. ASU 2014-09 is effective for annual reporting periods beginning after December 15, 2017, including interim periods within that reporting period, which for the Company is January 1, 2018.

ASU 2014-09 provides for two implementation methods to the Company, (i) full retrospective application to all periods from January 1, 2015 onwards for revenue recognized in relation to collaborations; or (ii) application of the standard from January 1, 2018, onwards to active collaborations with an adjustment to retained earnings as of December 31, 2017, to include the cumulative adjustment to revenue recognized in prior periods in relation to active collaborations. The Company has selected the cumulative effect method to adopt the standard and will not use practical expedients at initial application. The Company has one active collaboration arrangement with Bristol Myers Squibb ("BMS"). As a result of the cumulative effect method the Company will not apply the requirements of ASU 2014-09 to any comparative periods presented and therefore the impact assessment applies to BMS collaboration agreement only.

The Company is finalizing its evaluation of the impact of adopting this standard. The Company has considered the new standard and preliminarily expect that the revenue recognition for the existing license will not be materially impacted based on the transfer of the services over the performance obligation. Sales-based milestone payments and royalties will continue to be recognized in the statement of comprehensive income when earned. Collaboration revenues, which are typically related to reimbursements from collaborators for our performance and costs incurred of research and development services under the respective agreements, are recognized in the statement of comprehensive income on the basis of labor hours valued at a contractually agreed rate and as costs incurred.

ASU 2016-01: ASC 825 Recognition and Measurement of Financial Assets and Financial Liabilities

In January 2016, the FASB issued ASU 2016-01, Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities ("ASU 2016-01"). ASU 2016-01 addresses certain aspects of recognition, measurement, presentation and disclosure of financial instruments. ASU 2016-01 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017, which for the Company is January 1, 2018. The Company does not expect ASU 2016-01 to have a material impact on its consolidated financial statements.

ASU 2016-02: Leases

In February 2016, the FASB issued ASU 2016-02, Leases ("ASU 2016-02"). The standard amends the existing accounting standards for lease accounting, including requiring lessees to recognize most leases on their balance sheets and making targeted changes to lessor accounting. ASU 2016-02 is effective for annual periods in fiscal years beginning after December 15, 2019. Early adoption is permitted. The new leases standard requires a modified retrospective transition approach for all leases existing at, or entered into after, the date of initial application with an option to use certain transition relief. The Company does expect ASU 2016-02 to have a material impact on its consolidated financial statements, primarily from recognition of a right-of-use asset and lease liability in the balance sheet and a shift of cash outflows from operating activities to financing activities.

ASU 2016-05: Derivatives and Hedging: Effect of Derivative Contract Novations on Existing Hedge Accounting Relationships

In March 2016, the FASB issued ASU 2016-05, Derivatives and Hedging: Effect of Derivative Contract Novations on Existing Hedge Accounting Relationships ("ASU 2016-05") and ASU 2016-06, Derivatives and Hedging: Contingent Put and Call Options in Debt Instruments. Both ASUs address issues regarding hedge accounting. The ASUs are effective for fiscal years, and interim periods within those years, beginning after December 15, 2017, which for the Company is January 1, 2018. The Company does not expect ASU 2016-05 or ASU 2016-06 to have a material impact on its consolidated financial statements.

ASU 2017-09: Compensation (topic 718)- scope of modification accounting

In May 2017, the FASB issued ASU 2017-09, Compensation-stock compensation (topic 718)- scope of modification accounting ("ASU 2017-09"), which provides clarity regarding the applicability of modification accounting in relation to share-based payment awards. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The effective date for the standard is for fiscal years beginning after December 15, 2017, which for the Company is January 1, 2018. Early adoption is permitted. The new standard is to be applied prospectively. The Company does not expect ASU 2017-09 to have a material impact on its consolidated financial statements.

3. Fair value measurement

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

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

The Company's only material financial assets measured at fair value using Level 1 inputs is cash and cash equivalents.

Liabilities measured at fair value using Level 3 inputs consisted of contingent consideration and derivative financial instruments. Changes in Level 3 items during the years ended December 31, 2017, 2016 and 2015 are as follows:

	Contingent consideration	Derivative financial instruments	Total
		in thousands	
Balance at December 31, 2014	**$ 1,767**	**$ 251**	**$ 2,018**
Issuance of financial instruments	—	(10,060)	(10,060)
Allocation to shareholders' equity	—	3,614	3,614
Losses recognized in profit or loss	1,339	7,162	8,501
Currency translation effects	(180)	(130)	(310)
Balance at December 31, 2015	**$ 2,926**	**$ 837**	**$ 3,763**
Gains recognized in profit or loss	(1,080)	(785)	(1,865)
Currency translation effects	(8)	10	2
Balance at December 31, 2016	**$ 1,838**	**$ 62**	**$ 1,900**
Exercises of convertible loan warrants	—	(631)	(631)
Losses recognized in profit or loss	3,002	2,192	5,194
Contingent consideration paid	(1,181)	—	(1,181)
Currency translation effects	305	12	317
Balance at December 31, 2017	**$ 3,964**	**$ 1,635**	**$ 5,599**

Contingent consideration

In connection with the Company's acquisition of InoCard GmbH ("InoCard") in 2014, the Company recorded contingent consideration related to amounts potentially payable to InoCard's former shareholders. In August 2017, the

Company and the former shareholders amended the 2014 sale and purchase agreement to waive certain of the Company's obligations regarding the development of the acquired program pursuant to a plan to be agreed between the Company and InoCard's former shareholders. The parties also modified the conditions of the agreed milestone payments, including a reduction of the percentage of any future milestone that can be settled in the form of Company ordinary shares from 100% to 50%. The Company recorded $2.3 million in research and development cost in the year ended December 31, 2017, related to the increase in fair value of the contingent consideration resulting from these modifications. The Company made $1.2 million in milestone payments during the year ended December 31, 2017, 50% of which were settled through the issuance of 64,648 restricted ordinary shares on October 2, 2017.

The amounts payable in accordance with the amended sale and purchase agreement are contingent upon realization of the following milestones as amended:

- early candidate nomination of product by related party;
- acceptance of investigational new drug application by the United States Food and Drug Administration or an equivalent filing in defined Western European countries or Japan;
- completion of dosing of all patients in the first clinical study; and
- full proof of concept of the product in humans after finalization of the first clinical study.

The valuation of the contingent liability is based on significant inputs not observable in the market such as the probability of success ("POS") of achieving certain research milestones (estimated as likely for the first three milestones as of the balance sheet date), the time at which the research milestones are expected to be achieved (ranging from 2018 to 2021), as well as the discount rate applied, which represents a Level 3 measurement. The POS as well as the discount rate both reflect the probability of achieving a milestone as of a specific date. In June 2017, the Company replaced the risk-adjusted discount rate of 30.0% with the Company's weighted average rate of capital of 14.5% to reflect the full integration of the acquired business into the Company's operation. All of the above resulted in a $0.3 million increase of the liability. As of December 31, 2017, the Company's weighted average rate of capital is 12.0%.

The fair value of the contingent liability as of December 31, 2017 amounted to $4.0 million (December 31, 2016: $1.8 million). Varying the timing of the milestones, the discount rate and the POS of unobservable inputs results in the following fair value changes:

	December 31, 2017
	in thousands
Change in fair value	
Moving out of all milestones by 6 months	$ (212)
Increasing the POS for the first milestone by 20%	1,207
Decreasing the POS for the first milestone by 20%	(1,207)
Reducing the discount rate from 12.0% to 2.0%	1,239
Increasing the discount rate from 12.0% to 22.0%	(617)

Derivative financial instruments

The Company issued derivative financial instruments related to its collaboration with Bristol-Meyers Squibb Company ("BMS") and in relation to the issuance of the Hercules Technology Growth Corp. ("Hercules") loan facility. The fair value of these derivative financial instruments as of December 31, 2017, was $1.6 million (December 31, 2016: $0.1 million), and these derivative financial instruments are described in more detail below.

BMS collaboration

On April 6, 2015 ("Execution Date"), the Company entered into agreements with BMS. Pursuant to the terms of the agreements, BMS was required to purchase from the Company a certain number of shares such that:

- BMS would own 4.9% of the issued and outstanding ordinary shares of the Company immediately after the approval of the collaboration by the Company's shareholders ("First Closing"); and

- prior to December 31, 2015 BMS would own 9.9% of the issued and outstanding ordinary shares of the Company immediately after such purchase ("Second Closing").

The purchase price per ordinary share related to the First Closing was agreed at $33.84 per share at the Execution Date.

The purchase price per ordinary share related to the Second Closing on August 7, 2015, was $29.67, which was equal to 110% of the Volume Weighted Average price ("VWAP") for the 20 trading days ending on the date that is 5 days prior to the Second Closing. The timing of the investment was at the sole discretion of BMS.

Additionally, BMS was granted two warrants:

- a warrant allowing BMS to purchase a specific number of uniQure ordinary shares such that its ownership will equal 14.9% immediately after such purchase. The warrant can be exercised on the later of (i) the date on which the Company receives from BMS the Target Designation Fees (as defined in the collaboration agreements) associated with the first six New Targets (as defined in the collaboration agreements); and (ii) the date on which BMS designates the sixth New Target; and

- a warrant allowing BMS to purchase a specific number of uniQure ordinary shares such that its ownership will equal 19.9% immediately after such purchase. The warrant can be exercised on the later of (i) the date on which uniQure receives from BMS the Target Designation Fees associated with the first nine New Targets; and (ii) the date on which BMS designates the ninth New Target.

Pursuant to the terms of the BMS Agreements the exercise price, in respect of each warrant, is equal to the greater of (i) the product of (A) $33.84, multiplied by (B) a compounded annual growth rate of 10% and (ii) the product of (A) 1.10 multiplied by (B) the 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.

On the Execution Date, the Company recorded derivative financial instruments related to the First Closing, Second Closing and the two warrants at a combined fair value of $10.1 million (recorded as an asset). The Company evaluated the Share Subscription Agreement and the Collaboration Agreement (see note 4, "Collaboration arrangements and concentration of credit risk") as one agreement.

The Company recorded a loss of $7.3 million in non-operating income/ (expense) related to the changes in fair value of the derivative financial asset related to the First Closing between the Execution Date and June 12, 2015. On June 12, 2015, the Company issued 1.1 million of its ordinary shares to BMS for aggregate cash proceeds of $37.6 million, thereby extinguishing the derivative financial asset at its fair value of $5.0 million at this date and raising $32.6 million equity. After the extinguishment the equity raised from on the sale of ordinary shares in excess of the market price of $29.37 per share was recorded in additional paid- in capital as these amounts result from an investment decision made by BMS.

The Company recorded a loss of $0.3 million in non-operating income/ (expense) related to changes in fair value of the derivative financial liability related to the Second Closing between the Execution Date and August 7, 2015. On August 7, 2015, the Company issued 1.3 million of its ordinary shares to BMS at $29.67 per ordinary share for aggregate cash proceeds of $37.9 million, thereby extinguishing the derivative financial liability at its fair value of $1.4 million at this date and raising $39.3 million equity. After the extinguishment, the equity raised from on the sale of ordinary shares in excess of the market price of $23.64 per share was recorded in additional paid-in capital as these amounts result from an investment decision made by BMS.

The fair value of the warrants as of December 31, 2017 is $1.3 million (December 31, 2016: $0.1 million). During the year ended December 31, 2017, the Company recognized a $1.2 million loss in non-operating income / expense (December 31, 2016: $0.5 million gain; December 31, 2015: $0.5 million gain) related to fair value changes of the BMS warrants. The exercise of the warrants is expected to occur within 2 and 3 years after the balance sheet date. The Company classified the derivative financial liabilities as non-current at the balance sheet date.

The Company used Monte-Carlo simulations to determine the fair market value of the BMS warrants. The valuation model incorporated several inputs, including the underlying share price at both the Execution Date and on May

21, 2015, the effective date of the collaboration agreement ("Effective Date") as well as at the balance sheet date, the risk-free rate adjusted for the period affected, an expected volatility based on a peer group analysis, 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 assumes BMS will exercise the warrants only if it is financially rational to do so.

The Company conducted a sensitivity analysis to assess the impact on changes in assumptions on the fair value. Specifically, the Company examined the impact on the fair market of the warrants by increasing the volatility by 10% to 85%. A further sensitivity analysis was performed assuming the exercise date of the warrants would occur one year later than what was assumed in the initial valuation. The table below illustrates the impact on the fair market valuation associated with these changes in assumptions as of December 31, 2017.

	Total warrants in thousands
Base case	$ 1,298
Increase volatility by 10% to 85%	457
Extend exercise dates by one year	161

Hercules loan facility

On June 14, 2013, the Company entered into a venture debt loan facility (the "Original Facility") with Hercules Technology Growth Capital, Inc. ("Hercules") (see note 8, "Long-term debt") pursuant to a Loan and Security Agreement (the "Loan Agreement") which included a warrant maturing on February 5, 2019. The warrant was not closely related to the host contract and was accounted for separately as a derivative financial liability measured at fair value though profit or loss. The warrant included in the Original Facility remained in place following the 2014 and 2016 amendments of the loan. The fair value of this derivative, recorded in other current liabilities, as of December 31, 2017 is $0.3 million (December 31, 2016: $0.0 million). During the year ended December 31, 2017, uniQure recognized a $0.3 million loss in other non-operating income / (expense) (December 31, 2016: $0.3 million gain; December 31, 2015: $0.0 million) related to fair value changes of the Hercules warrants.

4. Collaboration arrangements and concentration of credit risk

In the year ended December 31, 2017, the Company generated all collaboration and license revenues from its Collaboration and License Agreement with BMS, and its Co-Development Agreement for hemophilia B with Chiesi Farmaceutici S.p.A. ("Chiesi").

On April 19, 2017, the Company and Chiesi entered into an agreement to terminate the Glybera Commercialization Agreement following the Company's decision to not seek renewal with the European Medicines Agency of the marketing authorization for Glybera by October 2017 ("Glybera Termination Agreement"). In July 2017, the Company and Chiesi terminated their co-development agreement in respect of the hemophilia B program ("hemophilia B Termination Agreement"). As a result, the Company holds the global rights to the development of the hemophilia B program and is not required to provide any further services to Chiesi.

Since June 2015, BMS has been considered a related party given the significance of its equity investment in the Company (December 31, 2017: 2.4 million ordinary shares or 7.6% of outstanding ordinary shares).

Services to the Company's collaboration partners are rendered by the Dutch operating entity. Total collaboration and license revenue generated from these partners are as follows:

	Years ended December 31,		
	2017	2016	2015
Bristol Myers Squibb	$ 8,461	$ 16,959	$ 4,677
Chiesi Farmaceutici S.p.A (up to June 30, 2017)	4,646	8,139	5,901
Total	**$ 13,107**	**$ 25,098**	**$ 10,578**

Amounts owed from these partners in relation to the collaboration are as follows:

	December 31, 2017	December 31, 2016
	in thousands	
Bristol Myers Squibb	$ 1,586	$ 5,500
Chiesi Farmaceutici S.p.A	—	3,680
Total	**$ 1,586**	**$ 9,180**

BMS collaboration

In May 2015, the Company closed a Collaboration and License Agreement with BMS (the "BMS Collaboration Agreement") that provides exclusive access to the Company's gene therapy technology platform for multiple targets in cardiovascular (and other target specific) diseases. The collaboration included the Company's proprietary gene therapy program for congestive heart failure, which aims to restore the heart's ability to synthesize S100A1, a calcium sensor and master regulator of heart function, and thereby improve clinical outcomes for patients with reduced ejection fraction. Beyond cardiovascular diseases, the agreement also included the potential for a target exclusive collaboration in other disease areas. In total, the companies may collaborate on ten targets, including AMT-126.

The Company is conducting the discovery, non-clinical, analytical and process development activities and is responsible for manufacturing of clinical and commercial supplies using the Company's vector technologies and industrial, proprietary insect-cell based manufacturing platform. BMS reimburses the Company for all its research and development efforts in support of the Collaboration, and will lead the clinical development and regulatory activities across all programs. BMS will also be solely responsible for commercialization of all products from the collaboration.

The Company evaluated the BMS Collaboration Agreement and determined that it is a revenue arrangement with multiple elements. The Company's substantive deliverables under the BMS Collaboration Agreement include an exclusive license to its technology in the field of cardiovascular disease, research and development services for specific targets chosen by BMS and general development of the Company's proprietary vector technology, participation in the Joint Steering Committee, and clinical and commercial manufacturing. The Company concluded that the BMS Collaboration Agreement consists of three units of accounting, including (i) technology (license and target selections), know-how and manufacturing in the field of gene therapy and development and active contribution to the development through the Joint Steering Committee participations, (ii) provision of employees, goods and services for research activities for specific targets and (iii) clinical and commercial manufacturing. The Company determined that the license does not have stand-alone value to BMS without the Company's know-how and manufacturing technology through the participation of the Joint Steering Committee and accordingly, they were combined into one unit of accounting.

License revenue – BMS

As of May 21, 2015, the effective date of the BMS Collaboration Agreement, the Company recorded deferred revenue of $60.1 million. On July 31, 2015, BMS selected the second, third and fourth collaboration targets, triggering a $15.0 million target designation payment to the Company. The Company is entitled to an aggregate of $16.5 million in target designation payments upon the selection of the fifth through tenth collaboration targets. The Company will also be eligible to receive research, development and regulatory milestone payments of up to $254.0 million for AMT-126 and up to $217.0 million for each of the other selected targets, if milestones are achieved. The Company determined that the contingent payments under the BMS Collaboration Agreement relating to research, development and regulatory milestones do not constitute substantive milestones and will not be accounted for under the milestone method of revenue recognition. The events leading to these payments solely depend on BMS' performance. Accordingly, any revenue from these contingent payments would be allocated to the first unit of accounting noted above and recognized over the expected performance period.

License revenue is recognized over an expected performance period of 19 years on a straight-line basis commencing on May 21, 2015. The expected performance period is reviewed quarterly and adjusted to account for changes, if any, in the Company´s estimated performance period. The estimated performance period did not change in 2017.

The Company recognized $4.1 million license revenue for the year ended December 31, 2017 (December 31, 2016: $3.9 million, December 31, 2015: $2.4 million).

Additionally, the Company is eligible to receive net sales-based milestone payments and tiered high single to low double-digit royalties on product sales. These revenues will be recognized when earned.

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 such first commercial sale if there is no such exclusivity.

Collaboration revenue – BMS

The Company provides target-specific research and development services to BMS. Collaboration revenue related to these contracted services is recognized when earned.

The Company generated $4.3 million collaboration revenue for the year ended December 31, 2017 (December 31, 2016: $13.0 million; December 31, 2015: $2.3 million).

Manufacturing revenue – BMS

BMS and the Company also entered into Master Clinical Supply Agreement in April 2017 for the Company to supply gene therapy products during the clinical as well as into a binding term sheet to supply gene therapy products during the commercial phase to BMS. Revenues from product sales will be recognized when earned. To date the Company has not supplied any clinical and commercial gene therapy product to BMS.

Chiesi collaboration

In 2013, the Company entered into two agreements with Chiesi, one for the co-development and commercialization of the hemophilia B program (the “Hemophilia Collaboration Agreement”) and one for the commercialization of Glybera (the “Glybera Agreement”, and together with the Collaboration Agreement, the “Chiesi Agreements”) in Europe and selected territories.

In April 2017, the parties agreed to terminate the Glybera Agreement. As of October 2017, the Company is not required to supply Glybera to Chiesi. In July 2017, the parties terminated the Hemophilia Collaboration Agreement and the Company reacquired rights associated with its hemophilia B program in Europe and selected territories.

License revenue – Chiesi

Upon the closing of the Chiesi Agreements on June 30, 2013, the Company received €17.0 million ($22.1 million) in non-refundable up-front payments. The Company determined that the up-front payments constituted a single unit of accounting that should be amortized as license revenue on a straight-line basis over the performance period of July 2013 through September 2032. In July 2017, the Company fully released the outstanding deferred revenue and recorded $13.8 million other income during the year ended December 31, 2017.

The Company recognized $0.0 million license revenue for the year ended December 31, 2017 (December 31, 2016: $1.0 million; December 31, 2015: $1.0 million). The Company recognized the license revenue for the year ended December 31, 2017, net of a $0.5 million reduction for amounts previously amortized and repaid by the Company in accordance with the Glybera Termination Agreement in 2017.

Collaboration revenue – Chiesi

Prior to the termination of the Hemophilia Collaboration Agreement up to June 30, 2017, Chiesi reimbursed the Company for 50% of the agreed research and development efforts related to hemophilia B. These reimbursable amounts have been presented as collaboration revenue.

The Company generated $4.6 million collaboration revenue for the year ended December 31, 2017 (December 31, 2016: $7.2 million; December 31, 2015: $4.9 million) from the co-development of hemophilia B.

5. Property, plant and equipment, net

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

	December 31, 2017	December 31, 2016
	in thousands	
Leasehold improvements	$ 32,297	$ 30,582
Laboratory equipment	15,976	14,166
Office equipment	2,304	2,710
Construction-in-progress	745	313
Total property, plant, and equipment	51,322	47,771
Less accumulated depreciation	(17,041)	(12,069)
Property, plant and equipment, net	**$ 34,281**	**$ 35,702**

Total depreciation expense was $7.0 million for the year ended December 31, 2017 (December 31, 2016: $5.5 million, December 31, 2015: $4.4 million). Depreciation expense is allocated to research and development to the extent it relates to the Company's manufacturing facility and equipment. All other depreciation expenses are allocated to selling, general and administrative expense.

Investment in new Amsterdam facility

In 2017, the Company invested $1.9 million (2016: $13.0 million) into its new facility located at the Paasheuvelweg in Amsterdam.

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

	December 31, 2017	December 31, 2016
	in thousands	
Lexington, Massachusetts (United States of America)	$ 17,177	$ 19,552
Amsterdam (the Netherlands)	17,104	16,150
Total	**$ 34,281**	**$ 35,702**

6. Intangible assets

a. Acquired licenses

The following table presents the Company's acquired licenses as of December 31:

	December 31, 2017	December 31, 2016
	in thousands	
Licenses	$ 9,551	$ 7,799
Less accumulated amortization and impairment	(5,575)	(3,952)
Licenses, net	**$ 3,976**	**$ 3,847**

All intangible assets are owned by uniQure biopharma B.V, a subsidiary of the Company. The acquired licenses have a weighted average remaining life of 14.9 years.

As of December 31, 2017, the estimated future amortization expense for each of the five succeeding years and the period thereafter is as follows:

Years	Amount in thousands
2018	$ 300
2019	284
2020	285
2021	280
2022	276
Thereafter	2,551
Total	**$ 3,976**

The carrying amount of the Company's licenses by licensor is set out below.

	December 31, 2017	December 31, 2016
	in thousands	
Protein Sciences Corporation	$ 2,340	$ 2,194
St. Jude Children's Hospital	707	659
Other	929	994
Total	**$ 3,976**	**$ 3,847**

The amortization expense related to licenses for the year ended December 31, 2017 was $1.0 million (December 31, 2016: $0.3 million; December 31, 2015: $0.4 million). All amortization was included in research and development expenses, except for $0.6 million related to the termination of the Chiesi collaboration, which was presented in other expense in the year ended December 31, 2017.

Protein Sciences Corporation

In 2016, the Company renegotiated its existing license contract with Protein Sciences Corporation for the exclusive use of its *expresSF+* ("SF+") insect cell line to provide the Company with an exclusive royalty free, perpetual right and license to the licensed technology in the field of AAV-based gene therapy.

Glybera impairment

Triggered by the first commercial sale of Glybera in September 2015, the Company assessed the value-in-use of Glybera related licenses (Xenon and Ampliphi). Accordingly, the Company recognized an impairment loss of $1.3 million in the year ended December 31, 2015, which was included in research and development expense.

b. Acquired research and development ("Acquired R&D")

The Acquired R&D asset was acquired as part of the acquisition of InoCard in July 2014 and relates to the AMT-126 program. The carrying amount as at December 31, 2017 is $5.6 million (December 31, 2016: $4.5 million).

7. Accrued expenses and other (non) current liabilities

Accrued expenses and other current liabilities include the following items:

	December 31, 2017	December 31, 2016
	in thousands	
Accruals for services provided by vendors-not yet billed	$ 2,348	$ 3,824
Personnel related accruals and liabilities	5,646	5,559
Other current liabilities	844	383
Total	**$ 8,838**	**$ 9,766**

According to the Glybera Termination Agreement the Company is responsible for terminating the Phase IV post-

approval study. The Company recorded $0.9 million of expenses (presented as other expenses) during the year ended December 31, 2017, related to such costs. As of December 31, 2017, the accrued liability was $0.6 million of which $0.3 million is included in other non-current liabilities.

In December 2016, the Company and Extera Partners agreed to settle an arbitration case for a total amount of $2.9 million paid in December 2016 (including legal and related settlement costs). The expense is presented as selling, general and administrative expense in the consolidated statements of operations and comprehensive loss.

Restructuring plan

In November 2016, the Company announced a plan to restructure its activities resulting from a company-wide strategic review with the aim of refocusing its pipeline, consolidating its manufacturing capabilities into its Lexington, Massachusetts site, reducing operating costs and enhancing overall execution. At various dates between December 2016 and December 2017, the Company entered into termination agreements with certain employees. The Company expects to complete the restructuring in early 2018. Depending on the individual case pattern the Company accrues the related termination costs over the service period or at the date of communication to the employees. Changes in accrued termination benefits (included in research and development expenses) for the year ended December 31, 2017, are detailed in the table below:

	Accrued termination benefits
	in thousands
Balance at December 31, 2016	**$ 1,148**
Accrued through profit and loss	2,018
Payments	(2,599)
Currency translation effects	58
Balance at December 31, 2017	**$ 625**

Other non-current liabilities.

Other non-current liabilities include deposits collected in relation to a sub-lease arrangement as well as the non-current portion of the Glybera exit costs.

8. Long-term debt

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”). The 2016 Amended Facility extended the maturity date from June 30, 2018, to May 1, 2020. As at December 31, 2017, and December 31, 2016, $20.0 million was outstanding. The interest rate is adjustable and is the greater of (i) 8.25% or (ii) 8.25% plus the prime rate less 5.25%. Under the 2016 Amended Facility, the interest rate will initially be 8.25% per annum with a back-end fee of 4.85% and a facility fee of 0.75% of the outstanding loan amounts. The interest-only payment period was extended by 12 months to November 2018 as a result of raising more than $50.0 million in equity financing in October 2017.

The amortized cost of the 2016 Amended Facility, was $20.8 million as of December 31, 2017, compared to $20.2 million as of December 31, 2016, and is recorded net of discount and debt issuance costs. The foreign currency gain on the loan was $2.6 million in 2017 (December 31, 2016: loss of $0.9 million; December 31, 2015: loss of $2.2 million). The fair value of the loan approximates its carrying amount.

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

Years	Amount
	in millions
2017	$ 2.2
2016	2.2
2015	2.5

As a covenant in the 2016 Amended 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 the outstanding balance of principal due and 50% of worldwide cash reserves. This restriction on the cash reserves only relates to the location of the cash reserves, and such cash reserves can be used at the discretion of the Company. In combination with other covenants, the 2016 Amended Facility restricts the Company's ability to, among other things, incur future indebtedness and obtain additional debt financing, to make investments in securities or in other companies, to transfer assets, to perform certain corporate changes, to make loans to employees, officers and directors, and to make dividend payments and other distributions. The Company secured the facilities by pledging the shares in its subsidiaries, substantially all its receivables, moveable assets as well as the equipment, fixtures, inventory and cash of uniQure Inc.

The 2016 Amended 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, 2017, the Company was in compliance with all covenants and provisions.

The aggregate maturities of the loan, including $4.0 million of coupon interest payments and financing fees, for each of the three years subsequent to December 31, 2017, are as follows:

Years	Amount in thousands
2018	$ 2,890
2019	14,188
2020	6,882
Total	**$ 23,960**

9. Shareholders' equity

As of December 31, 2017, the Company's authorized share capital is €3.0 million (exchange rate as of December 31, 2017, of 1.19913 $ / €; $3.6 million), divided into 60,000,000 ordinary shares, each with a nominal value of €0.05. Under Dutch law, the authorized share capital is the maximum capital that the Company may issue without amending its articles of association.

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.

As of December 31, 2017, and 2016 and 2015 the Company's reserves were restricted for payment of dividends for accumulated foreign currency translation losses of $4.9 million, $6.6 million and $6.8 million, respectively.

On October 27, 2017, the Company completed its follow-on public offering announced on October 23, 2017. The Company issued and sold 5,000,000 ordinary shares at $18.25 per ordinary share, resulting in gross proceeds to the Company of approximately $91.3 million. The net proceeds to the Company from this offering were approximately $85.3 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company. The Company capitalized $0.5 million of expenses related to this offering (deducted from additional paid in capital in the accompanying consolidated balance sheet).

On September 15, 2017, the Company filed a prospectus supplement to the prospectus dated May 15, 2017, and entered into a sales agreement (the "Sales Agreement") with Leerink Partners LLC ("Leerink") to establish an "at the market" equity offering program pursuant to which Leerink can sell, with the Company's authorization, up to 5 million ordinary shares at prevailing market prices from time to time. The Company will pay Leerink a commission equal to 3% of the gross proceeds of the sales price of all shares sold through it as sales agent under the Sales Agreement. The Company has not yet sold any ordinary shares under the Sales Agreement and has not received any gross proceeds.

In December 2017 the Company issued a total of 114,172 restricted ordinary shares in relation to the exercise of 128,710 warrants issued to former lenders of a loan, which was converted into equity in July 2013 prior to the Company's initial public offering. The ordinary shares were issued at an exercise price of €10.10, or approximately $12.0 depending on the foreign exchange rate as of the date of warrant exercise. Certain of these lenders (Forbion and Coller) continue to qualify as related parties to the Company.

On April 15, 2015, the Company issued 3,000,000 ordinary shares at a public offering price of $29.50 per share, with net proceeds, after deducting underwriting discounts and net of offering expenses of $82.5 million.

In the year ended December 31, 2015 the Company issued shares to BMS upon extinguishment of derivative obligations following the collaboration agreement:

	Ordinary shares		Additional paid-in capital	Total shareholders' equity
	No. of shares	Amount		
	in thousands, except share and per share amounts			
Issuance of shares at $33.84 per share on June 12, 2015	1,112,319	$ 61	$ 37,579	$ 37,640
Extinguishment of derivative upon issuance of shares on June 12, 2015	—	—	(4,972)	(4,972)
Issuance of shares at $29.67 per share on August 7, 2015	1,275,789	71	37,782	37,853
Extinguishment of derivative upon issuance of shares on August 7, 2015	—	—	1,410	1,410
Balance at December 31, 2015	**2,388,108**	**$ 132**	**$ 71,799**	**$ 71,931**

10. Share-based compensation

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

	Years ended December 31,		
	2017	2016	2015
Research and development - employees	$ 3,945	$ 3,302	$ 2,162
Selling, general and administrative - employees	6,335	2,242	3,026
Research and development - non-employees	—	670	6,429
Total	**$ 10,280**	**$ 6,214**	**$ 11,617**

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

	Years ended December 31,		
	2017	2016	2015
Award type			
Share options	$ 3,246	$ 5,187	$ 10,469
Restricted share units ("RSUs")	2,588	528	1,148
Performance share units ("PSUs")	4,446	499	—
Total	**$ 10,280**	**$ 6,214**	**$ 11,617**

As of December 31, 2017, the unrecognized compensation cost related to unvested awards under the various share-based compensation plans were:

Award type	Unrecognized compensation costs	Weighted-average remaining period for recognition
	in thousands	in years
Share options	$ 6,773	2.79
Restricted share units	2,548	1.64
Performance share units	5,041	2.07
Total	**$ 14,362**	**2.33**

The Company satisfies the exercise of share options and vesting of RSUs and PSUs through newly issued 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 characteristics similar to the 2014 Plan (classified as "Other Plans"). The Company previously had a 2012 Equity Incentive Plan (the "2012 Plan") and issued options to purchase ordinary shares to the shareholders of 4D in connection with a collaboration and license agreement between the Company and 4D dated as of January 2014 (classified as "Other Plans").

2014 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 and 2016, uniQure shareholders approved amendments of the 2014 Plan, increasing the shares authorized for issuance by 3,000,000 in 2016 (2015: 1,070,000) to a total of 5,601,471.

Share options

Under the 2014 Plan, share options are granted 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, straight-line over years two, three and four. Certain grants to non-executive directors vest in full after one year. Any options that vest must be exercised by the tenth anniversary of the initial grant date.

The following table summarizes option activity under the Company's 2014 Plan for the year ended December 31, 2017:

	2014 plan			
	Options	Weighted average exercise price	Weighted average remaining contractual life	Aggregate intrinsic value
			in years	in thousands
Outstanding at December 31, 2016	**1,812,766**	**$ 12.47**	**$ 7.92**	**$ —**
Granted	995,350	$ 6.38		
Forfeited	(415,743)	$ 8.79		
Expired	(162,388)	$ 14.78		
Exercised	(198,552)	$ 9.39		
Outstanding at December 31, 2017	**2,031,433**	**$ 10.35**	**7.75**	**19,580**
Fully vested and exercisable at December 31, 2017	729,067	$ 13.22	6.08	5,121
Outstanding and expected to vest at December 31, 2017	1,302,366	$ 8.75	8.69	14,459
Outstanding and expected to vest at December 31, 2016	1,172,377	$ 12.41		
Total weighted average grant date fair value of options issued during the period (in million)		$ 3.8		
Granted to directors and officers during the period (options, $ in million)	684,500	$ 4.4		
Proceeds from option sales (in million)		$ 1.8		

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

	Options	Weighted average grant-date fair value
Granted, 2017	995,350	$ 3.78
Granted, 2016	899,178	6.54
Granted, 2015	566,500	12.19
Vested, 2017	469,147	7.11
Forfeited, 2017	(415,743)	5.12

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

	Options	Weighted average grant-date fair value
Outstanding and expected to vest, 2017	1,302,366	$ 5.12
Outstanding and expected to vest, 2016	1,172,377	7.07

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	2017	2016	2015
Expected volatility	75%-80%	75%	75%
Expected terms (in years)	10 years	10 years	6.11 and 10 years
Risk free interest rate	2.39% - 2.81%	0.16% - 2.67%	0.57% - 0.62%
Expected dividends	0%	0%	0%

The Hull & White option model captures early exercises by assuming that the likelihood of exercises will increase when the share price reaches defined multiples of the strike price. This analysis is performed over the full contractual term. The following table summarizes information about options exercised during the years ended December 31:

	Exercised during the year	Intrinsic value in thousands
2017	198,552	$ 1,291
2016	87,425	345
2015	92,932	1,697

Restricted Share Units

The following table summarizes the RSUs activity for the year ended December 31, 2017:

	RSU	
	Number of shares	Weighted average grant-date fair value
Non-vested at December 31, 2016	**307,063**	**$ 9.11**
Granted	428,350	$ 6.00
Vested	(166,000)	$ 9.31
Forfeited	(60,750)	$ 7.06
Non-vested at December 31, 2017	**508,663**	**$ 6.68**
Total fair value of RSUs awarded during the period (in million)		$ 2.6
Granted to directors and officers during the period (shares, $ in million)	255,000	$ 1.5

RSUs vest over one to three years. RSUs granted in March 2017 to the Company's Chief Executive Officer will vest equally over two years from the date of grant and RSUs granted to non-executive directors will vest one year from the date of grant.

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

	Granted during the year	Weighted average grant-date fair value
2017	428,350	$ 6.00
2016	358,678	9.05
2015	—	N/A

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

	Total fair value in thousands
2017	$ 2,917
2016	2,296
2015	N/A

Performance Share Units (PSUs)

The following table summarizes the PSUs activity for the year ended December 31, 2017:

	PSU	
	Number of shares	Weighted average grant-date fair value
Non-vested at December 31, 2016	**111,564**	**$ 5.76**
Granted	550,570	$ 17.15
Vested	(133,060)	$ 11.09
Forfeited	(18,000)	$ 5.76
Non-vested at December 31, 2017	**511,074**	**$ 16.73**
Total fair value of PSUs awarded during the period (in million)		$ 9.4
Granted to directors and officers during the period (shares, $ in million)	527,995	$ 9.0

The performance share units granted for the year ended December 31, 2017 will vest on the third anniversary of the grant, subject to the grantee's continued employment. PSU grants are linked to specific performance criteria as determined by the Board of Directors and were earned based on the actual achievement of this specific criteria during the years ended December 31, 2017 and December 31, 2016. The grants made to six executives who left the Company in 2017 were accelerated as of the date of entering into their respective termination agreements.

The following table summarizes information about the weighted average grant-date fair value, determined at of the date these were earned, of PSUs granted during the years ended December 31:

	Granted during the year	Weighted average grant-date fair value
2017	550,570	$ 17.15
2016	111,564	$ 5.76
2015	-	N/A

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

	Total fair value in thousands
2017	$ 1,730
2016	N/A
2015	N/A

In September 2016, the Company awarded PSUs to its Chief Executive Officer, subject to the successful implementation of the strategic plan. The earning of these PSUs was based on the Board's assessment of the Chief Executive Officer's performance through December 31, 2017.

The Company did not grant PSUs in the year ended December 31, 2015, and no PSUs vested in the year ended December 31, 2015.

Other Plans

Under Rule 5653(c)(4) of the NASDAQ Global Select Market, the Company grants share options and RSUs to officers as a material inducement to enter into employment with the Company. In 2017, the Company granted 175,000 inducement RSUs with a grant date fair value of $1.0 million to one officer.

The following table summarizes option activity under the Company's Other Plans for the year ended December 31, 2017:

	Other plans			
	Options	Weighted average exercise price	Weighted average remaining contractual life	Aggregate intrinsic value
			in years	in thousands
Outstanding at December 31, 2016	**187,500**	**$ 17.93**	**6.39**	**$ —**
Granted	300,000	$ 6.90		
Expired	(62,500)	$ 27.82		
Outstanding at December 31, 2017	**425,000**	**$ 8.69**	**9.08**	**4,633**
Fully vested and exercisable	46,875	$ 12.98	8.33	310
Outstanding and expected to vest	378,125	$ 8.16	9.17	4,323
Total weighted average grant date fair value of options issued during the period (in million)		$ 1.2		

The fair value of the inducement grant options was estimated at the date of grant using the Hull & White option pricing model with the same assumptions as used in determining the fair value of options issued under the 2014 Plan.

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

	Exercised during the year	Intrinsic value in thousands
2017	—	$ —
2016	152,436	2,694
2015	304,872	6,155

In January 2014, the Company entered into a collaboration and license agreement with 4D to discover and optimize AAV vectors. In consideration of this collaboration, the Company granted options to the shareholders of 4D to purchase an aggregate of 609,744 ordinary shares. At October 1, 2014, 25% of the options vested (expiring at December 28, 2014), 50% of the options vested at January 31, 2015 (expiring at December 28, 2015) and the remainder on January 31, 2016 (expiring at December 28, 2016). Given the relatively short vesting period and the low exercise price of €0.05 compared to the share price, the Company used the intrinsic value for measurement purposes as proxy for the fair value of the options granted. The fair value continues to be re-measured until vesting of the instruments granted on a tranche-by-tranche basis. The related share-based compensation expenses are recognized as research and development cost.

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

	Granted during the year	Weighted average grant-date fair value
Granted, 2017	300,000	$ 4.15
Granted, 2016	125,000	$ 7.63
Granted, 2015	1,000,000	$ 10.60
Vested, 2017	46,875	$ 7.63

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

	Granted during the year	Weighted average grant-date fair value
Outstanding and expected to vest, 2017	378,125	$ 4.87
Outstanding and expected to vest, 2016	125,000	$ 7.63

The Company's former CEO Dan Soland forfeited 800,000 options granted in December 2015 upon his resignation in September 2016.

2012 Plan

The following table summarizes option activity under the Company's 2012 Plan for the year ended December 31, 2017:

	2012 plan			
	Options	Weighted average exercise price	Weighted average remaining contractual life	Aggregate intrinsic value
			in years	in thousands
Outstanding at December 31, 2016	**483,006**	**€ 5.13**	**4.13**	**$ 810**
Exercised	(405,188)	€ 5.04		
Forfeited	(5,000)	€ 3.07		
Expired	—	€ —		
Outstanding, fully vested and exercisable at December 31, 2017	**72,818**	**€ 5.77**	**3.00**	**922**
Proceeds from option sales (in million)		$ 2.3		

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

	Exercised during the year	Intrinsic value
		in thousands
2017	405,188	$ 1,176
2016	510,547	4,381
2015	449,838	9,272

11. Expenses by nature

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

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Employee-related expenses	$ 46,373	$ 42,260	$ 31,398
Laboratory and development expenses	17,737	21,054	10,874
Office and housing expenses	9,327	10,384	7,075
Legal and advisory expenses	8,121	11,715	12,209
Depreciation, amortization and impairment expenses	6,779	6,089	6,324
Patent and license expenses	817	1,348	1,342
Non-employee share-based compensation expenses	—	670	6,429
Other operating expenses	7,653	4,989	6,857
Total	**$ 96,807**	**$ 98,509**	**$ 82,508**

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

	Years ended December 31,		
	2017	2016	2015
	in thousands, except for employee numbers		
Wages and salaries	$ 25,131	$ 24,999	$ 19,274
Share-based compensation expenses	10,280	5,544	5,188
Consultant expenses	4,758	5,873	3,037
Social security costs	2,077	1,824	1,440
Health insurance	1,536	1,099	828
Pension costs-defined contribution plans	802	1,088	608
Other employee expenses	1,789	1,833	1,023
Total	**$ 46,373**	**$ 42,260**	**$ 31,398**
Number of employees at the end of the period	202	251	198

12. Other non-operating income / (expense)

Other non-operating income / (expense) consists of changes in the fair value of derivative financial instruments.

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Other non-operating income:			
Derivative gains	$ —	$ 785	$ 423
Total other non-operating income:	—	785	423
Other non-operating expense:			
Derivative losses	(2,192)	—	(7,587)
Finance expenses	(243)	—	—
Total other non-operating expense:	(2,435)	—	(7,587)
Other non-operating (expense) / income, net	**$ (2,435)**	**$ 785**	**$ (7,164)**

The Company recorded a net loss of $1.2 million for the year ended December 31, 2017, compared to a net gain of $0.5 million and a net loss of $7.2 million for the year ended December 31, 2016 and December 31, 2015, respectively, related to the derivative financial instruments issued as part of its collaboration with BMS and a net loss of $0.3 million for the year ended December 31, 2017 (December 31, 2016: $0.3 million gain; December 31, 2015: $0.0 million gain) related to warrants issued to Hercules (see note 3, “Fair value measurement”). Also, the Company recognized a $0.7 million loss for the year ended December 31, 2017, related to warrants issued in connection with the 2013 convertible loan.

13. Income taxes

a. Income tax benefit / (expense)

No current tax charges or liabilities were recorded in 2017, 2016 and 2015 by our Dutch and U.S entities since these entities generated losses. Due to the uncertainty surrounding the realization of favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company’s otherwise recognizable net deferred tax assets.

For the years ended December 31, 2017, 2016 and 2015, loss before income taxes consists of the following:

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Dutch operations	$ (60,966)	$ (51,107)	$ (63,304)
U.S. operations	(18,493)	(21,221)	(20,406)
Foreign operations	—	99	448
Total	**$ (79,459)**	**$ (72,229)**	**$ (83,262)**

The income tax benefit / (expense) for the years ended December 31, 2017, 2016 and 2015, consists of the following:

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Current benefit / (expense)			
Dutch operations	$ —	$ —	$ —
U.S. operations	—	—	—
Foreign operations	(10)	(51)	(51)
Deferred benefit / (expense)			
Dutch operations	209	(1,094)	714
U.S. operations	—	—	—
Foreign operations	—	—	516
Total income tax benefit / (expense)	**$ 199**	**$ (1,145)**	**$ 1,179**

b. Tax rate reconciliation

The reconciliation of the Dutch statutory income tax rate to the Company's effective tax rate for the years ended December 31, 2017, 2016 and 2015, is as follows:

	Years ended December 31,		
	2017	2016	2015
	in thousands		
Net loss before tax for the period	$ (79,459)	$ (72,229)	$ (83,262)
Expected tax benefit / (expense) at the tax rate enacted in the Netherlands (25%)	19,865	18,057	20,816
Difference in tax rates between the Netherlands and foreign countries	1,664	1,905	1,816
Net change in valuation allowance	(17,358)	(20,054)	(16,301)
Non-deductible expenses	(3,248)	(1,323)	(4,984)
Deductible expenses directly recognized in equity	—	—	168
Change in fair value of contingent consideration	(724)	270	(336)
Income tax benefit / (expense)	**$ 199**	**$ (1,145)**	**$ 1,179**

Non-deductible expenses predominantly relate to share-based compensation expenses for an amount of $2.5 million in 2017 (2016: $1.6 million; 2015: $2.9 million) and non-deductible results on derivative financial instruments of $0.5 million (2016: nil; 2015: $1.9 million).

c. Significant components of deferred taxes

The tax effects of temporary differences that give rise to significant portions of deferred tax assets and deferred tax liabilities at December 31, 2017 and 2016 are as follows:

	Years ended December 31,	
	2017	2016
	in thousands	
Deferred tax assets:		
Net operating loss carryforwards	$ 73,207	$ 59,468
Intangible assets	924	1,621
Property, plant and equipment	173	1,412
Deferred revenue	17,930	19,997
Accrued expenses and other current liabilities	1,657	144
Gross deferred tax asset	$ 93,891	$ 82,642
Less valuation allowance	(93,682)	(82,642)
Net deferred tax asset	$ 209	$ —
Long-term loan to foreign operations	(209)	—
Net deferred tax liability	$ (209)	$ —
Net deferred tax asset / (liability)	**$ —**	**$ —**

Changes in the valuation allowance were as follows:

	Years ended December 31,		
	2017	2016	2015
	in thousands		
January 1,	$ 82,642	$ 65,593	$ 49,997
Changes recorded in profit and loss	19,080	20,054	16,301
Changes recorded in profit and loss related to US tax reform	(1,722)	—	—
Currency translation effects	(6,318)	(3,005)	(705)
December 31,	**$ 93,682**	**$ 82,642**	**$ 65,593**

The valuation allowance at December 31, 2017 was primarily related to net operating loss carryforwards that, in the judgment of management, are not more-likely than-not to be realized. Management considered projected future taxable income and tax-planning strategies in making this assessment.

In the U.S., the tax act known as the Tax Cuts and Jobs Act ("the Act") was enacted on December 22, 2017. The Act reduces the corporate tax rate from 34% to 21%, effective January 1, 2018. As a foreign domiciled entity, the most significant impact of the Act relates to the tax rate applicable to the Company's U.S. operating entity, resulting in a $1.7 million reduction of both the gross deferred tax asset and the valuation allowance.

According to Dutch income tax law, a tax loss carry-forward expires nine years after the end of the respective period.

The Dutch fiscal unity has as of December 31, 2017 an estimated $246.0 million (2016: $182.0 million; 2015: $137.0 million) of taxable losses that can be offset in the following nine years. The expiration dates of these Dutch losses, is summarized in the following table. In the year ended December 31, 2017 unused tax losses of $24.5 million (December 31, 2016: $0.0 million) expired.

	2018	2019	2020	2021	2022
	in thousands				
Loss expiring	$ 20,037	21,736	19,757	14,867	25,301

There are no unrecognized tax benefits for the years ended December 31, 2017, 2016 and 2015.

14. Basic and diluted earnings per share

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, all potentially dilutive ordinary shares would have an antidilutive effect, if converted, and thus have been excluded from the computation of loss per share.

The potentially dilutive ordinary shares are summarized below:

	Years ended December 31,		
	2017	2016	2015
	ordinary shares		
BMS warrants	6,800,000	3,587,333	3,088,027
Stock options under 2014 Plan	2,031,433	1,812,766	1,448,226
Non-vested RSUs and earned PSUs	1,194,737	418,627	179,068
Stock options (other)	425,000	187,500	1,152,436
Stock options under 2012 Plan	72,818	483,006	1,077,944
Warrants	37,175	37,175	37,175
Total potential dilutive ordinary shares	**10,561,163**	**6,526,407**	**6,982,876**

15. Leases

The Company leases various office space and laboratory space under operating lease agreements:

Lexington, Massachusetts / United States

In July 2013, uniQure entered into a lease for a facility in Lexington, Massachusetts, United States. The term of the lease commenced in November 2013 and was set for 10 years and is non-cancellable. The lease for this facility terminates in 2024, and subject to the provisions of the lease, may be renewed for two subsequent five-year terms. The lease provides for annual minimum increases in rent, based on a consumer price index

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 Company consolidated its three Amsterdam sites into the new site at the end of May 2017. The lease for the new facility terminates in 2032, with an option to extend in increments of five-year periods. The lease contract provides for annual minimum increases in rent, 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. The minimum rentals to be received during the ten-year term amount to $11.1 million as of December 31, 2017.

As of December 31, 2017, aggregate minimum lease payments (excluding payments from the sub-lease agreement) for the calendar years and lease incentives received were as follows:

	Lexington	Amsterdam	Total
		in thousands	
2018	$ 1,849	$ 2,023	$ 3,872
2019	1,903	2,023	3,926
2020	1,956	2,023	3,979
2021	2,009	2,023	4,032
2022	2,063	2,023	4,086
Thereafter	2,827	18,203	21,030
Total minimum lease payments	**$ 12,607**	**$ 28,318**	**$ 40,925**
Deferred rent related to lease incentives-non current	$ 4,826	$ 4,288	$ 9,114
Deferred rent related to lease incentives-current	737	—	737

Rent expense is calculated on a straight-line basis over the term of the lease, and considers $11.8 million of lease incentives received. Aggregate rent expense was as follows:

	Years ended December 31,		
	2017	2016	2015
Rent expense-Lexington	$ 1,103	$ 1,103	$ 1,103
Rent expense-Amsterdam	2,503	2,871	366
Total rent expense	**$ 3,606**	**$ 3,974**	**$ 1,469**

16. Commitments and contingencies

a. Royalties and milestones

In the course of its business, the Company enters as a licensee into contracts with other parties with regard to 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.

b. Grant commitments

The Company's predecessor entity received a technical development loan from the Dutch government in relation to the development of our now abandoned product, Glybera. The Company is required to repay the grant through a percentage of revenue derived from product sales of Glybera up to December 31, 2019. Any grant balance remaining at this date will be forgiven. The Company decided not to renew its marketing authorization for Glybera in the European Union, which expired in October 2017. The Company does not expect to derive any revenue from Glybera.

17. Related party transaction

On August 7, 2017, the Company appointed Dr. Sander van Deventer as its Chief Scientific Officer and General Manager of its Amsterdam site. Dr. van Deventer served on the Company's Board until September 14, 2017. Dr. van Deventer has resigned as Managing Partner of Forbion Capital Partners by August 1, 2017, and now is an operating partner with Forbion Capital Partners for up to 50% of his time. Dr. van Deventer is entitled to €200,000 gross annual salary ("Base Salary"), including an 8% holiday allowance to be paid annually in May based upon the previous year's gross annual salary. Dr. van Deventer will also be eligible for a bonus amounting to a maximum of 40% of his annual gross salary, such amount to be determined by the Board. On September 20, 2017, Dr. van Deventer was granted an option to purchase 150,000 shares with an exercise price of $8.49, in accordance with the Company's Amended and Restated 2014 Share Incentive Plan.

18. Subsequent events

None.

EXHIBIT INDEX

Exhibit No.	Description
3.1	Amended Articles of Association of the Company. (incorporated by reference to Exhibit 1.1 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission)
10.1	2014 Share Incentive Plan (incorporated by reference to Exhibit 10.1 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission).
10.2	Form of Inducement Share Option Agreement under 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.2 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission).
10.3	Form of Share Option Agreement under 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.3 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission).
10.4t*	Form of Restricted Stock Unit Award under the 2014 Share Incentive
10.5t*	Form of Performance Stock Unit Award under the 2014 Share Incentive Plan
10.6	Employment Agreement dated December 9, 2014 between uniQure, Inc. and Matthew Kapusta (incorporated by reference to Exhibit 10.6 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission).
10.7	Amendment to the Employment Agreement between uniQure, Inc. and Matthew Kapusta, dated March 14, 2017 (incorporated by reference to Exhibit 10.7 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission).
10.8	Amendment to the Employment Agreement between uniQure, Inc. and Matthew Kapusta, dated October 26, 2017 (incorporated by reference to Exhibit 10.1 of the Company's quarterly report on form 10-Q (file no. 001-36294) for the period ending on September 31, 2017 filed with the Securities and Exchange Commission).
10.10	Patent License Agreement (L-107-2007), effective as of May 2, 2007, by and between the Company and the National Institutes of Health, as amended on December 31, 2009, May 31, 2013 and November 11, 2013 (incorporated by reference to Exhibit 10.1 of the Company's quarterly report on form 10-Q (file no. 001-36294) for the period ending on March 31, 2017 with the Securities and Exchange Commission).
10.11	Patent License Agreement (L-116-2011), effective as of August 10, 2011, by and between the Company and National Institutes of Health, as amended on May 31, 2013 and November 11, 2013 (incorporated by reference to Exhibit 10.2 of the Company's quarterly report on form 10-Q (file no. 001-36294) for the period ending on March 31, 2017 filed with the Securities and Exchange Commission).
10.15	Warrant Agreement, dated as of September 20, 2013, by and among the Company, uniQure Biopharma B.V. and Hercules Technology Growth Capital, Inc. (incorporated by reference to Exhibit 10.18 of the Company's registration statement on form F-1 (file no. 333-193158) filed with the Securities and Exchange Commission).
10.18	Lease relating to 113 Hartwell Avenue, Lexington, Massachusetts, dated as of July 24, 2013, by and between the Company and King113 Hartwell LLC (incorporated by reference to Exhibit 10.28 of the Company's registration statement on form F-1 (file no. 333-193158) filed with the Securities and Exchange Commission).
10.19	Business Acquisition Agreement, dated as of February 16, 2012, by and among Amsterdam Molecular Therapeutics (AMT) Holding N.V., the Company and the other Parties listed therein (incorporated by reference to Exhibit 10.29 of the Company's registration statement on form F-1 (file no. 333-193158) filed with the Securities and Exchange Commission).
10.20	Deed of Assignment of Certain Assets and Liabilities of Amsterdam Molecular Therapeutics (AMT) Holding N.V., dated as of April 5, 2012, by and among Amsterdam Molecular Therapeutics (AMT) Holding B.V., Amsterdam Molecular Therapeutics (AMT) Holding IP B.V. and Amsterdam Molecular Therapeutics (AMT) Holding N.V. (incorporated by reference to Exhibit 10.30 of the Company's registration statement on form F-1 (file no. 333-193158) filed with the Securities and Exchange Commission).

10.21	Agreement for Transfer of Certain Assets and Liabilities of Amsterdam Molecular Therapeutics (AMT) Holding N.V., dated as of February 16, 2012, by and among Amsterdam Molecular Therapeutics (AMT) Holding B.V., Amsterdam Molecular Therapeutics (AMT) Holding IP B.V. and Amsterdam Molecular Therapeutics (AMT) Holding N.V. (incorporated by reference to Exhibit 10.31 of the Company's registration statement on form F-1 (file no. 333-193158) filed with the Securities and Exchange Commission).
10.22†	Collaboration and License Agreement, dated January 17, 2014, by and between uniQure biopharma B.V. and 4D Molecular Therapeutics, LLC (incorporated by reference to Exhibit 10.32 of the Company's registration statement on form F-1 (file no. 333-193158) filed with the Securities and Exchange Commission).
10.26	Second Amended and Restated Loan and Security Agreement, dated as of May 6, 2016 by and among uniQure Biopharma B.V., uniQure, Inc., uniQure IP B.V., the Company's subsidiaries listed therein, and Hercules Technology Growth Capital, Inc (incorporated by reference to Exhibit 10.30 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission
10.27†	Collaboration and License Agreement by and between uniQure Biopharma B.V. and Bristol-Myers Squibb Company dated April 6, 2015 (incorporated by reference to Exhibit 4.30 of the Company's annual report on form 20-F (file no. 001-36294) filed with the Securities and Exchange Commission).
10.28†	Share Subscription Agreement by and between uniQure N.V. and Bristol-Myers Squibb Company dated April 6, 2015 (incorporated by reference to Exhibit 4.31 of the Company's annual report on form 20-F (file no. 001-36294) filed with the Securities and Exchange Commission).
10.29†	Investor Agreement by and between uniQure Biopharma B.V. and Bristol-Myers Squibb Company dated April 6, 2015 (incorporated by reference to Exhibit 4.32 of the Company's annual report on form 20-F (file no. 001-36294) filed with the Securities and Exchange Commission).
10.30†	Seventh Collaboration Warrant Agreement dated April 6, 2015 issued to Bristol-Myers Squibb Company (incorporated by reference to Exhibit 4.33 of the Company's annual report on form 20-F (file no. 001-36294) filed with the Securities and Exchange Commission).
10.31†	Tenth Collaboration Warrant Agreement dated April 6, 2015 issued to Bristol-Myers Squibb Company (incorporated by reference to Exhibit 4.34 of the Company's annual report on form 20-F (file no. 001-36294) filed with the Securities and Exchange Commission).
10.32	Lease relating to Paasheuvelweg 25, dated as of March 7, 2016, by and between 52 IFH GmbH & Co. KG and uniQure biopharma B.V. (incorporated by reference to Exhibit 10.36 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission).
10.34	Employment Agreement dated August 4, 2017 between uniQure biopharma B.V. and Sander van Deventer (incorporated by reference to Exhibit 10.2 of the Company's quarterly report on form 10-Q (file no. 001-36294) for the period ending on June 30, 2017 filed with the Securities and Exchange Commission).
10.35	Employment Agreement dated July 10, 2017 between uniQure, Inc. and Scott McMillan (incorporated by reference to Exhibit 10.3 of the Company's quarterly report on form 10-Q (file no. 001-36294) for the period ending on June 30, 2017 filed with the Securities and Exchange Commission).
10.36	Employment Agreement dated July 15, 2017 between uniQure biopharma B.V. and Christian Klemt (incorporated by reference to Exhibit 10.4 of the Company's quarterly report on form 10-Q (file no. 001-36294) for the period ending on June 30, 2017 filed with the Securities and Exchange Commission).
10.37†	Assignment and License Agreement dated April 17, 2017 between Professor Paolo Simioni and uniQure biopharma B.V. (incorporated by reference to Exhibit 10.1 of the Company's periodic report on form 8-K (file no. 001-36294) filed on October 19, 2017 with the Securities and Exchange Commission).
10.38	Sales Agreement dated September 15, 2017 by and between uniQure N.V. and Leerink Partners LLC (incorporated by reference to Exhibit 10.1 of the Company's periodic report on form 8-K (file no. 001-36294) filed on September 18, 2017 with the Securities and Exchange Commission).
14.1	Code of Ethics (incorporated by reference to Exhibit 14.1 of the Company's annual report on form 10-K (file no. 001-36294) for the period ending December 31, 2016 filed with the Securities and Exchange Commission).
21.1*	Subsidiaries of the Company
23.1*	Consent of Independent Registered Public Accounting Firm

24.1*	Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K)
31.1*	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer
31.2*	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer
32.1*	Section 1350 Certification
101*	The following materials from the Company's Annual Report on Form 10-K for the year ended December 31, 2017, formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Income (Loss), (iii) Consolidated Statements of Stockholders' Equity, (iv) Consolidated Statements of Cash Flows and (v) Notes to Consolidated Financial Statements.

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

* Filed herewith

t Indicates a management contract or compensatory plan or arrangement.

SIGNATURES

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

UNIQURE, N.V.

By: /s/ MATHEW KAPUSTA
Matthew Kapusta
Chief Executive Officer
(Principal Executive and Financial Officer)

POWER OF ATTORNEY

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

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

Signatures	Title	Date
/s/ MATHEW KAPUSTA Matthew Kapusta	Chief Executive Officer, Chief Financial Officer and Director (Principal Executive and Financial Officer)	March 14, 2018
/s/ CHRISTIAN KLEMT Christian Klemt	Chief Accounting Officer	March 14, 2018
/s/ PHILIP ASTLEY SPARKE Philip Astley Sparke	Director	March 14, 2018
/s/ JACK KAYE Jack Kaye	Director	March 14, 2018
/s/ DAVID SCHAFFER David Schaffer	Director	March 14, 2018
s/ PAULA SOTEROPOULOS Paula Soteropoulos	Director	March 14, 2018
/s/ MADHAVAN BALACHANDRAN Madhavan Balachandran	Director	March 14, 2018
/s/ JEREMY P. SPRINGHORN Jeremy P. Springhorn	Director	March 14, 2018

March 14, 2018

Exhibit 10.4

uniQure N.V.

Restricted Share Unit Agreement
Granted Under 2014 Share Incentive Plan, As Amended and Restated effective as of June 15, 2016

NOTICE OF GRANT

This Restricted Share Unit Grant Agreement (this "**Agreement**") is made as of the Grant Date between uniQure N.V., a public limited company incorporated under the laws of the Netherlands (the **"Company"**) and the Participant.

1. Grant Date:

2. Participant Information:
Participant:

3. Number of time-based restricted share units ("**Restricted Share Units")**:

This Agreement includes this Notice of Grant and the following General Terms and Conditions (attached as Exhibit A), which are expressly incorporated by reference in their entirety herein.

This Agreement, including the General Terms and Conditions, supersedes all written and/or oral arrangements previously made between the Company and the Participant on the subject of this Agreement.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the Grant Date by signing below or by electronic acceptance.

uniQure N.V.	**Participant**
By:	By:
Name: Matt Kapusta	Name:
Title: CEO	Title:

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uniQure N.V.

Restricted Share Unit Agreement
Granted Under 2014 Share Incentive Plan, Amended and Restated effective as of June 15, 2016

EXHIBIT A
General Terms and Conditions

1. Restricted Share Unit Grant. This Restricted Share Unit Grant Agreement (this "**Agreement**") evidences the grant by the Company, on the Grant Date to the Participant, of the number Restricted Share Units listed in the Notice of Grant, subject to the terms, restrictions and conditions set forth in this Agreement and the uniQure N.V. 2014 Share Incentive Plan, as amended and restated, Amended and Restated effective as of June 15, 2016 (the "**Plan**"). Pursuant to this Agreement, the Company hereby grants to the Participant the right to receive ordinary shares of the Company ("**Ordinary Shares**") in the amount and on the terms set forth in this Agreement upon the satisfaction of the requirements of the vesting schedule set forth in Section 3, below. No Ordinary Shares shall be issued to the Participant on the Grant Date. Unless otherwise defined herein, capitalized terms used in this Agreement shall have the meanings set forth in the Plan.

2. Shareholder Rights. Prior to the issuance, if any, of Ordinary Shares pursuant to the terms of this Agreement and the Plan, the Participant shall not (a) have any of the rights or privileges of a shareholder of the Company, including the right to vote the Ordinary Shares underlying the Restricted Share Units, (b) have the right to receive any dividends or other distributions, and (c) have any interest in any fund or specific assets of the Company by reason of this Agreement.

3. Vesting.

(a) The Restricted Share Units shall become vested over three (3) years as follows: _____ (each, a "**Vesting Date**"), if the Participant continues to be employed by the Company or a subsidiary of the Company employing the Participant (the "**Employer**") from the Date of Grant until such date.

(b) If the Participant ceases to be employed by the Employer for any reason prior to the date that the Restricted Share Units are vested, the Participant shall forfeit all unvested Restricted Share Units and the Participant will not have any rights with respect to any such unvested Restricted Share Units.

(c) Notwithstanding this Section 3, if a Reorganization Event occurs before the Restricted Share Units are fully vested, the Participant's unvested Restricted Share Units shall become fully vested immediately upon such termination, provided that the Participant was employed by the Employer on the date of the Reorganization Event.

4. Issuance.

(a) The Restricted Share Units that become vested pursuant to Section 3 above shall be settled by the Company on the first business day following the date that the Restricted Share Units vest (the "**Settlement Date**"). Settlement will be made with respect to the Restricted Share

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Units in the form of Ordinary Shares, with each vested Restricted Share Unit equivalent to one Ordinary Share. In no event shall any fractional shares be issued.

(b) The obligation of the Company to deliver the Ordinary Shares to the Participant following the date that the Restricted Share Units vest in accordance with Section 3 above shall be subject to all applicable laws, rules, and regulations and such approvals by governmental agencies as may be deemed appropriate to comply with relevant securities laws and regulations.

5. Nonassignability of Ordinary Shares. The right to receive Ordinary Shares may not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution applicable to such Participant, except as permitted under the Plan or by the Supervisory Board or Board of Directors of the Company, as the case may be (the "**Board**"). Any attempt to sell, assign, transfer, pledge or otherwise encumber the right to receive Ordinary Shares contrary to the provisions of this Agreement and the Plan, and the levy of any execution, attachment or similar process upon the right to receive the shares, shall be null, void and without effect.

6. Provisions of the Plan. This grant is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which will be furnished to the Participant.

7. Withholding. No Ordinary Shares will be issued unless and until the Participant pays to the Employer, or makes provision satisfactory to the Employer for payment of, any national, federal, state and local or other income, national insurance, social and employment taxes required by law to be withheld in respect of this grant. Without limiting the generality of the forgoing, on the Settlement Date, the Participant shall cause to be sold such number of Ordinary Shares as shall be required such that the proceeds thereof shall be sufficient to cover all amounts required to be withheld by the Company in respect of tax, and shall cause the proceeds thereof to be remitted to the Company.

8. No Employment or Other Rights. This grant shall not confer upon the Participant any right to be retained by or in the employ or service of the Employer and shall not interfere in any way with the right of the Employer to terminate the Participant's employment or service at any time. The right of the Employer to terminate the Participant's employment or service pursuant to the terms of the Participant's employment agreement, if any, is specifically reserved.

9. Recoupment Policy. The Participant agrees that the Participant will be subject to any applicable clawback and recoupment policies, share trading policies and other policies that may be applicable to the Participant as an employee of the Employer, as in effect from time to time, whether or not approved before or after the Grant Date.

10. Assignment by Company. The rights and protections of the Company hereunder shall extend to any successors or assigns of the Company and to the Company's parents, subsidiaries, and affiliates. This Agreement may be assigned by the Company without the Participant's consent.

11. Notice. Any notice to the Company provided for in this Agreement shall be addressed to the Head of Human Resources or the Chief Financial Officer at their respective corporate address at the Company, and any notice to the Participant shall be addressed to such Participant at the

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current address shown on the payroll of the Employer, or to such other address as the Participant may designate to the Employer in writing. Any notice shall be delivered by hand, sent by telecopy or enclosed in a properly sealed envelope addressed as stated above, registered and deposited with postage prepaid.

12. Nature of the Grant. In accepting the Restricted Share Units, the Participant acknowledges that:

(a) the Plan is established voluntarily by the Company, it provides for certain criteria in order to be eligible to receive an award, it is restricted in time, it is discretionary in nature and it may be modified, amended, suspended or terminated by the Company at any time, unless otherwise provided in the Plan and this Agreement;

(b) the grant of the Restricted Share Units is voluntary and occasional and does not create any contractual or other right to receive future grants, or benefits in lieu of grants, even if grants have been granted repeatedly in the past;

(c) all decisions with respect to future grants, if any, will be at the sole discretion of the Board;

(d) the Participant is voluntarily participating in the Plan;

(e) the Restricted Share Units are an extraordinary item that do not constitute compensation of any kind for services of any kind rendered to the Company or the Employer, and which is outside the scope of the Participant's employment or consultancy agreement of his or her corporate mandate, if any;

(f) the Restricted Share Units are not part of normal or expected compensation or salary for any purposes, including, but not limited to, calculation of any severance, resignation, termination, redundancy, end of service payments, bonuses, long-service awards, pension, retirement or welfare benefits or similar payments and in no event should be considered as compensation for, or relating in any way, to past services for the Company or the Employer;

(g) in the event that the Participant is not an employee of the Company, the Restricted Share Units and the Participant's participation in the Plan will not be interpreted to form an employment or service contract or relationship with the Company;

(h) the future value of the underlying Ordinary Shares is unknown and cannot be predicted with certainty; if the Participant's Restricted Share Units never vest, the Participant will not be eligible to receive any Ordinary Shares; and

(i) in consideration of the Restricted Share Units, no claim or entitlement to compensation or damages shall arise from termination of the Restricted Share Units or from any decrease in value of the Restricted Share Units or Ordinary Shares that may be or have been acquired resulting from termination of the Participant's employment, consultancy or corporate mandate by or with the Company or the Employer (for any reason whatsoever and whether or not in breach of contract or local laws) and the Participant irrevocably releases the Company and the Employer from any such claim that may arise.

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13. **Data Privacy. The Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of his or her personal data as described in this agreement by and among, as applicable, his or her Employer or contracting party and the Company for the exclusive purpose of implementing, administering and managing his or her participation in the Plan.**

The Participant understands that the Company holds certain personal information about him or her, including, but not limited to, his or her name, home address and telephone number, work location and phone number, date of birth, hire date, details of all Restricted Share Units or any other entitlement to Ordinary Shares awarded, cancelled, exercised, vested, unvested or outstanding in the Participant's favor, for the purpose of implementing, administering and managing the Plan ("Personal Data"). The Participant understands that Personal Data may be transferred to any third parties assisting in the implementation, administration and management of the Plan, that these recipients may be located in the Participant's country or elsewhere and that the recipient's country may have different data privacy laws and protections than the Participant's country. The Participant understands that he or she may request a list with the names and addresses of any potential recipients of the Personal Data by contacting his or her local human resources representative. The Participant authorizes the recipients to receive, possess, use, retain and transfer the Personal Data, in electronic or other form, for the purposes of implementing, administering and managing his or her participation in the Plan, including any requisite transfer of such Personal Data as may be required to a broker or other third party with whom the Participant may elect to deposit any Ordinary Shares acquired pursuant to the Restricted Share Units. The Participant understands that Personal Data will be held only as long as is necessary to implement, administer and manage his or her participation in the Plan. The Participant understands that he or she may, at any time, view Personal Data, request additional information about the storage and processing of Personal Data, require any necessary amendments to Personal Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. The Participant understands, however, that refusing or withdrawing his or her consent may affect his or her ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, the Participant understands that he or she may contact his or her local human resources representative.

14. Section 409A. This Agreement is not intended to constitute or result in deferred compensation subject to the requirements of section 409A of the Code. However, to the extent any amount payable under this Agreement is subsequently determined to constitute deferred compensation subject to the requirements of section 409A of the Code, this Agreement shall be administered in accordance with the requirements of section 409A of the Code. In such case, distributions shall only be made on an event and in a manner permitted by section 409A of the Code, including the six month delay for specified employees consistent with Section 11(g) of the Plan, if applicable. To the extent that any provision of this Agreement would cause a conflict with the requirements of section 409A of the Code, or would cause the administration of this Agreement to fail to satisfy the requirements of section 409A of the Code, such provision shall be deemed null and void to the extent permitted by applicable law. In no event shall the Participant, directly or indirectly, designate the calendar year of redemption. This Agreement may be amended without the consent of the Participant in any respect deemed by the Board to be necessary in order to preserve compliance with Section 409A of the Code. Each distribution

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pursuant to this Agreement shall be deemed a separate payment for purposes of Section 409A of the Code.

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March 14, 2018

Exhibit 10.5

uniQure N.V.

Performance Share Unit Agreement
Granted Under 2014 Share Incentive Plan, Amended and Restated effective as of June 15, 2016

NOTICE OF GRANT

This Performance Share Grant Unit Agreement (this "**Agreement**") is made as of the Grant Date between uniQure N.V., a public limited company incorporated under the laws of the Netherlands (the "**Company**") and the Participant.

1. Grant Date:

2. Participant Information:
Participant:
3. Number of performance-based restricted share units ("**Performance Share Units**"):

This Agreement includes this Notice of Grant and the following General Terms and Conditions (attached as Exhibit A), which are expressly incorporated by reference in their entirety herein.

This Agreement, including the General Terms and Conditions, supersedes all written and/or oral arrangements previously made between the Company and the Participant on the subject of this Agreement.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the Grant Date by signing below or by electronic acceptance.

uniQure N.V.	**Participant**
By:	By:
Name: Matthew Kapusta	Name:
Title: CEO	Title:

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uniQure N.V.

Performance Share Unit Agreement
Granted Under 2014 Share Incentive Plan, Amended and Restated effective as of June 15, 2016

EXHIBIT A
General Terms and Conditions

1. Performance Share Unit Grant.

(a) This Performance Share Unit Grant Agreement (this "**Agreement**") evidences the grant by the Company, on the Grant Date to the Participant, of the number of Performance Based Share Units listed in the Notice of Grant (the "**Target Award**"), subject to the terms, restrictions and conditions set forth in this Agreement and the uniQure N.V. 2014 Share Incentive Plan, amended and restated effective as of June 15, 2016 (the "**Plan**"). Pursuant to this Agreement, the Company hereby grants to the Participant the right to receive ordinary shares of the Company ("**Ordinary Shares**") in the amount and on the terms set forth in this Agreement upon achievement of the Performance Goals (as defined on Exhibit B) during the 2018 calendar year (the "**Performance Period**") and satisfaction of the requirements of the Vesting Schedule, both as set forth on Exhibit B attached hereto. No Ordinary Shares shall be issued to the Participant on the Grant Date. Unless otherwise defined herein, capitalized terms used in this Agreement shall have the meanings set forth in the Plan.

(b) The Board of Directors of the Company (the "**Board**") shall, as soon as practicable, certify (i) the extent, if any, to which, the Performance Goals have been achieved with respect to the Performance Period, and (ii) the number of Ordinary Shares, if any, earned upon attainment of the Performance Goals. Such certification shall be final, conclusive and binding on the Participant, and on all other persons, to the maximum extent permitted by law. In the event that the Board makes a final determination that a specific Performance Goal has not been achieved, the Participant shall have no further rights to receive Ordinary Shares pursuant to such Performance Goal hereunder.

(c) The Board may at any time prior to the final determination of whether the Performance Goals have been attained, change the Performance Goals or change the weighting of the Performance Goals to reflect any change in the Participant's responsibility level or position or any other factor deemed relevant by the Board during the course of the period beginning on the Grant Date and ending on the last day of the Performance Period.

2. Shareholder Rights. Prior to the issuance, if any, of Ordinary Shares pursuant to the terms of this Agreement and the Plan, the Participant shall not (a) have any of the rights or privileges of a shareholder of the Company, including the right to vote the Ordinary Shares underlying the Performance Share Units, (b) have the right to receive any dividends or other distributions, and (c) have any interest in any fund or specific assets of the Company by reason of this Agreement.

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3. Vesting.

(a) The Ordinary Shares subject to this Agreement will become earned based on the actual level of performance achieved with respect to the Performance Goals during the Performance Period on the terms set forth on Exhibit B and as determined by the Board and the earned Performance Share Units will become vested if the Participant satisfies the requirements of the Vesting Schedule set forth on Exhibit B.

(b) If the Participant ceases to be employed by the Company or a subsidiary of the Company employing the Participant (the "**Employer**") prior to the Vesting Date (as defined in Exhibit B) as a result of a termination by the Employer without Cause (as defined below) or the Participant's resignation for Good Reason (as defined below), as of the Vesting Date, the Participant shall be entitled to the number of Performance Share Units earned pursuant to the Performance Goals as of the date of termination.

(c) If the Participant ceases to be employed by the Employer for any reason prior to the applicable Vesting Date, other than due to a termination without Cause or the Participant's resignation for Good Reason, the Participant shall forfeit all Performance Share Units and the Participant will not have any rights with respect to Performance Share Units that have not yet become vested as of the date the Participant ceases to be employed by the Employer, irrespective of the level of achievement of the Performance Goals; provided, however, that if such termination is a result of the death or permanent disability of the Participant, the Performance Share Units shall not be forfeited and shall remain subject to vesting pursuant to the terms hereof and exercisable by the Participant or his or her estate, as the case may be.

(d) For purposes of this agreement, the following terms have the following meanings:

(e) "**Good Reason**" means (I) a material reduction in the Participant's base compensation, (II) a material reduction in the Participant's authority, responsibilities or duties, (III) a material change in the geographic location at which the Participant must provide services for the Employer, or (IV) a material breach by the Company of this Agreement or by the Employer of the terms of the written employment agreement under which the Participant provides services to the Employer, if applicable; provided that the Participant provides the Employer notice of the event constituting Good Reason within 30 days following the occurrence of the event, the Employer fails to cure the event constituting Good Reason within 30 days following receipt of such notice and the Participant ceases employment with the Employer within 10 days following the end of the Employer's 30-day cure period.

(f) "**Cause**" means willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Employer (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Employer), as determined by the Employer, which determination shall be conclusive. The Participant's employment shall be considered to have been terminated for Cause if the Employer determines on or before, or within 30 days after, the Participant's resignation, that termination for Cause was warranted.

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4. Issuance.

(a) Ordinary Shares equal to the number of Performance Share Units that the Participant earns upon achievement of the Performance Goals and becomes vested in the right to receive in accordance with the Vesting Schedule, in each case, as set forth on Exhibit B, shall be issued to the Participant in accordance with Exhibit B.

(b) The obligation of the Company to deliver the Ordinary Shares to the Participant following the Vesting Date shall be subject to all applicable laws, rules, and regulations and such approvals by governmental agencies as may be deemed appropriate to comply with relevant securities laws and regulations.

5. Nonassignability of Ordinary Shares. The right to receive Ordinary Shares may not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution applicable to such Participant, except as permitted under the Plan or by the Board. Any attempt to sell, assign, transfer, pledge or otherwise encumber the right to receive Ordinary Shares contrary to the provisions of this Agreement and the Plan, and the levy of any execution, attachment or similar process upon the right to receive the shares, shall be null, void and without effect.

6. Provisions of the Plan. This grant is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which will be furnished to the Participant.

7. Withholding. No Ordinary Shares will be issued unless and until the Participant pays to the Employer, or makes provision satisfactory to the Employer for payment of, any national, federal, state and local or other income, national insurance, social and employment taxes required by law to be withheld in respect of this grant. Without limiting the generality of the forgoing, on the Settlement Date, the Participant shall cause to be sold such number of Ordinary Shares as shall be required such that the proceeds thereof shall be sufficient to cover all amounts required to be withheld by the Company in respect of tax, and shall cause the proceeds thereof to be remitted to the Company.

8. No Employment or Other Rights. This grant shall not confer upon the Participant any right to be retained by or in the employ or service of the Employer and shall not interfere in any way with the right of the Employer to terminate the Participant's employment or service at any time. The right of the Employer to terminate the Participant's employment or service pursuant to the terms of the Participant's employment agreement, if any, is specifically reserved.

9. Recoupment Policy. The Participant agrees that the Participant will be subject to any applicable claw back and recoupment policies, share trading policies and other policies that may be applicable to the Participant as an employee of the Employer, as in effect from time to time, whether or not approved before or after the Grant Date.

10. Assignment by Company. The rights and protections of the Company hereunder shall extend to any successors or assigns of the Company and to the Company's parents, subsidiaries,

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and affiliates. This Agreement may be assigned by the Company without the Participant's consent.

11. Notice. Any notice to the Company provided for in this Agreement shall be addressed to the Head of Human Resources or Chief Financial Officer at their corporate address at the Company, and any notice to the Participant shall be addressed to such Participant at the current address shown on the payroll of the Employer, or to such other address as the Participant may designate to the Employer in writing. Any notice shall be delivered by hand, sent by telecopy or enclosed in a properly sealed envelope addressed as stated above, registered and deposited with postage prepaid.

12. Nature of the Grant. In accepting the Performance Share Units, the Participant acknowledges that:

(a) the Plan is established voluntarily by the Company, it provides for certain criteria in order to be eligible to receive an award, it is restricted in time, it is discretionary in nature and it may be modified, amended, suspended or terminated by the Company at any time, unless otherwise provided in the Plan and this Agreement;

(b) the grant of the Performance Share Units is voluntary and occasional and does not create any contractual or other right to receive future grants, or benefits in lieu of grants, even if grants have been granted repeatedly in the past;

(c) all decisions with respect to future grants, if any, will be at the sole discretion of the Board;

(d) the Participant is voluntarily participating in the Plan;

(e) the Performance Share Units are an extraordinary item that do not constitute compensation of any kind for services of any kind rendered to the Company or the Employer, and which is outside the scope of the Participant's employment or consultancy agreement of his or her corporate mandate, if any;

(f) the Performance Share Units are not part of normal or expected compensation or salary for any purposes, including, but not limited to, calculation of any severance, resignation, termination, redundancy, end of service payments, bonuses, long-service awards, pension, retirement or welfare benefits or similar payments and in no event should be considered as compensation for, or relating in any way, to past services for the Company or the Employer;

(g) in the event that the Participant is not an employee of the Company, the Performance Share Units and the Participant's participation in the Plan will not be interpreted to form an employment or service contract or relationship with the Company;

(h) the future value of the underlying Ordinary Shares is unknown and cannot be predicted with certainty; if the Participant's Performance Share Units never vest, the Participant will not be eligible to receive any Ordinary Shares; and

(i) in consideration of the Performance Share Units, no claim or entitlement to compensation or damages shall arise from termination of the Performance Share Units or from

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any decrease in value of the Performance Share Units or Ordinary Shares that may be or have been acquired resulting from termination of the Participant's employment, consultancy or corporate mandate by or with the Company or the Employer (for any reason whatsoever and whether or not in breach of contract or local laws) and the Participant irrevocably releases the Company and the Employer from any such claim that may arise.

13. **Data Privacy. The Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of his or her personal data as described in this agreement by and among, as applicable, his or her Employer or contracting party and the Company for the exclusive purpose of implementing, administering and managing his or her participation in the Plan.**

The Participant understands that the Company holds certain personal information about him or her, including, but not limited to, his or her name, home address and telephone number, work location and phone number, date of birth, hire date, details of all Performance Share Units or any other entitlement to Ordinary Shares awarded, cancelled, exercised, vested, unvested or outstanding in the Participant's favor, for the purpose of implementing, administering and managing the Plan ("Personal Data"). The Participant understands that Personal Data may be transferred to any third parties assisting in the implementation, administration and management of the Plan, that these recipients may be located in the Participant's country or elsewhere and that the recipient's country may have different data privacy laws and protections than the Participant's country. The Participant understands that he or she may request a list with the names and addresses of any potential recipients of the Personal Data by contacting his or her local human resources representative. The Participant authorizes the recipients to receive, possess, use, retain and transfer the Personal Data, in electronic or other form, for the purposes of implementing, administering and managing his or her participation in the Plan, including any requisite transfer of such Personal Data as may be required to a broker or other third party with whom the Participant may elect to deposit any Ordinary Shares acquired pursuant to the Performance Share Units. The Participant understands that Personal Data will be held only as long as is necessary to implement, administer and manage his or her participation in the Plan. The Participant understands that he or she may, at any time, view Personal Data, request additional information about the storage and processing of Personal Data, require any necessary amendments to Personal Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. The Participant understands, however, that refusing or withdrawing his or her consent may affect his or her ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, the Participant understands that he or she may contact his or her local human resources representative.

14. Section 409A. It is intended that the Performance Share Units awarded hereunder shall comply with the requirements of Section 409A of the Code (and any regulations and guidelines issued thereunder) or an exemption, and this Agreement shall be interpreted on a basis consistent with such intent. Payments shall only be made on an event and in a manner permitted by Section 409A of the Code, including the six-month delay for specified employees consistent with Section 11(g) of the Plan, if applicable. This Agreement may be amended without the consent of the

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Participant in any respect deemed by the Board to be necessary in order to preserve compliance with Section 409A of the Code.

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EXHIBIT B

Target Award:

Performance Period:

Performance Goals:

Vesting Schedule:

Issuance Schedule:

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Exhibit 21.1

March 14, 2018

SUBSIDIARIES OF UNIQURE N.V.

Name of Subsidiary	Jurisdiction of Organization
uniQure biopharma B.V.	The Netherlands
uniQure IP B.V.	The Netherlands
uniQure Inc.	Delaware
uniQure GmbH	Germany

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-216701) and Form S-8 (No. 333-222051, No. 333-218005 and No. 333-197887) of uniQure N.V. of our report dated March 14, 2018 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers Accountants N.V.

R.M.N. Admiraal RA
Amsterdam, The Netherlands
March 14, 2018

Exhibit 31.1

Certification of Chief Executive Officer

I, Matthew Kapusta, certify that:

1. I have reviewed this Annual Report on Form 10-K of uniQure N.V.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Chief Executive Officer
March 14, 2018

Exhibit 31.2

Certification of Chief Financial Officer

I, Matthew Kapusta, certify that:

1. I have reviewed this Annual Report on Form 10-K of uniQure N.V.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Chief Financial Officer
March 14, 2018

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Annual Report of uniQure N.V. (the "Company") on Form 10-K for the period ended December 31, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Matthew Kapusta, Chief Executive Officer and Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1 the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2 the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

By: /s/ MATTHEW KAPUSTA

Matthew Kapusta
Chief Executive Officer and
Chief Financial Officer
March 14, 2018

A signed original of this written statement required by Section 906 has been provided to uniQure N.V. and will be retained by uniQure N.V. and furnished to the SEC or its staff upon request.