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**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, 2018

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

Indicate by check mark 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", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

The aggregate market value of the voting and non-voting ordinary shares held by non-affiliates of the registrant as of June 30, 2018 was \$1,403.4 million, based on the closing price reported as of June 29, 2018 on the NASDAQ Global Select Market.

As of February 26, 2019, the registrant had 37,626,300 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 2019 Annual Meeting of Shareholders to be filed with the Securities and Exchange Commission no later than April 30, 2019 and to be delivered to shareholders in connection with the 2019 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 1 “Business,” Part 1, Item 1A “Risk Factors,” 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 are only predictions based on management’s current views and assumptions and involve risks and uncertainties, and actual results could differ materially from those projected or implied. The most significant factors known to us that could materially adversely affect our business, operations, industry, financial position or future financial performance include those discussed in Part 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 one-time administered treatments with potentially curative results for patients suffering from genetic and other devastating diseases. We are working to advance 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. In January 2019, we commenced the dosing phase of a pivotal study of AMT-061, our lead product candidate for patients with hemophilia B. Also, in January 2019, we received notice from the U.S. Food and Drug Administration (“FDA”) of the clearance of our Investigational New Drug (“IND”) application for AMT-130, our product candidate for patients with Huntington’s disease, thereby enabling us to initiate our Phase I/II clinical study. In November 2018 we announced the expansion of our research pipeline to include additional novel gene therapy candidates for treating additional indications, including hemophilia A, Fabry disease and spinocerebellar ataxia Type 3 (“SCA3”).

We believe our gene therapy technology platform and manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost and time to market. We produce our adeno-associated virus based, or AAV-based, gene therapies in our own facilities with a proprietary, commercial-scale, current good manufacturing practices (“cGMP”), compliant, manufacturing process. We believe our Lexington, Massachusetts-based facility is one of the world’s leading, most versatile, gene therapy manufacturing facilities.

#### Key events

##### Commencing a pivotal study of hemophilia B lead candidate (“AMT-061”)

On February 4, 2019, we announced the dosing of the first patient in our Phase III HOPE-B hemophilia B pivotal trial. The trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of AMT-061. After the six-month lead-in period, patients will receive a single intravenous administration of AMT-061. The primary endpoint of the study will be based on the Factor IX (“FIX”) activity level achieved following the administration of AMT-061, and the secondary endpoints will measure annualized FIX replacement therapy usage, annualized bleed rates and safety. Patients enrolled in the HOPE-B trial will be tested for the presence of pre-existing neutralizing antibodies to AAV5 but will not be excluded from the trial based on their titers.

In February 2019, we presented updated data from our Phase IIb dose-confirmation study of AMT-061, which demonstrated that all three patients experienced increasing and sustained FIX levels after a one-time administration of AMT-061. Twelve weeks after administration, mean FIX activity for the three patients was 38% of normal, exceeding threshold FIX levels generally considered sufficient to significantly reduce the risk of bleeding events. The first patient achieved FIX activity of 48% of normal at 16 weeks after administration. FIX activity in the second patient was 25% of normal at 14 weeks following administration and in the third patient was 51% of normal at 12 weeks after administration. Based on the data obtained through December 13, 2018, no patient experienced a material loss of FIX activity, reported any bleeding events or required any infusions of FIX replacement therapy. AMT-061 has been well-tolerated, with no serious adverse events reported and no patients requiring any immunosuppression therapy.

##### Preparing for the clinical development of Huntington product candidate (“AMT-130”)

In January 2019, our IND application for AMT-130 was cleared by the FDA, thereby enabling us to initiate our planned Phase I/II clinical study. The Phase I/II study is expected to be a randomized, double-arm, blinded, imitation surgery-controlled trial conducted at three surgical sites and at least two non-surgical sites in the U.S. The primary objective of the study is to evaluate the safety, tolerability and efficacy of AMT-130 at two doses.

Expanding our preclinical pipeline and proprietary technology platform

In November 2018, we announced the expansion of our research pipeline with three new AAV-based product candidates. Our lead preclinical candidate, AMT-180, is a novel hemophilia A gene therapy candidate that we believe has the potential to treat all hemophilia A patients, including those with past and current inhibitors. Our next most advanced preclinical candidates, AMT-190 and AMT-150, are differentiated gene therapy candidates for the treatment of Fabry disease and SCA3, respectively.

Also, in November 2018, we presented our miQURE™ gene silencing technology platform. miQURE is uniQure's novel technology platform designed to degrade disease-causing genes, without off-target toxicity, and induce silencing of the entire target organ through secondary exosome-mediated delivery. Preclinical studies of miQURE-based gene therapies have demonstrated several important advantages, including enhanced tissue-specificity, improved nuclear and cytoplasmic gene lowering and no off-target effects associated with impact on the normal cellular miRNA or mRNA mechanisms. Gene therapy candidates designed with miQURE incorporate proprietary, therapeutic miRNA constructs that can be delivered using AAVs to potentially provide long-lasting activity. miQURE technology has been incorporated in our gene therapy product candidate for Huntington's disease, and is expected to be applied to our gene therapy candidate for SCA3.

Financing

In May 2018, we raised \$138.4 million through a follow-on public offering of 5.2 million ordinary shares at \$28.50 per ordinary share.

In December 2018, we increased our existing \$20 million credit facility to \$35 million, extended the maturity by three years to May 31, 2023 and extended the interest-only period by at least two years to November 2020.

**Our Mission and Strategy**

Our mission is to deliver curative gene therapies that transform the lives of patients.

Our strategy to achieve this mission is to:

***Advance the development of AMT-061, a potentially best-in-class treatment of hemophilia B.*** 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 European Medicines Agency ("EMA") on what we believe is an expedited clinical development plan. We initiated the lead in phase of our pivotal study program in 2018, and we dosed the first patient in January 2019.

***Maintain our leadership position in commercial-scale AAV manufacturing.*** We have established cGMP, commercial-scale manufacturing capabilities for AAV-based gene therapies in our state-of-the-art Lexington, Massachusetts facility. 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 and central-nervous system ("CNS") diseases.*** Beyond our lead clinical program for hemophilia B and our Huntington's program, 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 four clinical trials conducted in 25 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.

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**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 with third parties.

**Continue to expand our intellectual property portfolio.** We have established what we believe is a leading intellectual property portfolio covering various aspects of our technology and programs, including (i) elements of our gene therapy constructs, such as AAV vectors, promoters and transgenes, 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 is provided below:

Product/Product Candidate	Vector	Gene	Indication	Development Stage			Comments
				Pre-clinical	Phase I/II	Phase III	
<b>Liver directed diseases</b>							
AMT-061	AAV5	FIX-Padua	Hemophilia B	✓	✓	✓	Enrolling and dosing patients in phase III study Conducting IND-enabling studies
AMT-180	AAV5		Hemophilia A	✓			
AMT-190	AAV5		Fabry disease	✓			
<b>Central nervous system directed diseases</b>							
AMT-130	AAV5	HTT	Huntington's disease	✓	✓		Preparing to initiate a Phase I/II study
AMT-150			Spinocerebellar Ataxia Type 3	✓			Conducting preclinical studies
<b>Partnered programs</b>							
Undisclosed programs partnered with Bristol-Myers Squibb				✓			

**Liver-directed diseases**

**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 patients with hemophilia B that is designed to restore Factor IX (“FIX”) activity, an essential protein for blood clotting. AMT-061 includes an AAV5 vector incorporating our patent-protected FIX-Padua variant (“FIX-Padua”). AMT-061 is identical in structure to our first-generation hemophilia B product candidate, AMT-060, apart from two nucleotide substitutions in the coding sequence for FIX. The FIX-Padua

variant 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 ninefold increase in FIX activity compared to the wild-type protein, which was incorporated in AMT-060. All other critical quality attributes of AMT-061 are expected to be comparable to those of AMT-060, as AMT-061 utilizes the same AAV5 capsid and proprietary insect cell-based manufacturing platform.

AMT-061 is intended to be delivered by IV-infusion, without immunosuppressant therapy, through the peripheral vein in a single treatment session for approximately 30 minutes.

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

AAV5-based gene therapies have been demonstrated to be generally safe and well-tolerated in a multitude of clinical trials, including four uniQure trials conducted in 25 patients in hemophilia B and other indications. 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, cytotoxic T-cell-mediated immune response to the capsid or material loss of FIX activity. An independent clinical trial has demonstrated that AAV5 has the lowest prevalence of preexisting neutralizing antibodies compared to other AAV vectors. Data from our clinical, preclinical and nonclinical studies suggest that all, or nearly all patients may be eligible for treatment with AMT-061.

The FDA has agreed that AMT-061 will fall under the existing Breakthrough Therapy Designation and IND for AMT-060, and the EMA has also agreed that AMT-061 will fall under the current priority medicines (“PRIME”) designation.

In June 2018, we announced the enrollment of the first patient in the Phase III HOPE-B pivotal study of AMT-061. The Phase III HOPE-B pivotal trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of AMT-061. Approximately 50 adult hemophilia B patients classified as severe or moderately severe will be enrolled in a six-month observational period during which time they will continue to use their current standard of care to establish a baseline control. After the six-month lead-in period, patients will receive a single IV-administration of AMT-061. The primary endpoint of the study will be based on the FIX activity level achieved following the administration of AMT-061, and the secondary endpoints will measure annualized FIX replacement therapy usage, annualized bleed rates and safety. Patients enrolled in the HOPE-B trial will be tested for the presence of pre-existing neutralizing antibodies to AAV5 but will not be excluded from the trial based on their titers. In January 2019 we dosed the first patient in our HOPE-B pivotal trial.

In September 2018, we completed the dosing of a Phase IIb dose-confirmation study of AMT-061. The Phase IIb study is an open-label, single-dose, single-arm, multi-center trial being conducted in the United States. The objective of the study was to evaluate the safety and tolerability of AMT-061 and confirm the dose based on FIX activity at six weeks after administration. Three patients with severe hemophilia were enrolled in this study and received a single intravenous infusion of  $2 \times 10^{13}$  genome copies per kilogram (“gc/kg”). Patients are evaluated for the presence of pre-existing neutralizing antibodies to AAV5 but not excluded from the trial on this basis. We will continue to follow patients for a total 52 weeks to assess FIX activity, bleeding rates and usage of FIX replacement therapy, and will monitor the three patients for five years to evaluate the safety of AMT-061.

In December 2018, the study's Data Monitoring Committee evaluated initial data from the Phase IIb study and confirmed the dose of  $2 \times 10^{13}$  gc/kg for the Phase III pivotal trial. In February 2019, we presented updated data from the Phase IIb dose-confirmation study, which demonstrated that all three patients experienced increasing and sustained FIX levels after a one-time administration of AMT-061. Twelve weeks after administration, mean FIX activity for the three patients was 38% of normal, exceeding threshold FIX levels generally considered sufficient to significantly reduce the risk of bleeding events. The first patient achieved FIX activity of 48% of normal at 16 weeks after administration. FIX activity in the second patient was 25% of normal at 14 weeks following administration and in the third patient was 51% of normal at 12 weeks after administration. Based on the data obtained through December 13, 2018, no patient experienced a material loss of FIX activity, reported any bleeding events or required any infusions of FIX replacement therapy. AMT-061 has been well-tolerated, with no serious adverse events reported and no patients requiring any immunosuppression therapy.

#### *Intellectual Property for AMT-061*

In 2017, we acquired intellectual property from Professor Paolo Simioni ("Dr. Simioni"), a hemophilia expert at the University of Padua, Italy. The intellectual property includes U.S. Patent Number 9,245,405, which covers compositions of FIX-Padua nucleic acids and polypeptides (proteins), as well as their therapeutic uses.

In May 2018, the U.S. Patent and Trademark Office ("USPTO") granted us a second patent, U.S. Patent Number 9,982,248, which covers methods of treating coagulopathies (bleeding disorders), including hemophilia B, using AAV-based gene therapy with nucleic acid encoding the hyperactive FIX Padua variant. The FIX Padua variant is a Factor IX protein carrying a leucine at the R338 position, often called the "FIX-Padua" or "Padua mutant".

In addition to the U.S. patent, in February 2018, the Canadian Intellectual Property Office granted Patent Number 2,737,094, which covers FIX-Padua nucleic acids for use in gene therapy and FIX-Padua polypeptides for use in FIX replacement therapy. We are also currently pursuing European patents directed toward therapeutic uses of FIX-Padua nucleic acids and polypeptides.

#### *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, our first-generation hemophilia B product candidate, 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 Children's Research Hospital. The study is a five-year, open-label, uncontrolled, single-dose, dose-ascending multi-center trial that includes two cohorts, with the low-dose cohort using a treatment of  $5 \times 10^{12}$  gc/kg and the second-dose cohort using  $2 \times 10^{13}$  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.

In December 2018, we presented long-term clinical data from our ongoing Phase I/II study of AMT-060, including up to two and a half years of follow-up. The data demonstrated that AMT-060 continues to be safe and well-tolerated, with no new serious adverse events and no development of inhibitors. All ten patients sustained increases in FIX activity and improvements in their disease state as measured by reduced usage of FIX replacement therapy and decreased bleeding frequency.

All five patients in the second dose cohort of  $2 \times 10^{13}$  gc/kg continue to be free of routine prophylaxis at up to two years after treatment. During the last 12 months of observation, the mean annualized bleeding rate was 0.5 bleeds, representing an 88% reduction compared to the year prior to treatment. During the same period, the usage of FIX replacement therapy declined 93% compared to the year prior to treatment. Mean FIX activity increased from 7.1% in the first year after treatment to 8.3% in the second year and was 8.9% of normal at the last measurement.



Hemophilia A program (AMT-180)

*Hemophilia A Disease and Market Background*

Hemophilia A, also called factor VIII (“FVIII”) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation, a change in a gene. More than half of the patients have the severe form of hemophilia A. Patients with severe hemophilia A experience bleeding following an injury and may have frequent spontaneous bleeding episodes, often into their joints and muscles. Hemophilia A occurs in approximately one in 5,000 live births. Approximately 30 percent of patients with severe hemophilia A will develop an inhibitor that neutralizes the infused FVIII activity. Historically, this patient population has been underserved due to past exclusion from gene therapy research in clinical development.

*Our Development of AMT-180 for Hemophilia A*

AMT-180 is a novel hemophilia A gene therapy that we believe has the potential to treat all hemophilia A patients including those with past and current inhibitors. AMT-180 is a one-time, intravenously-administered, AAV5-based gene therapy incorporating a proprietary modified Factor IX gene, Super9™, that has been demonstrated in preclinical studies to circumvent inhibitors to FVIII. A proof-of-concept study indicated that administration of Super9 resulted in clinically relevant FVIII mimetic activity in hemophilia A mice and was not associated with hypercoagulability in wild-type mice. Another study in non-human primates indicated that a single dose of AMT-180 resulted in expression levels that translate into FVIII mimetic activity expected to be clinically relevant in hemophilia A patients with or without inhibitors. In addition, Super9 induced clinically relevant thrombin activation in FVIII-depleted human plasma with or without inhibitors. These data indicate that AMT-180 may lead to durable expression in hemophilia A patients and may provide long-term prevention of bleeds. In early 2019, we initiated IND-enabling studies of AMT-180.

Fabry disease program (AMT-190)

*Fabry Disease and Market Background*

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

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

*Our Development of AMT-190 for Fabry Disease*

AMT-190 is a one-time, intravenously-administered, AAV5-based gene therapy designed to circumvent GLA antibodies that can inhibit efficacy in Fabry patients. AMT-190 incorporates a modified version of  $\alpha$ -N-acetylgalactosaminidase (“NAGA”), a protein that is structurally similar to the GLA protein but is not recognized by GLA-neutralizing antibodies. As such, AMT-190 has the potential to be a more effective, longer-term treatment of Fabry disease. In cultured cells and in a study in wild-type mice, AMT-190 resulted in clinically relevant GLA activity. In a preclinical proof-of-concept study, Fabry mice were injected with a single dose of AMT-190, resulting in modified NAGA expression with subsequent GLA-activity in plasma. At two- and four-weeks post-dosing, this GLA activity already translated to up to fifty percent reduction in lyso-Gb3 levels. We believe that these studies demonstrate proof-of-concept of AMT-190 as a gene therapy candidate for Fabry disease. We believe that a one-time administration of AMT-190 could potentially lead to long-term expression of GLA in the liver, kidneys and heart, with no loss of expression due to inhibitors. We plan to conduct additional pre-clinical tests during 2019.

**Central Nervous System diseases**

Huntington’s Disease

*Huntington’s Disease and Market Background*

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

*Our Development of AMT-130 for Huntington’s Disease*

AMT-130 is our gene therapy candidate targeting Huntington’s disease that utilizes an AAV vector carrying an engineered micro-RNA (“miRNA”) designed to silence the HTT. AMT-130 is our lead product candidate developed using our miQURE technology, a proprietary, one-time administered gene silencing platform. AMT-130 has received orphan drug designation from the FDA and Orphan Medicinal Product Designation from the EMA. AMT-130 is intended to be administered directly into the brain via a stereotactic, magnetic resonance imaging guided catheter.

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

- One-time administration in the striatum of disease modifying therapy;
- Strong HTT knockdown in both deep structures and cortex;
- Use of proprietary miQURE platform.

In April 2017, we presented preclinical data on AMT-130 in transgenic mini pigs. 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, 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 which demonstrated significant improvements in both motor-coordination and survival, as well as a dose-dependent, sustained reduction in HTT.

In April 2018, we presented an overview of preclinical data establishing proof-of-concept for AMT-130 at the 2018 American Academy of Neurology Annual Meeting in Los Angeles, California. Data from multiple studies in Huntington’s disease animal models across three different species showed that a single intraparenchymal administration of AMT-130 into the striatum, resulted in a dose-dependent and sustained reduction of mutant huntingtin protein

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("mHTT") in both the deep structures of the brain and the cortex. Specifically, we presented data from the ongoing preclinical study in transgenic minipigs, one of the largest Huntington's disease animal models available, demonstrating significant reductions in human mHTT by a median of 68% in the striatum and a median of 47% in the frontal cortex at 6 months after administration of AMT-130.

In January 2019 our IND application for AMT-130 was cleared by the FDA, thereby enabling us to initiate our planned Phase I/II clinical study. The Phase I/II study is expected to be a randomized, double-arm, blinded, imitation surgery-controlled trial conducted at three surgical sites in the U.S., with at least two non-surgical sites. The primary objective of the study is to evaluate the safety, tolerability and efficacy of AMT-130 at two doses.

### Spinocerebellar Ataxia Type 3 program

#### *Spinocerebellar Ataxia type 3 and Market Background*

SCA3 is a central nervous system disorder. SCA3, also known as Machado-Joseph disease, is caused by a CAG-repeat expansion in the ATXN3 gene that results in an abnormal form of the protein ataxin-3. Patients with SCA3 experience brain degeneration that results in movement disorders, rigidity, muscular atrophy and paralysis. There is currently no treatment available that slows the progressive course of this lethal disease.

Prevalence of Spinocerebellar Ataxia Type 3 is estimated to be one to two per 100,000 with significant geographical and ethnic variations: the highest prevalence has been found in the Azores (Flores Island (1/239)), intermediate prevalence rates in Portugal, Germany, the Netherlands, China and Japan, and lower prevalence in North America, Australia and India. SCA3 is the most common form of ADCA1 in most genetically characterized populations.

#### *Our preclinical SCA3 program*

AMT-150 is a one-time, intrathecally-administered, AAV gene therapy incorporating our proprietary miQURE™ silencing technology that is designed to halt ataxia in early manifest SCA3 patients. In an in-vitro study with human Induced Pluripotent Stem ("IPS") derived neurons, AMT-150 has been shown to lower the human ataxin-3 protein by 65%, without any off-target effects. We also performed a proof-of-concept in-life study in SCA3 mice demonstrating that AMT-150 was able to lower toxic ataxin-3 protein by 65% in the brain stem after a single administration. Further studies in non-human primates demonstrate the ability to distribute and express a reporter gene at a clinically relevant level in the most degenerated brain regions in SCA3. These preclinical studies demonstrate that a single administration of AMT-150 results in sustained expression and efficient processing with on-target engagement. They also demonstrate that AMT-150 appears to be safe due to the lack of off-target activity. In 2019 we intend to initiate large animal studies to demonstrate safety and efficacy.

### **Bristol-Myers Squibb Collaboration**

In 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"). We are supporting BMS in 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.

#### *Collaboration on cardiovascular and other diseases focused targets*

In total, the companies may collaborate on ten targets, including cardiovascular targets and potentially targets in other areas. BMS initially designated four research targets, including S100A1 for congestive heart failure ("AMT-126"). BMS and we in October 2018 completed a heart function proof-of-concept study of AMT-126 in a pre-clinical animal model of heart failure. The study demonstrated deoxyribonucleic acid ("DNA") delivery and expression of S100A1 in the myocardium, thereby validating our vector delivery platform in the animal model. The data did not show a benefit on heart function at six months, and consequently, the Joint Steering Committee for the collaboration has chosen to discontinue work on S100A1. We expect that BMS will replace the S100A1 collaboration target with another cardiovascular target and that we and BMS will continue working on the other collaboration targets under the collaboration.

*Equity arrangements*

After entering into the collaboration in 2015 BMS acquired 2.4 million or 9.9% of our outstanding shares following the issuance for aggregate consideration of \$75.5 million. As of December 31, 2018, BMS held 6.4% of our outstanding ordinary shares. We have also granted BMS two warrants. BMS may at its option acquire, at a premium to the market, an additional number of shares such that BMS owns 14.9% and 19.9%, respectively, 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 standstill 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 in June 2019 (or fifth anniversary in June 2020 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.

## **New Technology Development**

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

We have a significant effort dedicated to designing and screening novel AAV capsids 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 a “rational design” approach.

We are also utilizing a “directed evolution” approach to identifying next-generation AAV capsids, which involves a capsid 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 for the discovery and optimization of next-generation AAV capsids targeting the liver and the brain. We have identified several promising next-generation AAV capsids 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 and function to activate transcription of the gene into messenger RNA. Synthetic promoters, which do not exist in nature, are optimally tailored to drive gene expression 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. One such promoter from the Synpromics collaboration is being utilized in our AMT-180 program for the treatment of hemophilia A.

## **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.

## **Intellectual Property**

### ***Introduction***

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

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

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

Because most patent applications throughout the world are confidential for 18 months after the earliest claimed priority date, and since the publication of discoveries in the scientific and patent literature often lags 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, copyrights, licenses, trademarks, trade secrets and other intellectual property rights.

### ***Patent Portfolio***

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

We file the initial patent applications for our commercially important technologies in both Europe and the United States. For the same technologies, we typically file international patent applications under the 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, 2018, our intellectual property portfolio included the following rights:

- 23 patent families that we own;
- 7 patent families that we exclusively in-license; and
- 1 patent family that we non-exclusively in-license.

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As of December 31, 2018, the geographic breakdown of our owned and exclusively in-licensed patent portfolio was as follows:

- 24 issued U.S. patents;
- 13 granted European patents;
- 5 pending PCT patent applications;
- 16 pending U.S. patent applications;
- 19 pending European patent applications; and
- 56 pending and 48 granted patent applications in other jurisdictions.

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

### ***Our Manufacturing and Technology Platform Patent Portfolios***

We own a patent family directed to large scale production of AAV vectors in insect cells relating to first-generation technology developed by uniQure for improvement of manufacturing 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.

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 includes issued patents in the United States, Europe, Japan, Australia, China and other jurisdictions and pending applications in the United States, Europe and other jurisdictions. The standard 20-year term for patents in this family will expire in 2028. Another patent family contains two issued patents in the United States 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 directed to improved AAV manufacturing with regard to capsid protein expression. One such patent family includes issued patents issued in the United States, Europe, and other jurisdictions. The standard 20-year term for patents in this family will expire in 2026. Another such patent family contains pending patent applications in the United States, Europe and other jurisdictions. The standard 20-year term for patents in this family will expire in 2035. A third such patent family includes a PCT application that we filed in 2018 directed to large scale production of parvoviral particles in insect cells. The standard 20-year term for patents in this family, if issued, will expire in 2038.

We own a patent family directed to a proprietary baculovirus removal process that contributes to developing regulatory-compliant AAV vector products. This family contains 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 directed 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 patent family directed to AAV5 administration technology through intrathecal 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 patent family directed to AAV5 administration technology in patients utilizing an immunoabsorption procedure. This family includes a PCT-application and a concomitantly filed US patent application. The standard 20-year term of patents in this family, if issued, will expire in 2037.

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We own a patent family directed to AAV5 administration technology in patients combined with an intralipid infusion procedure. This family includes a PCT-application. The standard 20-year term of patents in this family, if issued, will expire in 2038.

We own a patent family directed to AAV gene therapy vectors comprising liver-specific promoters. This family includes a provisional application in the United States, which was filed in 2018. The standard 20-year term of patents in this family, if filed and issued, will expire in 2039.

We own a patent family directed to gene therapy involving microRNA, including the treatment of neurodegenerative diseases and the monitoring of the effects of such treatment. This family includes a provisional application in the United States, which was filed in 2018. The standard 20-year term of patents in these families, if filed and issued, will expire in 2039.

### ***Our Patent Portfolio Related to Development Programs***

#### Hemophilia B

We own a patent family, including patents and patent applications, directed 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 patents have been issued in the United States, Europe, and Canada. Further applications are pending in the United States, Europe, and Hong Kong. The issued patents include 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. The standard 20-year patent term of patents in this family will expire in 2029.

On June 13, 2018, we were granted European Patent 2337849 directed to a Factor IX polypeptide protein. European patent law provides for a nine-month period during which third parties may file oppositions to issued patents. On December 21, 2018, we received notice that an opposition was filed by Strawman Limited, which we believe was filed on behalf of an anonymous third party. The opposition seeks revocation of our patent on the grounds that it is not new, does not involve an inventive step and several other reasons. The opposition period expires on March 13, 2019, and additional oppositions could be filed until that deadline. Following the deadline, a schedule of proceedings will be set by the European Patent Office to address the opposition. We expect that we will vigorously defend our patent in any opposition proceedings.

#### Huntington's disease

We own a patent family directed to gene therapy treatment of Huntington's disease within AMT-130. This family includes an issued patent in the United States and pending patent applications in the US, Europe and other jurisdictions. The standard 20-year term of patents in this family will expire in 2035.

#### Hemophilia A (AMT-180) and SCA3 (AMT-150)

We own a patent family directed to AAV-based gene therapies for treatment of hemophilia A and SCA3. This family includes a provisional application in the United States, which was filed in 2018. The standard 20-year term of patents in these families, if filed and issued, will expire in 2039.

### **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+* 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**

*Padua*

On April 17, 2017, we entered into an Assignment and License Agreement with Dr. Simioni (the “Padua Assignment”). Pursuant to the Padua Assignment, we acquired from Dr. Simioni all right, title and interest in a patent family covering the variant of the Factor IX gene, carrying an R338L mutation (FIX-Padua; “Padua IP”). Under the Padua Assignment, we have also licensed certain know-how included in the Padua IP. We 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.

*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.

*Rockefeller University*

In 2018 we entered into a Tangible Material License Agreement with Rockefeller University, NY. The non-exclusively licensed materials are used to develop and commercialize a diagnostic test and allow us to screen patients who will be treated with uniQure’s therapeutic products. The license with Rockefeller has granted us sublicensing rights under specific conditions in order to conduct all activities necessary to develop and commercialize on its own behalf within the field of use.

We paid a one-time execution fee and will pay an annual fee until commercialization of the diagnostic test occurs. If we commercialize the diagnostic test, we will pay Rockefeller University a tiered annual fee based on the number of diagnostic tests sold.

### Huntington's disease and SCA3

#### *Cold Spring Harbor Laboratory ("CSHL")*

In 2015, we entered into a license agreement with CSHL in which CSHL granted to us an exclusive, sublicensable license to develop and commercialize certain of CSHL's patented RNAi-related technology for use in connection to the treatment or prevention of Huntington's disease. The standard 20-year patent term for the licensed patents expires in 2031.

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

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

### Hemophilia A

#### *DRK Blutspendedienst ("DRK")*

In 2018, we entered into a research and option agreement with DRK-Blutspendedienst Baden-Wuerttemberg-Hessen GmbH. Under the agreement, we received an option to exclusively license from DRK patents and other intellectual property in the area of FIX variants potentially useful in treating Hemophilia A and Hemophilia B, and the parties agreed to undertake a research plan to allow us to evaluate whether we desire to exercise the option. The option expires in April 2019. The associated Assignment and License Agreement (ALA) will, if executed, give us a worldwide exclusive, sublicensable license to develop and commercialize under the DRK patents FIX-variants for the treatment of Hemophilia by gene therapy. The standard 20-year patent terms for the patents and patent applications that are the subject of this research and option agreement will expire in 2029 and 2034 respectively. Under the proposed terms of the ALA, we would pay an option fee, milestone payments when certain development milestones are achieved, and a single-digit royalty on net sales of products commercialized under the DRK patents. If we do not meet certain development milestones in either field of hemophilia A or hemophilia B, we could lose our license to the DRK intellectual property in that field. We are currently negotiating with DRK the terms of a proposal to apportion the rights to intellectual property that was created during the term of the research and option agreement, which may affect the final terms of the ALA.

### Fabry's disease

#### *Tokyo Metropolitan Institute of Medical Science ("TMIMS")*

In 2018, we entered into a license agreement with TMIMS. Under the agreement, TMIMS granted us an exclusive, sublicensable license to develop and commercialize certain TMIM's patented modified alpha-N-acetylgalactosaminidases for the treatment of Fabry by gene therapy. The standard 20-year patent term for the patent families which are the subject of this license agreement expire in 2026 and 2028.

Under the terms of the license agreement we will pay development milestones and a single-digit royalty on net sales of a commercialized product.

### ***Trade Secrets***

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

### **Trademarks**

uniQure is a registered trademark in various jurisdictions including the United States and the European Union. In 2018, we applied for trademark protection for the marks miQURE and Super9, related to our gene silencing and hemophilia technologies, respectively. We may seek trademark protection for other product candidates and technologies as and when appropriate.

### **Competition**

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

We are aware of numerous companies focused on developing gene therapies in various indications, including AGTC, Abeona Therapeutics, Adverum Biotechnologies, Allergan, Ally Therapeutics, Audentes Therapeutics, AVROBIO, Axovant Sciences, Bayer, BioMarin, bluebird bio, Expression Therapeutics, Freeline Therapeutics, Generation Bio, Genethon, GlaxoSmithKline, Homology Medicines, Lysogene, Meigenics, Milo Therapeutics, Nightstar, Novartis, Pfizer, REGENXBIO, Renova Therapeutics, Rocket, Pharmaceuticals, Sangamo BioSciences, Sanofi, Selecta Biosciences, Sarepta, Shire, Solid Biosciences, Spark Therapeutics, Takara, Ultragenyx, Vivet Therapeutics, 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, nucleic acid, antisense, RNAi, gene editing and other therapeutic modalities under development or commercialized at pharmaceutical and biotechnology companies such as Alnylam, Amgen, Bayer, Biogen, BioMarin, CSL Behring, Dicerna, Ionis, LogicBio, Novartis, Novo Nordisk, Pfizer, Translate Bio, Roche, Sangamo, Sanofi, Shire, Sobi, Spark, Wave Biosciences, 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 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 (“FDCA”) 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 (“cGMP”) regulations;
- submission to the FDA of an IND application which allows human clinical trials to begin unless the FDA objects within 30 days; the sponsor of an IND or its legal representative must be based in the United States
- approval by an independent institutional review board (“IRB”) and Institutional Biosafety Committee (“IBC”) before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with the FDA’s 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”);
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product’s identity, strength, quality and purity, as well as selected clinical trial sites and investigators to determine GCP compliance;
- approval of the BLA by the FDA, in consultation with an FDA advisory committee, if deemed appropriate by the FDA; and
- compliance with any post-approval commitments, including Risk Evaluation and Mitigation Strategies (“REMS”), and post-approval studies required by the FDA.

### ***Human Clinical Studies in the United States under an IND***

Clinical trials involve the administration of the investigational biologic to human subjects under the supervision of qualified investigators in accordance with cGCP requirements, which includes requirements for informed consent, study conduct, and IRB review and approval. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of an IND. A clinical trial may not proceed in the United States unless and until an IND becomes effective, which is 30 days after its receipt by the FDA unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on hold. INDs include preclinical study reports, together with manufacturing information, analytical data, any available clinical data or literature, and proposed clinical study protocols among other things.

The protocol and informed consent documents must also be approved by an IRB. In the case of gene therapy studies, an IBC at the local level must also review and maintain oversight over the particular study, in addition to the IRB. The FDA, an IRB, and IBC, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk or that research requirements are not being met. Information about certain clinical trials, including results, must be submitted within specific timeframes for listing on the ClinicalTrials.gov website. Subsequent clinical protocols and amendments must also be submitted to an active IND but are not subject to the 30-day review period imposed on an original IND. There is a risk that once a new protocol or amendment is submitted to an active IND there may be an extended period before the FDA may comment or provide feedback. This may result in a need to modify an ongoing clinical trial to incorporate this feedback or even a clinical hold of the trial. There is also risk that FDA may not provide comments or feedback but may ultimately disagree with the design of the study once a BLA is submitted.

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

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

Additional kinds of data may also help support a BLA or NDA, such as patient experience data and real world evidence. Real world evidence may also be used to assist in clinical trial design or support an NDA for already approved products. For genetically targeted populations and variant protein targeted products intended to address an unmet medical need in one or more patient subgroups with a serious or life threatening rare disease or condition, the FDA may allow a sponsor to rely upon data and information previously developed by the sponsor or for which the sponsor has a right of reference, that was submitted previously to support an approved application for a product that incorporates or utilizes the same or similar genetically targeted technology or a product that is the same or utilizes the same variant protein targeted drug as the product that is the subject of the application.

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

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

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

#### ***FDA Guidance Governing Gene Therapy Products***

The FDA has issued various guidance documents regarding gene therapies that outline additional factors that the FDA will consider at each of the above stages of development and which 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 via long-term follow-up.

### ***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, among other consequences. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

### ***FDA Programs to Expedite Product Development***

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

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, enacted in 2012, a sponsor can request designation of a product candidate as a breakthrough therapy. A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Products designated as breakthrough therapies are eligible for rolling review, intensive guidance on an efficient development program beginning as early as Phase 1 trials, and a commitment from the FDA to involve senior managers and experienced review staff in a proactive collaborative, cross disciplinary review.

Biologics studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means the FDA may approve the product based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. A biologic candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug or biologic from the market on an expedited basis. All promotional materials for drug or biologic candidates approved under accelerated regulations are subject to prior review by the FDA.

### ***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 \$2.5 million in fiscal year 2019; products with orphan designation are exempt from the BLA filing fee. The sponsor of an approved BLA is also subject to annual program user fees for each, currently exceeding \$309,000 in fiscal year 2019. Orphan products may also be exempt from program fees provided that certain criteria are met. These fees are typically increased annually. The FDA has agreed to specified performance goals in the review of BLAs.

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

The FDA may request additional information rather than accept an application for filing. In this event, the application must be refiled with the additional information. The refiled application is also subject to review before the FDA accepts it for review. Once the submission is accepted, the FDA begins an in-depth substantive review. The FDA will assign a date for its final decision for the product (the PDUFA action date) but can 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, including boxed warnings; require that post-approval studies, including Phase IV clinical trials, be conducted to further assess a biologic's efficacy and safety after approval; or require testing and surveillance programs to monitor the product after commercialization. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. The FDA may also not approve label statements that are necessary for successful commercialization and marketing.

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

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. The results of such tests, along with samples, are submitted to FDA for approval before the lot may be 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 ("BPCIA") which amended the Public Health Service Act ("PHSA") authorized the FDA to approve biosimilars under Section 351(k) of the PHSA. Under the BPCIA, 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



and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. An application for a biosimilar product may not be submitted to the FDA until four years following approval of the reference product, and it may not be approved until 12 years thereafter. These exclusivity provisions only apply to biosimilar companies and not companies that rely on their own data and file a full BLA. Moreover, this exclusivity is not without limitation. certain changes and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the twelve-year exclusivity period. Further, the twelve-year exclusivity market period in the U.S. for biologics has been controversial and may be shortened in the future.

#### ***Orphan Drug Exclusivity***

Under the Orphan Drug Act of 1983, the FDA may designate a biological product as an orphan drug if it is intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a biological product available in the United States for treatment of the disease or condition will be recovered from sales of the product. 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-130 for the treatment of Huntington's disease; meaning that they would receive orphan drug exclusivity if they are the first products approved for their respective indications.

#### ***Pediatric Exclusivity***

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

#### ***Regenerative Advanced Therapy Designation***

The 21<sup>st</sup> Century Cures Act became law in December 2016 and created a new program under Section 3033 in which the FDA has authority to designate a product as a regenerative medicine advanced therapy ("RMAT"). A drug is eligible for a RMAT designation if: 1) it is a regenerative medicine therapy which is a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except those products already regulated under Section 361 of the Public Health Service ("PHS") Act, 2) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and 3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. A RMAT must be made with the submission of an IND or as an amendment to an existing IND. FDA will determine if a product is eligible for RMAT designation within 60 days of submission. Advantages of the RMAT designation include all the benefits of the fast track and breakthrough therapy designation programs, including early interactions with the FDA. These early interactions may be used to discuss potential surrogate or intermediate endpoints to support accelerated approval. In 2017 FDA stated in draft guidance that human gene therapies, including genetically modified cells, that lead to a sustained effect on cells or tissues, may meet the definition of a regenerative therapy.

### ***FDA Regulation of Companion Diagnostics***

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 with therapeutics, such as establishing clinical validity, study design, the appropriate patient population and when the FDA will require that the companion diagnostic and the drug be approved simultaneously. The guidance issued in August 2014 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 and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payers and independent non-profit healthcare research organizations such as the Institute for Clinical and Economic Review (“ICER”) are also increasingly challenging the prices charged for medical products and services and examining the medical necessity, budget-impact and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third party payers do not consider a product to be cost-effective compared to other available therapies and or the standard of care, they may not cover the product after approval as a benefit under their plans or, if they do, measures including prior authorization and step throughs could be required and or the level of payment may not be sufficient to allow a company to sell its products at a profit. The U.S. federal and state governments and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid 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 choose to provide low coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on drug pricing. 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 clinical trial application ("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.

Market access can be expedited through the grant of conditional authorization for a medicine that may fulfil unmet needs which may be granted provided that the benefit-risk balance of the product is positive. The benefit-risk balance is likely to be positive if the applicant is able to provide comprehensive data and the benefit to public health of the medicinal product's immediate availability on the market outweighs the risks due to need for further data. Such authorizations are valid for one year and can be renewed annually. The holder will be required to complete specific obligations (ongoing or new studies, and in some cases additional activities) with a view to providing comprehensive data

confirming that the benefit-risk balance is positive. Once comprehensive data on the product have been obtained, the marketing authorization may be converted into a standard marketing authorization (not subject to specific obligations). Initially, this is valid for 5 years, but can be renewed for unlimited validity. Applicants for conditional authorizations can benefit from early dialogue with EMA through scientific advice or protocol assistance and discuss their development plan well in advance of the submission of a marketing-authorization application. Other stakeholders (e.g. health technology assessment bodies) can be included.

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

The European Union also provides for a system of regulatory data and market exclusivity. According to Article 14(11) of Regulation (EC) No 726/2004, as amended, and Article 10(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.

Under Regulation (EC) No 141/20003 as amended (Orphan Drug Regulation, 'ODR') a product can benefit from orphan drug status if it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European Community (EC) when the application is made. The principle benefit of such status is 10 years' market exclusivity once they are approved preventing the subsequent approval of similar medicines with similar indications.

Additional rules apply to medicinal products for pediatric use under Regulation (EC) No 1901/2006, as amended. Potential incentives include a six-month extension of any supplementary protection certificate granted pursuant to Regulation (EC) No 469/2009, however not in cases in which the relevant product is designated as an orphan medicinal product pursuant to the ODR. Instead, medicinal products designated as orphan medicinal product may enjoy an extension of the ten-year market exclusivity period granted under Regulation (EC) No 141/2000, as amended, to twelve years subject to the conditions applicable to orphan drugs.

#### *Manufacturing and 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 legislature or responsible national authority. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. Other member states allow companies to determine the prices for their medicines, but monitor and control company profits and may limit or restrict reimbursement. 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, 2018, we had a total of 212 employees, 98 of whom are based in Amsterdam, The Netherlands, and 114 in Lexington, Massachusetts. As of December 31, 2018, 40 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 works council in the Netherlands.

## **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 seek to deliver to patients suffering from rare and other devastating diseases single treatments with potentially curative results. Our business was founded in 1998 and was initially operated through our predecessor company, Amsterdam Molecular Therapeutics (AMT) Holding N.V. (“AMT”). In 2012, AMT undertook a corporate reorganization, pursuant to which uniQure B.V. acquired the entire business and assets of AMT and completed a share-for-share exchange with the shareholders of AMT. Effective February 10, 2014, in connection with 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.

From our initial public offering until December 31, 2018 we were an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (“JOBS Act”). On the last business day of our second quarter in fiscal year 2018 the aggregate worldwide market value of ordinary shares held by our non-affiliate shareholders exceeded \$700 million. As a result, as of December 31, 2018, we were considered a large accelerated filer and as a consequence lost our status as an emerging growth company. We are therefore no longer permitted to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are emerging growth companies.

Our website address is [www.uniqure.com](http://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 “Investors & Newsroom: 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. 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**

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

All of our product candidates are in research or early development. We have not generated any revenues from the sale of products and do not expect to do so for at least the next several years. Our lead product candidates, AMT-061 and AMT-130, and any of our other potential product candidates will require extensive preclinical and/or clinical testing and regulatory approval prior to commercial use. Our research and development efforts may not be successful. Even if our clinical development efforts result in positive data, our product candidates may not receive regulatory approval or be successfully introduced and marketed at prices that would permit us to operate profitably.

***We 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 different stages of 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 authorization to conduct the clinical trials or a regulatory authority decision that the clinical trial should not proceed;
- delays in obtaining required 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 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 clinical trial sites. Clinical trial sites may not have the adequate infrastructure established to handle gene therapy products or may have difficulty finding eligible patients to enroll into a trial.

In addition, we or 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. Also, patients may be reluctant to enroll in gene therapy trial where there are other therapeutic alternatives available or that may become available, which may be for various reasons including uncertainty about the safety or effectiveness of the therapeutic and the possibility that treatment with the therapeutic would preclude future gene therapy treatments.

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 materially harm our business, financial conditions 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, our product candidate that 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 from 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.

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 using a more sensitive antibody assay. Since we did not observe any ill-effects or correlation between the level of anti-AAV5 antibodies and clinical outcomes, patients who have anti-AAV5 antibodies will be permitted to enroll in our planned pivotal study of AMT-061. Since we only have been able to test a limited number of patients and have limited clinical and pre-clinical data, it is possible that future clinical studies may not confirm these results, and if so, negatively impact the outcome of our study.

In advance of treating patients in the pivotal study of AMT-061, we conducted a short study to confirm the dose expected to be used in the pivotal trial. The dose-confirmation study enrolled three patients, who were administered a single dose of  $2 \times 10^{13}$  gc/kg. We have relied on the short-term data from this study, including FIX activity and safety outcomes during the weeks following administration of AMT-061, to confirm the dose to be used in the pivotal study. Following the results of this study, our Data Monitoring Committee confirmed the dose of  $2 \times 10^{13}$  gc/kg for administration in the pivotal study. Given the limited number of patients and short follow-up period, data from this study may exhibit significant variability and differ materially from the future results of our planned pivotal study of AMT-061.

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

***Fast track product, breakthrough therapy, priority review, or 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. A fast track product designation is designed to facilitate the clinical development and expedite the review of drugs intended to treat a serious or life-threatening condition and which demonstrate the potential to address an unmet medical need. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to speed the FDA marketing application review timeframe for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. PRIME is a scheme provided by the EMA, and is analogous to BTM in the US, 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 scheme, interaction and communication between the regulatory agency and the sponsor of the trial can help to identify the most efficient path for clinical development. Sponsors of 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 to twelve 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. RMAT 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 business, results of operations and financial position and materially adversely affect our share price.

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

We seek to expand our product pipeline 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, 2018, 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. As of December 31, 2018, no serious adverse events have been reported in our Phase IIb hemophilia B trial with AMT-061.

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. If any of these events should occur, it may have a material adverse effect on our business, financial condition and results of operations.

### **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, financial condition and results of operations.

***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 any of our manufacturing processes, even minor deviations from the normal process, could result in insufficient yield, product deficiencies or manufacturing failures that result in adverse patient reactions, lot failures, insufficient inventory, product recalls and product liability claims. Additionally, we may not be able to scale up some or all of our manufacturing processes that may result in delays in regulatory approvals or otherwise adversely affect our ability to manufacture sufficient amounts of our products.

Many factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, 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 materially harm our business.

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

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

### **Risks Related to Regulatory Approval of Our Products**

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

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

The process of obtaining marketing approval for our product candidates in the 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. While there are a number of gene therapy product candidates under development, in the United States, FDA has only approved a limited number of gene therapy products, to date. Accordingly, regulators, like FDA, may have limited experience with the review and approval of marketing applications for gene therapy products.

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 continue to evolve, and agencies at both the U.S. federal and state level, as well as congressional committees and foreign governments, have sometimes expressed interest in further regulating biotechnology. In the United States, there have been a number of changes relating to gene therapy development over the last year. By example, FDA issued a number of new guidance documents on human gene therapy development, one of which was specific to human gene therapy for hemophilia and another of which was specific to rare diseases. Moreover, the U.S. National Institutes of Health, which also has authority over research involving gene therapy products, issued a proposed rule in October 2018, seeking to streamline the oversight of such protocols and reduce duplicative reporting requirements that are already captured within existing regulatory frameworks. Moreover, the European Commission conducted a public consultation in early 2013 on the application of EU legislation that governs advanced therapy medicinal products, including gene therapy products, which could result in changes in the data we need to submit to the EMA for our product candidates to gain regulatory approval or change the requirements for tracking, handling and distribution of the products which may be associated with increased costs. In addition, divergent scientific opinions among the various bodies involved in the review process may result in delays, require additional resources and ultimately result in rejection. FDA, the EMA, and other regulatory authorities will likely continue to revise and further update its approach to gene therapies in the coming years. These regulatory agencies, committees and advisory groups and the new regulations and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenues to maintain our business.

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

Regulatory authorities in some jurisdictions, including the 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 and FDA, however, may subsequently approve a similar drug for the same indication during the first product's market exclusivity if the EMA or FDA 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. The inability to obtain or failure to maintain adequate product exclusivity for our product candidates could have a material adverse effect on our business prospects, results of operations and financial conditions.

***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
- obtaining 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 may be impacted by the prevalence of neutralizing antibodies to the capsids, which are an integral component of our gene therapy constructs. Patients that have pre-existing antibodies to a particular capsid may not be eligible for administration of a gene therapy that includes this particular capsid. For example, 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. However, we did not observe any ill-effects or correlation between the level of anti-AAV5 antibodies and clinical outcomes in these three patients, suggesting that patients who have anti-AAV5 antibodies may still be eligible for AAV5-based gene therapies. Since we only have been able to test a limited number of patients and have limited clinical and pre-clinical data, 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, if approved.

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

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

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

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

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

We are aware of numerous companies focused on developing gene therapies in various indications, including AGTC, Abeona Therapeutics, Adverum Biotechnologies, Allergan, Ally Therapeutics, Audentes Therapeutics, AVROBIO, Axovant Sciences, Bayer, BioMarin, bluebird bio, Expression Therapeutics, Freeline Therapeutics, Generation Bio, Genethon, GlaxoSmithKline, Homology Medicines, Lysogene, Megenics, Milo Therapeutics, Nightstar, Novartis, Pfizer, REGENXBIO, Renova Therapeutics, Rocket, Pharmaceuticals, Sangamo BioSciences, Sanofi, Selecta Biosciences, Sarepta, Shire, Solid Biosciences, Spark Therapeutics, Takara, Ultragenyx, Vivet Therapeutics, 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, nucleic acid, antisense, RNAi, gene editing and other pharmaceuticals under development or commercialized at pharmaceutical and biotechnology companies such as Alynham, Amgen, Bayer, Biogen, BioMarin, CSL Behring, Dicerna, Ionis, LogicBio, Novartis, Novo Nordisk, Pfizer, Translate Bio, Roche, Sangamo, Sanofi, Shire, Sobi, Spark, Wave Biosciences, 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 currently expect that BMS will replace the S100A1 research target with another research target. A decision by BMS not to actively pursue target indications or our inability to achieve milestones under the collaboration agreement could have a material adverse effect on our business, financial conditions and results of operations.



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

If 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, in part, upon a combination of in-licensed and owned patents to protect our intellectual property. Our success depends in a large part on our ability to obtain and maintain this protection in the 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. Our inability to obtain and maintain appropriate patent protection for any one of our products could have a material adverse effect on our business, financial conditions and results of operations.

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

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

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

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. 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.

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

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

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

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

Because we collaborate 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, most patients may not be able to afford treatment with our products and our revenues and gross margins will be adversely affected, and our business will be harmed.

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

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 materially 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 \$83.3 million in the year ended December 31, 2018, \$79.3 million in 2017 and \$73.4 million in 2016. As of December 31, 2018, we had an accumulated deficit of \$535.5 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:

- execute our pivotal study for AMT-061;
- initiate clinical studies related to our Huntington's disease gene therapy program;
- advance multiple research programs related to gene therapy candidates targeting liver-directed and 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; and
- maintain, expand and protect our intellectual property portfolio, including in-licensing 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 materially adversely affected.

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

As of December 31, 2018, we had \$35.0 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 January 2021 through June 2023. 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, if we are found in violation thereof, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

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 would be able to market, sell and distribute any products for which we obtain marketing approval.

Efforts to ensure that our business arrangements with third parties will comply with applicable laws and regulations 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. The cost associated with any of these actions could be substantial and could cause irreparable harm to our reputation or otherwise have a material adverse effect on our business, financial condition and results of operations.

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

Many national and state laws govern the privacy and security of health information and other personal and private information. They often differ from each other in significant ways. For instance, the EU has adopted a comprehensive data protection law called the General Data Protection Regulation (“GDPR”) that took effect on May 25, 2018. The GDPR, together with the national legislation of the EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EU, security breach notifications, security and confidentiality of the personal data, and imposition of substantial potential fines for breaches of the data protection obligations. The GDPR imposes penalties for non-compliance of up to the greater of €20 million or 4% of worldwide revenue. Data protection authorities from the different EU member states may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the EU. Guidance on implementation and compliance practices are often updated or otherwise revised. The significant costs of compliance with, risk of regulatory enforcement actions under, and other burdens imposed by the GDPR as well as under other regulatory schemes throughout the world related to privacy and security of health information and other personal and private data could have an adverse impact on our business, financial condition and results of operations.

***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 that could have a material adverse effect on our business, financial condition and results of operations.

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

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

- decreased demand for any product candidates or products that we develop or sell;
- injury to our reputation and significant negative media attention;
- negative publicity or public opinion surrounding gene therapy;
- withdrawal of clinical trial participants;
- 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. In the event insurance coverage is insufficient to cover liabilities that we may incur, it could have a material adverse effect on our business, financial condition and results of operations.

***Healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.***

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

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, following passage of the Bipartisan Budget Act of 2018, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the reimbursement our customers may receive for our products. Further, there have been, and there may continue to be, judicial and Congressional challenges to certain aspects of the PPACA. For example, the U.S. Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additional legislative and regulatory changes to the PPACA, its implementing regulations and guidance and its policies, remain possible in the 116th U.S. Congress and under the Trump Administration. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

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

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

While we have not experienced a system failure, accident, cyber-attack or security breach that has resulted in a material interruption in our operations to date, we have experienced and addressed recent system failures, cyber-attacks and security breaches. In the future, such events could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal

and/or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business and the further development and commercialization of our product and product candidates could be delayed.

#### **Risks Related to Employee Matters and Managing Growth**

***Our future success depends on our ability to retain key executives 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 February 26, 2019, the sale price of our ordinary shares ranged from a high of \$59.45 to a low of \$4.72. The closing price on February 26, 2019, was \$53.56 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 50.8% of our issued shares (including such shares to be issued in relation to exercisable options to purchase ordinary shares) as at December 31, 2018. As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to control many matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could control the election of the board directors and the approval of any merger, consolidation or sale of all or substantially all our assets. These shareholders may have interests that differ from those of other of our shareholders and conflicts of interest may arise.

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

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

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

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

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

***We lost our status as an "emerging growth company" as of December 31, 2018.***

We were an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 ("JOBS Act"). On the last business day of our second quarter in fiscal year 2018 the aggregate worldwide market value of ordinary shares held by our non-affiliate shareholders exceeded \$700 million. As a result, as of December 31, 2018, we are considered a large accelerated filer and as a consequence lost our status as an emerging growth company. We therefore no longer are permitted to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions included:

- reduced disclosure obligations surrounding executive compensation in our periodic reports and proxy statements;
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved; 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.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. We are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

Meeting these disclosure requirements as well as the auditor attestation of our internal control over financial reporting will require that our management and other personnel devote a substantial amount of time to these compliance incentives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities costlier and more time-consuming. In order to meet these additional reporting requirements, we may be required to divert resources away from research and development efforts, which could have a material adverse effect on our business, financial condition and results of operations.

***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.

***Unfavorable global economic conditions, including those caused by political instability in the United States or by the U.K.'s departure from the European Union ("Brexit"), could adversely affect our business, financial condition or results of operations.***

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Political instability in the United States and surrounding Brexit has the potential to disrupt global economic conditions and supply changes. While we do not believe that our operations will be directly adversely affected by Brexit, we may not be able to anticipate the effects Brexit will have on our suppliers and collaborator. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payers or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

#### **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 or 2018. A corporation organized outside the United States generally will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which at least 75% of its gross income is passive income or on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held to produce passive income. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions. Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will continue to qualify as a PFIC in future taxable years. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate, and may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were considered a PFIC for the current taxable year or any future taxable year, a U.S. holder would be required to file annual information returns for such year, whether the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year. In certain circumstances a U.S. holder may be able to make certain tax elections that would lessen the adverse impact of PFIC status; however, in order to make such elections the U.S. holder will usually have to have been provided information about the company by us, and we do not intend to provide such information.

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

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

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

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

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

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

Although we 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 (as would be required under the law of most U.S. jurisdictions). As a result of these considerations our directors may take action that would be different than those that would be taken by a company organized under the law of some U.S. jurisdictions.

**Item 1B. Unresolved Staff Comments.**

None.

**Item 2. Properties.**

*Lexington, Massachusetts / United States*

We operate a 53,343 square feet GMP qualified manufacturing facility that we lease in Lexington, Massachusetts. In November 2018, we extended and expanded the facility by leasing an additional 30,655 square feet of the same building. The expanded and extended lease for the facility terminates in June 2029, and subject to the provisions of the lease, may be renewed for two subsequent five-year terms.

*Amsterdam / The Netherlands*

In 2016, we entered into leases for a total of approximately 111,000 square feet facility in Amsterdam. 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 the lessee 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”. 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 May 7, 2018, we completed a follow-on public offering of 5,175,000 ordinary shares at \$28.50 per ordinary share, resulting in gross proceeds to us of approximately \$147.5 million. The net proceeds from this offering were approximately \$138.4 million, after deducting underwriting discounts and commissions and other estimated offering expenses. We capitalized \$0.2 million of expenses (which are presented as a reduction of additional paid-in capital) related to this offering. 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. and Wells Fargo Securities, LLC acted as joint book-running managers. Chardan Capital Markets, LLC and H.C. Wainwright & Co., LLC acted as co-lead managers and Janney Montgomery Scott acted as co-manager.

The net proceeds of our follow-on offerings 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 424B5, which were filed with the Securities and Exchange Commission on October 26, 2017 and May 3, 2018. There has been no material change in the planned use of proceeds from our follow-on offering as described in our final prospectuses.

#### **Issuer Stock Repurchases**

We did not make any purchases of our ordinary shares during the year ended December 31, 2018. Our affiliates made purchases of our ordinary shares as described in “Unregistered Sales of Equity Securities” above.

**Holders**

As of February 26, 2019, there were approximately ten 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**

The table below provides information about our Ordinary Shares that may be issued under our 2014 Amended and Restated Share Option Plan (the “2014 Plan”), our predecessor plan, our Employee Share Purchase Plan and outside these plans as of December 31, 2018:

<b>Plan Category</b>	<b>(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights</b>	<b>(b) Weighted-average exercise price of outstanding options, warrants and rights (1)</b>	<b>(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))</b>
2012 Equity Incentive Plan (Equity Compensation Plan Approved by Security Holders)	32,567	\$ 5.23 (2)	—
2014 Restated Plan (Equity Compensation Plan Approved by Security Holders)	3,300,184 (3)	\$ 11.59	3,806,163
Employee Share Purchase Plan (Equity Compensation Plan Approved by Security Holders)	—	—	147,409
Equity Compensation Plans Not Approved by Security Holders (4)	300,000	6.90	— (5)
<b>Total</b>	<b>3,632,751</b>	<b>\$ 11.15</b>	<b>3,953,572</b>

- (1) The exercise price for our RSU and PSU awards is \$0.00 and is included in the weighted average exercise price of outstanding options, warrants and rights.
- (2) The exercise price of outstanding options is denominated in euro and translated to dollar at the foreign exchange rate as of December 31, 2018
- (3) The PSU Awards in the foregoing table are measured at 140% of target for the outstanding performance-based awards
- (4) These awards include inducement grants entered into by the Company outside of the 2014 Restated Plan and the predecessor plans.
- (5) At the 2018 annual general meeting of shareholders, our Board of Directors was granted the authority to issue a maximum of 19.9% of the Company’s aggregate issued capital outside of a public offering. Ordinary Shares may be issued as part of inducement or other option grants, but are not restricted to that purpose.



**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, 2018, 2017, and 2016 and the selected consolidated balance sheet data as of December 31, 2018 and 2017 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 years ended December 31, 2015 and 2014 and the selected consolidated balance sheets as of December 31, 2016 and 2015 from our audited consolidated financial statements not included in this Annual Report on Form 10-K. We derived the selected consolidated balance sheet as of December 31, 2014 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 as issued by the International Accounting Standards Board (“IASB”) 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,				
	2018	2017	2016	2015	2014
	in thousands, except per share data				
License revenues	\$ —	\$ 8	\$ 975	\$ —	\$ —
License revenues from related party (1)	7,528	4,121	3,940	3,335	1,173
Collaboration revenues	—	4,638	7,164	—	—
Collaboration revenues from related party	3,756	4,340	13,019	7,243	4,968
<b>Total revenues</b>	<b>11,284</b>	<b>13,107</b>	<b>25,098</b>	<b>10,578</b>	<b>6,141</b>
<b>Operating expenses:</b>					
Research and development expenses	(74,809)	(72,172)	(72,510)	(59,125)	(43,772)
Selling, general and administrative expenses	(25,305)	(24,635)	(25,999)	(23,383)	(17,073)
<b>Total operating expenses</b>	<b>(100,114)</b>	<b>(96,807)</b>	<b>(98,509)</b>	<b>(82,508)</b>	<b>(60,845)</b>
Other income	2,146	15,430	1,465	779	1,022
Other expense	(1,548)	(3,073)	—	—	—
<b>Loss from operations</b>	<b>(88,232)</b>	<b>(71,343)</b>	<b>(71,946)</b>	<b>(71,151)</b>	<b>(53,682)</b>
Interest income	2,729	117	70	121	220
Interest expense	(2,160)	(2,232)	(2,172)	(2,572)	(2,019)
Foreign currency (losses) / gains, net	4,382	(3,566)	1,034	(2,496)	5,148
Other non-operating (expense) / income, net	208	(2,435)	785	(7,164)	21
<b>Loss before income tax expense</b>	<b>(83,073)</b>	<b>(79,459)</b>	<b>(72,229)</b>	<b>(83,262)</b>	<b>(50,312)</b>
Income tax benefit / (expense)	(231)	199	(1,145)	1,179	535
<b>Net loss</b>	<b>\$ (83,304)</b>	<b>\$ (79,260)</b>	<b>\$ (73,374)</b>	<b>\$ (82,083)</b>	<b>\$ (49,777)</b>
<b>Other comprehensive income / (loss), net of income tax:</b>					
Foreign currency translation adjustments net of tax impact of \$(0.2) million for the year ended December 31, 2018 (2017: \$0.2 million, 2016: \$(1.1) million, 2015: \$0.7 million, 2014: \$0.5 million)	(5,261)	2,757	271	(1,556)	(5,387)
<b>Total comprehensive loss</b>	<b>\$ (88,565)</b>	<b>\$ (76,503)</b>	<b>\$ (73,103)</b>	<b>\$ (83,639)</b>	<b>\$ (55,164)</b>
Basic and diluted net loss per common share	\$ (2.34)	(2.94)	(2.93)	(3.72)	(2.91)

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- (1) Our license revenue for the year ended December 31, 2018 reflects the implementation of ASC 606 Revenue from Contracts with Customers using the modified retrospective method. See Note 4 to our consolidated financial statements.

	As of December 31,				
	2018	2017	2016	2015	2014
	in thousands				
Cash and cash equivalents	\$ 234,898	\$ 159,371	\$ 132,496	\$ 221,626	\$ 64,688
Total assets	273,906	209,644	190,265	262,663	104,683
Total debt	35,471	20,791	20,236	20,356	20,189
Accumulated deficit	(535,506)	(475,318)	(396,058)	(322,684)	(240,601)
<b>Total shareholders' equity</b>	<b>\$ 179,606</b>	<b>\$ 89,359</b>	<b>\$ 63,631</b>	<b>\$ 127,927</b>	<b>\$ 42,634</b>

**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, 2018 and 2017, respectively, is as follows:

	For the Quarter Ended (unaudited)			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	in thousands, except per share data			
Revenue	\$ 3,478	\$ 3,050	\$ 3,148	\$ 1,608
Net loss	(18,789)	(20,592)	(22,035)	(21,888)
Basic and diluted net loss per ordinary share	\$ (0.59)	\$ (0.57)	\$ (0.59)	\$ (0.59)

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, 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)

## **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 United States ("U.S. GAAP") and unless otherwise indicated are presented in U.S. dollars.*

*Except for the historical information contained herein, the matters discussed in this MD&A may be deemed to be forward-looking statements. Forward-looking statements are only predictions based on management's current views and assumptions and involve risks and uncertainties, and actual results could differ materially from those projected or implied. 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. In January 2019, we commenced the dosing phase of a pivotal study of AMT-061, our lead product candidate for patients with hemophilia B. Also, in January 2019, we received notice from the FDA of the clearance of our IND application for AMT-130, our product candidate for patients with Huntington's disease, thereby enabling us to initiate our Phase I/II clinical study. In November 2018, we announced the expansion of our research pipeline with novel gene therapy approaches to several additional indications, including hemophilia A, Fabry disease and SCA3.

We believe our gene therapy technology platform and manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost and time to market. We produce our adeno-associated virus based ("AAV-based") gene therapies in our own facilities with a proprietary, commercial-scale, current good manufacturing practices, or cGMP, 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

#### *AMT-061*

AMT-061, our lead gene therapy candidate that includes an AAV5 vector incorporating the Factor IX-Padua variant, is currently enrolling a pivotal study in patients with severe and moderately-severe hemophilia B. AMT-061 has been granted Breakthrough Therapy Designation by the United States Food and Drug Administration and access to the PRIME initiative by EMA.

In February 2019, we announced the dosing of the first patient in our Phase III HOPE-B hemophilia B pivotal trial. The trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of AMT-061. After the six-month lead-in period, patients will receive a single intravenous administration of AMT-061. The primary endpoint of the study will be based on the FIX activity level achieved following the administration of AMT-061, and the secondary endpoints will measure annualized FIX replacement therapy usage, annualized bleed rates and safety. Patients enrolled in the HOPE-B trial will be tested for the presence of pre-existing neutralizing antibodies to AAV5 but will not be excluded from the trial based on their titers.

In February 2019, we presented updated data from our Phase IIb dose-confirmation study. The Phase IIb study is an open-label, single-dose, single-arm, multi-center trial being conducted in the United States. The objective of the study was to evaluate the safety and tolerability of AMT-061 and confirm the dose based on FIX activity at six weeks after administration. Three patients with severe hemophilia were enrolled in this study and received a single intravenous infusion of  $2 \times 10^{13}$  gc/kg.

Data from the Phase IIb study of AMT-061 show that all three patients experienced increasing and sustained FIX levels after a one-time administration of AMT-061. Twelve weeks after administration, mean FIX activity for the three patients was 38% of normal, exceeding threshold FIX levels generally considered sufficient to significantly reduce the risk of bleeding events. The first patient achieved FIX activity of 48% of normal at 16 weeks after administration. FIX activity in the second patient was 25% of normal at 14 weeks following administration and in the third patient was 51% of normal at 12 weeks after administration. Based on the data obtained through December 13, 2018, no patient experienced a material loss of FIX activity, reported any bleeding events or required any infusions of FIX replacement therapy. AMT-061 has been well-tolerated, with no serious adverse events reported and no patients requiring any immunosuppression therapy.

#### *AMT-060*

In December 2018, we presented long-term follow data from our ongoing phase I/II trial of AMT-060, our first-generation gene therapy targeting hemophilia B. AMT-060 comprised an AAV5 vector carrying a gene cassette with the wild-type FIX gene. The data presented includes up to two and a half years of follow-up from the low-dose cohort and up to two years of follow-up from the second, higher-dose cohort.

Data from the Phase I/II study show that AMT-060 continues to be safe and well-tolerated, with no new serious adverse events and no development of inhibitors. All 10 patients sustained increases in FIX activity and improvements in their disease state as measured by reduced usage of FIX replacement therapy and decreased bleeding frequency. All five patients in the second dose cohort of  $2 \times 10^{13}$  gc/kg continue to be free of routine prophylaxis at up to two and one half years after treatment. During the last 12 months of observation, the mean annualized bleeding rate was 0.5 bleeds, representing an 88% reduction compared to the year prior to treatment. During the same period, the usage of FIX replacement therapy declined 93% compared to the year prior to treatment.

### Huntington program

AMT-130 is our gene therapy candidate targeting Huntington's disease that utilizes an AAV vector carrying a microRNA ("miRNA") specifically designed to silence the huntingtin gene. AMT-130 has received orphan drug designation from the FDA and Orphan Medicinal Product Designation from the EMA.

In January 2019, our IND application for AMT-130 was cleared by the FDA, thereby enabling us to initiate our planned Phase I/II clinical study. The Phase I/II study is expected to be a randomized, double-arm, blinded, imitation surgery-controlled trial conducted at three surgical sites in the U.S., with at least two non-surgical sites. The primary objective of the study is to evaluate the safety, tolerability and efficacy of AMT-130 at two doses.

In April 2018, we presented an overview of preclinical data establishing proof-of-concept for AMT-130 at the 2018 American Academy of Neurology Annual Meeting in Los Angeles, California. Data from multiple studies in Huntington's disease animal models across three different species show that a single intraparenchymal administration of AMT-130 into the striatum, resulted in a dose-dependent and sustained reduction of mutant huntingtin protein ("mHTT") in both the deep structures of the brain and the cortex. Specifically, we presented data from an ongoing preclinical study in transgenic minipigs, one of the largest Huntington's disease animal models available, demonstrating significant reductions in human mHTT by a median of 68% in the striatum and a median of 47% in the frontal cortex at 6 months after administration of AMT-130.

#### Preclinical programs

In November 2018, we announced the expansion of our research pipeline with novel AAV gene therapy approaches to treating hemophilia A, Fabry disease and Spinocerebellar Ataxia Type 3.

##### *Hemophilia A program*

AMT-180 is a novel hemophilia A gene therapy that we believe has the potential to treat all hemophilia A patients including those with past and current inhibitors. Approximately 30 percent of patients with severe hemophilia A will develop an inhibitor that neutralizes the infused Factor VIII ("FVIII") activity. This patient population has in the past been excluded from gene therapy approaches in clinical development.

AMT-180 is a one-time, intravenously-administered, AAV5-based gene therapy incorporating a proprietary modified Factor IX gene, Super9™, that has been demonstrated in preclinical studies to circumvent inhibitors to FVIII. A proof-of-concept study indicated that administration of Super9 resulted in clinically relevant FVIII mimetic activity in hemophilia A mice and was not associated with hypercoagulability in wild-type mice. Another study in non-human primates indicated that a single dose of AMT-180 resulted in expression levels that translate into FVIII mimetic activity expected to be clinically relevant in hemophilia A patients with or without inhibitors. In addition, Super9 induced clinically relevant thrombin activation in FVIII-depleted human plasma with or without inhibitors. These data indicate that AMT-180 may lead to durable expression in hemophilia A patients and may provide long-term prevention of bleeds. We plan to conduct additional IND enabling studies during 2019.

##### *Fabry disease program*

AMT-190 is a differentiated gene therapy for the treatment of Fabry disease. Fabry disease is an inherited lysosomal storage disorder caused by a defect in a gene that encodes for a protein called  $\alpha$ -galactosidase A (GLA). The GLA protein is an essential enzyme required to breakdown globotriaosylsphingosine ("Gb3") and lyso-globotriaosylsphingosine ("lyso-Gb3"). In patients living with Fabry disease, Gb3 and lyso-Gb3 accumulate in various cells throughout the body causing progressive clinical signs and symptoms of the disease. Current treatment options, which consist of bi-weekly intravenous enzyme replacement therapy, have no therapeutic benefit in patients with advanced renal or cardiac disease. Studies have also shown that a majority of male patients develop antibodies that inhibit the GLA protein and interfere with therapeutic efficacy.

AMT-190 is a one-time, intravenously-administered, AAV5-based gene therapy designed to circumvent GLA antibodies that can inhibit efficacy in Fabry patients. AMT-190 incorporates a modified version of  $\alpha$ -N-acetylgalactosaminidase ("NAGA"), a protein that is structurally similar to the GLA protein but is not recognized by GLA-neutralizing antibodies. As such, AMT-190 has the potential to be a more effective, longer-term treatment of Fabry disease.

In cultured cells and in a study in wild-type mice, AMT-190 resulted in clinically relevant GLA activity. In a preclinical proof-of-concept study, Fabry mice were injected with a single dose of AMT-190, resulting in modified NAGA expression with subsequent GLA-activity in plasma. At two- and four-weeks post-dosing, this GLA activity already translated to up to fifty percent reduction in lyso-Gb3 levels. These studies demonstrate proof-of-concept of AMT-190 as a gene therapy candidate for Fabry disease. A one-time administration of AMT-190 could potentially lead to long-term expression of GLA in the liver, kidneys and heart, with no loss of expression due to inhibitors. We plan to conduct additional pre-clinical tests through 2019.

*Spinocerebellar Ataxia Type 3 program*

AMT-150 is a gene therapy for SCA3, a central nervous system disorder. SCA3, also known as Machado-Joseph disease, is caused by a CAG-repeat expansion in the ATXN3 gene that results in an abnormal form of the protein ataxin-3. People with SCA3 experience brain degeneration that results in movement disorders, rigidity, muscular atrophy and paralysis. There is currently no treatment available that slows the progressive course of this lethal disease.

AMT-150 is a one-time, intrathecally-administered, AAV gene therapy incorporating the Company's proprietary miQURE™ silencing technology that is designed to halt ataxia in early manifest SCA3 patients. In an in-vitro study with human IPS derived neurons, AMT-150 has been shown to lower the human ataxin-3 protein by 65%, without any off-target effects. We also performed a proof-of-concept in-life study in SCA3 mice demonstrating that AMT-150 was able to lower toxic ataxin-3 protein by 65% in the brain stem after a single administration. Further studies in non-human primates demonstrate the ability to distribute and express a reporter gene at a clinically relevant level in the most degenerated brain regions in SCA3. These preclinical studies demonstrate that a single administration of AMT-150 results in sustained expression and efficient processing with on-target engagement. They also demonstrate that AMT-150 appears to be safe due to the lack of off-target activity.

We are currently performing studies in large animals to demonstrate further safety and efficacy and expect results in the fall of 2019.

BMS collaboration

We continue our research collaboration with our collaboration partner, Bristol-Myers Squibb ("BMS"), which includes research programs focused on cardiovascular and other diseases. BMS had designated four research targets to be researched, including S100A1 for congestive heart failure. BMS and we recently completed a heart function proof-of-concept study of AMT-126 in a pre-clinical animal model of heart failure. The study demonstrated DNA delivery and expression of S100A1 in the myocardium, thereby validating our vector delivery platform in the animal model. The data did not show a benefit on heart function at six months, and consequently, the Joint Steering Committee for the collaboration has chosen to discontinue work on S100A1. We expect that BMS will replace the S100A1 collaboration target with another cardiovascular target and that we and BMS will continue working on the other collaboration targets under the collaboration.

Padua-FIX patents

In 2017, we acquired intellectual property from Dr. Simioni. The intellectual property includes U.S. Patent Number 9,245,405, which covers compositions of FIX-Padua nucleic acids and polypeptides (proteins), as well as their therapeutic uses.

On May 29, 2018, the U.S. Patent and Trademark Office ("USPTO") granted us a second patent, U.S. Patent Number 9,982,248, which covers methods of treating coagulopathies (bleeding disorders), including hemophilia B, using AAV-based gene therapy with nucleic acid encoding the hyperactive FIX Padua variant. The FIX Padua variant is a Factor IX protein carrying a leucine at the R338 position, often called the "FIX-Padua" or "Padua mutant".

In addition to the U.S. patent, on February 20, 2018, the Canadian Intellectual Property Office granted Patent Number 2,737,094, which covers FIX-Padua nucleic acids for use in gene therapy and FIX-Padua polypeptides for use in FIX replacement therapy. We are also currently pursuing European and U.S. patents directed toward therapeutic uses of FIX-Padua nucleic acids and polypeptides.

On June 13, 2018, we were granted European Patent 2337849 directed to a Factor IX polypeptide protein. On December 21, 2018, we received notice that an opposition was filed by Strawman Limited in the United Kingdom. The opposition seeks revocation of our patent on the grounds that it is not new, does not involve an inventive step and several other reasons.

Intellectual Property Portfolio in Manufacturing

We continue to strengthen the intellectual property related to our proprietary insect cell-based AAV manufacturing process. In May 2018, we announced that the USPTO granted U.S. Patent Number 9,840,694, which includes claims covering nanofiltration to selectively remove potential residual baculovirus from the product. We believe this nanofiltration step is important for product quality and safety and that nanofiltration generally may be required to comply with viral clearance standards established by global regulatory authorities. Related patents were previously granted in Europe, Japan and several other jurisdictions.

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The 9,840,694 patent expands our intellectual property portfolio directed to large-scale manufacturing of AAV in insect cells using baculovirus vectors. Our portfolio includes multiple important molecular and process-related patents, as well as extensive know-how covering essential production, purification, and processing steps that are necessary for the large-scale insect cell-based manufacturing and for compliance with the regulatory authorities.

### Technology Platform Developments

In November 2018, we presented our miQURE™ gene silencing platform, which is designed to degrade disease-causing genes, without off-target toxicity, and induce silencing of the entire target organ through secondary exosome-mediated delivery. Gene therapy candidates designed with miQURE incorporate proprietary, therapeutic miRNA constructs that can be delivered using AAVs to potentially provide long-lasting activity. Preclinical studies of miQURE-based gene therapies have demonstrated several important advantages, including enhanced tissue-specificity, improved nuclear and cytoplasmic gene lowering and no off-target effects associated with impact to the cellular miRNA or messenger RNA (“mRNA”) transcriptome. miQURE technology has been incorporated in AMT-130, our investigational gene therapy for Huntington’s disease, and is expected to be applied to AMT-150 for SCA3.

In October 2018, we presented non-clinical data demonstrating that a next-generation synthetic promoter developed for liver-directed gene therapy capable of generating up to a 40-fold increase in expression compared to a reference promoter. A “promoter” is an essential component of a gene therapy construct that controls expression of a therapeutic protein. Most gene therapies incorporate natural promoters, which have limitations and may not optimize the expression of genes in specific target cells. Consequently, natural promoters may not be appropriate for gene therapies that require higher levels of gene expression and tissue specificity. The new promoter may enable us to tailor expression levels required for a specific therapeutic transgene.

Also, in October 2018, we presented new data demonstrating the ability to manufacture gene therapies using a 500-liter single-use, stirred tank reactor that has the potential to significantly increase manufacturing capacity and enhance scalability. We produce our AAV-based gene therapies in our state-of-the-art, Lexington-based manufacturing facility using a proprietary baculovirus expression vector system.

### Financing

On May 7, 2018, we completed a follow-on public offering of 5,175,000 ordinary shares at \$28.50 per ordinary share, resulting in gross proceeds to us of approximately \$147.5 million. The net proceeds from this offering were approximately \$138.4 million, after deducting underwriting discounts and commissions and other estimated offering expenses. We capitalized \$0.2 million of expenses (which are presented as a reduction of additional paid-in capital) related to this offering.

On December 6, 2018, we refinanced our existing \$20 million credit facility with Hercules Technology Growth Capital Inc. The transaction increased the facility to \$35 million, extended the maturity until June 1, 2023, extended the interest-only period from November 2018 to December 2020, or if we raise more than \$90 million in an offering or corporate transaction, to December 2021, and requires us to repay the facility in equal installments between the end of the interest-only period and the maturity date. The interest rate continues to be adjustable and is the greater of (i) 8.85% or (ii) 8.85% plus the prime rate less 5.50%. Under the refinancing, we have paid a facility fee of 0.50% and owe a back-end fee of 4.95% of the outstanding debt.

### Manufacturing Facility

In November 2018, we entered into an amendment to the lease on our facility in Lexington, Massachusetts. Pursuant to the terms of the original lease, we leased approximately 53,343 rentable square feet for a term through April 30, 2024. Pursuant to the amended lease, we have leased approximately 30,655 additional square feet of contiguous space for a term beginning June 1, 2019 and running through June 30, 2029. Additionally, we have extended the term of the lease of the original space through June 2029. The amended lease provides for an aggregate of \$15.8 million of rent for the expansion space and \$25.8 million of rent for the original space over the extended term. The amended lease provides for an additional contribution from the landlord of \$1.5 million, which may be used for alterations to the entire premises for a period of 18 months from the commencement of the term on the expansion space. We have two options to renew the amended lease for terms of five years each, as well as a right of first offer to lease any of the remaining approximately 20,000 square feet of space in the same building, if that space becomes available for rent.

### Leadership

On June 13, 2018, our shareholders voted to approve the appointment of Robert Gut, M.D., Ph.D. and David Meek as non-executive directors to our Board of Directors. On August 20, 2018, Dr. Gut was appointed as our Chief Medical Officer and he resigned as a non-executive director. On October 24, 2018, at an extraordinary general meeting, our shareholders voted to approve the appointment of Dr. Gut to our Board of Directors as an executive director.

## 2018 Financial Highlights

Key components of our results of operations include the following:

	Years ended December 31,		
	2018	2017	2016
Total revenues	\$ 11,284	\$ 13,107	\$ 25,098
Research and development expenses	(74,809)	(72,172)	(72,510)
Selling, general and administrative expenses	(25,305)	(24,635)	(25,999)
Net loss	(83,304)	(79,260)	(73,374)

As of December 31, 2018, we had cash and cash equivalents of \$234.9 million (December 31, 2017: \$159.4 million). We had a net loss of \$83.3 million in 2018, \$79.3 million in 2017 and \$73.4 million in 2016. As of December 31, 2018, we had an accumulated deficit of \$535.5 million (December 31, 2017: \$475.3 million). We anticipate that our loss from operations will increase in the future as we:

- Execute our pivotal study of AMT-061. 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);
- Initiate clinical studies for AMT-130 for our proprietary Huntington's disease gene therapy program;
- Advance multiple research programs related to gene therapy candidates targeting liver-directed, and 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. On an ongoing basis, we evaluate our estimates and judgments, including those related to the implementation of ASC 606 revenue recognition, BMS warrants, share-based payments, and the S100A1 research program. We base our assumptions, judgments and estimates on historical experience and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not clear from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies. 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 implementation of ASC 606 revenue recognition, BMS warrants, share-based payments, and the S100A1 research program 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.



**Adoption of ASC 606 revenue recognition on January 1, 2018**

On January 1, 2018 we adopted new revenue recognition policies in accordance with ASC 606. The new revenue recognition policies replace the existing policies in accordance with ASC 605. We elected to implement ASC 606 by applying it to active collaboration arrangements as of January 1, 2018 and to record a cumulative adjustment of revenue previously recognized to our accumulated loss as of December 31, 2017. The impact of implementing ASC 606 is summarized below:

- Recognized \$7.5 million of license revenue during the twelve months ended December 31, 2018, related to the collaboration with BMS compared to \$4.2 million that would have been recognized in accordance with the previous revenue recognition policies;
- Continued to present revenue recognized during the twelve months ended December 31, 2017, in accordance with the previous revenue recognition policies;
- Decreased the accumulated loss by \$24.9 million as of January 1, 2018 and decreased deferred revenue as of the same date by \$24.9 million.

In accordance with the previous revenue recognition policies we had concluded that the BMS collaboration agreement consisted of three performance obligations, (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, and (iii) clinical and commercial manufacturing. We determined that these three performance obligations are substantially identical with the performance obligations in accordance with our new revenue recognition policies:

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

**License Revenue**

We generate license revenue from a \$60.1 million upfront payment recorded on May 21, 2015, as well as \$15.0 million received in relation to the designation of the second, third and fourth collaboration target in August 2015. We are also entitled to an aggregate \$16.5 million in target designation payments upon the selection of the fifth to tenth collaboration target. We will also be eligible to receive research, development and regulatory milestone payments of up to \$254.0 million for a lead candidate target (which has been AMT-126) and up to \$217.0 million for each of the other selected targets, if milestones are achieved. We will include the variable consideration related to the selection of the fifth to tenth collaboration target, or any of the milestones, in the transaction price once it is considered probable that including these payments in the transaction price would not result in the reversal of cumulative revenue recognized. We might recognize significant amounts of License Revenue for services performed in prior periods if and when we consider this probable. Due to the significant uncertainty surrounding the development of gene-therapy product candidates and the dependence on BMS’s performance and decisions we so far did not consider this probable.

Additionally, we are eligible to receive net sales-based milestone payments and tiered mid-single to low double-digit royalties on product sales. The royalty term is determined on a licensed-product-by-licensed-product and country-by-country basis and begins on the first commercial sale of a licensed product in a country and ends on the expiration of the last to expire of specified patents or regulatory exclusivity covering such licensed product in such country or, with a customary royalty reduction, ten years after such first commercial sale if there is no such exclusivity. These revenues will be recognized when performance obligations are satisfied.

Under the previous revenue standard, we recognized License Revenue over the expected performance period on a straight-line basis commencing on May 21, 2015. In accordance with the new revenue recognition standards, we recognize License Revenue over the expected performance period based on our measure of progress towards the completion of certain activities related to our services. We determine such progress by comparing activities performed at the end of each reporting period with total activities expected to be performed. We estimate total expected activities using a number of unobservable inputs, such as the probability of BMS designating additional targets, the probability of successfully completing each phase and estimated time required to provide services during the various development stages. If available, we use product candidate specific research and development plans. Alternatively, we assume that completion of the pre-clinical phase requires an average of four years and that clinical development and commercial launch on average require 8.5 years to complete.

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The estimation of total services at the end of each reporting period involves considerable judgement. The estimated number of product candidates that BMS will pursue, significantly impacts the amount of License Revenue we recognize. For example, if we would increase the probability of all additional targets being designated by 10% then the revenue for the twelve months ended December 31, 2018, would have decreased by approximately \$2.2 million to \$5.3 million as we would be required to render more services in relation to the consideration received.

Collaboration and Manufacturing Revenue

The adoption of the new revenue recognition policies did not materially impact the recognition of Collaboration or Manufacturing Revenue.

**BMS warrants**

Pursuant to the terms of the BMS Agreements we granted BMS 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 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 BMS Agreements); and (ii) the date on which BMS designates the sixth New Target.
- 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 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.

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.

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, 2018 (December 31, 2017: 75%) for the warrants.

In March 2018, we reduced the probability of the warrants being exercised resulting in a reduction of the warrants fair value by \$1.1 million.

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 value 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, 2018.

	<u>Total warrants</u> <u>in thousands</u>
Base case	\$ 803
Increase volatility by 10% to 85%	236
Extend exercise dates by one year	55

### ***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.

### ***S100A1 research program***

In connection with our acquisition of the InoCard business (“InoCard”) in 2014, we recorded contingent consideration related to amounts potentially payable to InoCard’s former shareholders. The amounts payable in accordance with the sale and purchase agreement (as amended in August 2017) are contingent upon realization of milestones associated with the S100A1 protein research program. As part of this acquisition we acquired research and development assets. Based on the review of pre-clinical data associated with the program in 2018 we do not expect having to settle the milestone payments nor to recover the carrying amount of the acquired research and development assets. Accordingly, we recorded a \$3.8 million gain from releasing the contingent liability to profit and loss as well as a \$5.4 million impairment loss to reduce the asset’s carrying amount to its fair value of nil. This resulted in a net loss of \$1.6 million recorded within research and development expenses for the year ended December 31, 2018.

### ***Recent Accounting Pronouncements***

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

Effective January 1, 2018 we adopted new revenue recognition policies in accordance with ASC 606. The new revenue recognition policies replace the existing policies in accordance with ASC 605. We elected to implement ASC 606 by applying it to active collaboration arrangements as of January 1, 2018 and to record a cumulative adjustment of revenue previously recognized to the accumulated loss as of December 31, 2017.

#### ***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. ASU 2016-01 did not have a material impact on our consolidated financial statements.

#### ***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. Neither ASU 2016-05 nor ASU 2016-06 had a material impact on our 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. ASU 2017-09 did not have a material impact on our consolidated financial statements.

***Recent Accounting Pronouncements Not Yet Effective***

*ASU 2016-02: Leases*

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). Under the new guidance, lessees will be required to recognize the assets and liabilities that arise from operating leases. A lessee should recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. For leases with a term of 12 months or less, a lessee is permitted to make an accounting policy election by class of underlying asset not to recognize lease assets and lease liabilities. Lessees and lessors are required to recognize and measure leases at the beginning of the earliest period presented using a modified retrospective approach. ASU 2016-02 will be effective for the us beginning in the first quarter of 2019 and early application is permitted. We are finalizing our evaluation of the impact of adopting this standard including finalizing the population of leases which mainly consist of the lease agreements for the buildings. 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 balance sheet. The lease liability will be measured at the present value of the lease payments not yet paid discounted using the discount rate for the lease established at commencement date. The right-of-use asset will be valued at the amount of the lease liability adjusted for prepaid or accrued lease payments and the remaining balance of any lease incentives received. See Note 15 for current leases identified that at a minimum will be impacted by the standard. Lease cost will continue to be recognized on a straight-line basis within income from continuing operations. Payments arising from operating leases will be classified within operating activities.

*ASU 2018-13: Fair Value Measurement*

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820) which modifies the disclosure requirements on fair value measurements. The effective date for the standard is fiscal years beginning after December 15, 2019, which for us is January 1, 2020. Early adoption is permitted. The new disclosure requirements for changes in unrealized gains and losses in other comprehensive income for recurring Level 3 measurements, the range and weighted average of significant unobservable inputs and the amended requirements for the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively. We do not expect ASU 2018-13 to have a material impact on our consolidated financial statements.

**Results of Operations**

The following table presents a comparison of the twelve months ended December 31, 2018, 2017 and 2016.

	Years ended December 31,				
	2018	2017	2016	2018 vs 2017	2017 vs 2016
	in thousands				
Total revenues	\$ 11,284	\$ 13,107	\$ 25,098	\$ (1,823)	\$ (11,991)
<b>Operating expenses:</b>					
Research and development expenses	(74,809)	(72,172)	(72,510)	(2,637)	338
Selling, general and administrative expenses	(25,305)	(24,635)	(25,999)	(670)	1,364
<b>Total operating expenses</b>	<b>(100,114)</b>	<b>(96,807)</b>	<b>(98,509)</b>	<b>(3,307)</b>	<b>1,702</b>
Other income	2,146	15,430	1,465	(13,284)	13,965
Other expense	(1,548)	(3,073)	—	1,525	(3,073)
<b>Loss from operations</b>	<b>(88,232)</b>	<b>(71,343)</b>	<b>(71,946)</b>	<b>(16,889)</b>	<b>603</b>
Non-operating items, net	5,159	(8,116)	(283)	13,275	(7,833)
<b>Loss before income tax expense</b>	<b>(83,073)</b>	<b>(79,459)</b>	<b>(72,229)</b>	<b>(3,614)</b>	<b>(7,230)</b>
Income tax benefit / (expense)	(231)	199	(1,145)	(430)	1,344
<b>Net loss</b>	<b>\$ (83,304)</b>	<b>\$ (79,260)</b>	<b>\$ (73,374)</b>	<b>\$ (4,044)</b>	<b>\$ (5,886)</b>

*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 received or might receive from BMS and Chiesi (until June 2017). 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 recognize other revenue, such as sales milestone payments, when earned.

Our revenue for the years ended December 31, 2018, 2017 and 2016 was as follows:

	Years ended December 31,				
	2018	2017	2016	2018 vs 2017	2017 vs 2016
	in thousands				
License revenue	\$ 7,528	\$ 4,129	\$ 4,915	\$ 3,399	\$ (786)
Collaboration revenue BMS	3,756	4,340	13,019	(584)	(8,679)
Collaboration revenue Chiesi	—	4,638	7,164	(4,638)	(2,526)
<b>Total revenues</b>	<b>\$ 11,284</b>	<b>\$ 13,107</b>	<b>\$ 25,098</b>	<b>\$ (1,823)</b>	<b>\$ (11,991)</b>

We recognized \$7.5 million of BMS license revenue during the year ended December 31, 2018, in accordance with our new revenue recognition policies we adopted effective January 1, 2018. We recognized \$4.1 million and \$3.9 million license revenue for the years ended December 31, 2017 and 2016 in accordance with our previous revenue recognition policies.

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 for the year ended December 31, 2016. 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 a \$2.3 million up-front payment that we were required to repay in 2017 in accordance with the Glybera Termination Agreement.

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Collaboration revenue generated during year ended December 31, 2018, from research activities associated with our BMS-partnered programs, was \$3.8 million compared to \$4.3 million and \$13.0 million for the years ended December 31, 2017 and December 31, 2016, respectively. 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 for the year ended December 31, 2016.

### *Research and development expenses*

We expense research and development costs as incurred. Our research and development 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;
- Changes in the fair value of the contingent consideration related to our acquisition of InoCard as well as the impairment of in process research and development acquired;
- 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 have incurred costs related to the research, development and production of AMT-060 and AMT-061 for the treatment of hemophilia B. In the first quarter of 2015, we initiated a Phase I/II clinical trial of AMT-060. In June 2018, we initiated a pivotal study of AMT-061 and in September 2018, we completed dosing of a three-patient Phase IIb dose-confirmation study. In July 2017, we and Chiesi terminated our Hemophilia Collaboration Agreement. Accordingly, all future development expenses will be borne by us (previously Chiesi reimbursed 50% of such costs);
- *AMT-130 (Huntington's disease)*. We have incurred costs related to preclinical and nonclinical studies, as well as those associated with the preparation of the IND, which was submitted to the FDA and cleared in January 2019;
- *BMS partnered candidates*. We incur costs related to the preclinical development of BMS partnered candidates. Since May 2015, all costs related to these programs are reimbursed by BMS under our 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; and
- *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.

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, 2018 were \$74.8 million, compared to \$72.2 million and \$72.5 million for the years ended December 31, 2017 and 2016, respectively.

- We incurred \$32.4 million in personnel and consulting expenses in 2018 compared to \$31.4 million in 2017 and \$34.9 million in 2016. Our cost increased in 2018 by \$1.0 million primarily because of new personnel added during the year in our manufacturing and development organizations. Compared to 2016, our costs decreased in 2017 by \$3.5 million primarily related to our November 2016 strategic decision to consolidate our manufacturing in Lexington and to narrow the focus of our product pipeline;
- We incurred \$4.0 million in share-based compensation expenses in 2018 compared to \$3.9 million in 2017 and \$3.3 million in 2016. The increase in 2017 compared to 2016 of \$0.6 million was driven primarily by the recruitment of personnel to support the expansion of our proprietary and collaborator-sponsored programs;
- We recorded in 2018 \$0.1 million associated with termination benefits primarily attributable to our November 2016 restructuring, compared to \$1.8 million in 2017 and \$0.9 million in 2016;
- We incurred \$23.5 million in external services and costs related to the development of our product candidates in 2018, compared to \$17.3 million in 2017 and \$19.2 million in 2016. The increase in 2018 compared to 2017 of \$6.2 million was primarily related to the initiation of our dose-confirmation and pivotal studies for AMT-061 as well as costs related to the GLP toxicology study completed in 2018. The reduction in 2017 compared to 2016 of \$1.9 million was a result of the strategic reprioritization of certain product candidates;
- We incurred \$12.4 million in operating expenses and depreciation expenses related to our rented facilities in 2018, compared to \$14.4 million in 2017 and \$13.7 million in 2016. The decrease in 2018 compared to 2017 of \$2.0 million was largely the result of our decision to sublet part of our Amsterdam facility in 2018, as well as the costs incurred in 2017 from the termination of lease contracts associated with our former Amsterdam facilities. The increase in 2017 compared to 2016 of \$0.7 million primarily relates to the rental of temporary research space in Amsterdam in preparation of the build out of our new facility in Amsterdam;
- We recorded \$3.8 million in income related to a decrease in the fair value of the contingent consideration owed to the sellers of InoCard business in 2018 compared to an increase of \$3.0 million in 2017 and a decrease of \$1.1 million in 2016;
- We recorded in 2018 a \$5.4 million impairment loss on the in-process research and development asset acquired in the InoCard business combination in 2018. We recorded no such charge in either 2017 or 2016.

*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 and Chiesi 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, 2018 were \$25.3 million, compared to \$24.6 million and \$26.0 million for the years ended December 31, 2017 and 2016, respectively.

- We incurred \$8.9 million in personnel and consulting expenses in 2018 compared to \$8.4 million in 2017 and \$8.8 million in 2016;
- We incurred \$6.7 million of share-based compensation expenses in 2018 compared to \$6.3 million in 2017 and \$2.2 million in 2016. The increase in 2018 compared to 2017 of \$0.4 million is primarily related to the appreciation of our share price. The increase in 2017 compared to 2016 of \$4.1 million was primarily a result of equity grants offered to executives appointed in 2016, including our CEO;
- We incurred \$4.2 million in professional fees in 2018 compared to \$4.8 million in 2017 and \$5.9 million in 2016. We regularly incur accounting, audit and legal fees associated with operating as a public company. The decrease in 2017 compared to 2016 of \$1.1 million is related to nonrecurring expenditures incurred in 2016 related to the conversion of our financial reporting from IFRS to U.S. GAAP, Extera arbitration proceedings and the refinancing of our loan facility;
- We incurred settlement costs of \$1.5 million in 2016 in connection with our arbitration proceeding with Extera. No such costs were incurred in 2018 and 2017; and
- We incurred no costs associated with the Glybera global registry and Phase IV study during the year ended December 31, 2018, compared to \$0.3 million in 2017 and \$3.2 million in 2016. 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*

In 2018, we recognized \$1.0 million in income in the year ended December 31, 2018, from payments received from European authorities to subsidize our research and development efforts in the Netherlands compared to \$1.2 million in 2017 and \$1.5 million in 2016.

In January 2018, we began recognizing other income from the subleasing of a portion of our Amsterdam facility. We present expenses related to such income as other expense.

Following the termination of our collaboration with Chiesi in July 2017, we recognized \$13.8 million of income that was previously treated as deferred revenue. We recognized no such income in 2018 and 2016.

In 2017, we recognized other expense of \$1.7 million related to our decision to not seek renewal of the marketing authorization for the Glybera program, as well as the termination of our collaboration agreements with Chiesi. We did not recognize any such expenses in 2018 or 2016.

In 2017, we accrued \$0.6 million in contract termination costs, related to vacated facilities at our Amsterdam site. We did not recognize any such expenses in 2018 or 2016.

In 2017, we accrued \$0.8 million related to various exit activities conducted during the year. We did not recognize any such expenses in 2018 or 2016.



*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, 2018, 2017 and 2016 were as follows:

	Years ended December 31,				
	2018	2017	2016	2018 vs 2017	2017 vs 2016
	in thousands				
Interest income	\$ 2,729	\$ 117	\$ 70	\$ 2,612	\$ 47
Interest expense - Hercules debt	(2,160)	(2,232)	(2,172)	72	(60)
Foreign currency gains / (losses), net	4,382	(3,566)	1,034	7,948	(4,600)
Other non-operating (expense) / income	208	(2,435)	785	2,643	(3,220)
<b>Total non-operating (expense) / income, net</b>	<b>\$ 5,159</b>	<b>\$ (8,116)</b>	<b>\$ (283)</b>	<b>\$ 13,275</b>	<b>\$ (7,833)</b>

We raised \$85.3 million in our October 2017 and \$138.4 million in our May 2018 follow-on offering. The resulting increase in our cash on hand increased our interest income in the year ended December 31, 2018 to \$2.7 million compared to \$0.1 million in 2017 and \$0.1 million in 2016.

In 2018, we recognized a net foreign currency gain of \$4.4 million related to our borrowings from Hercules and our cash and cash equivalents, compared to a net loss of \$3.6 million in 2017 and a net gain of \$1.0 million in 2016.

In 2018, we recognized a \$0.2 million gain related to fair value changes of warrants, compared to a loss of \$2.2 million in 2017 and a gain of \$0.8 million in 2016.

**Financial Position, Liquidity and Capital Resources**

As of December 31, 2018, we had cash, cash equivalents and restricted cash of \$237.3 million. We currently expect that our cash and cash equivalents will be sufficient to fund operations into early 2021. The table below summarizes our consolidated cash flow data for the years ended December 31:

	Years ended December 31,		
	2018	2017	2016
	in thousands		
Cash, cash equivalents and restricted cash at the beginning of the period	\$ 161,851	\$ 134,324	\$ 222,869
Net cash used in operating activities	(76,037)	(64,270)	(72,189)
Net cash used in investing activities	(4,245)	(5,583)	(17,172)
Net cash generated from financing activities	157,961	90,074	2,445
Foreign exchange impact	(2,187)	7,306	(1,629)
<b>Cash, cash equivalents and restricted cash at the end of period</b>	<b>\$ 237,342</b>	<b>\$ 161,851</b>	<b>\$ 134,324</b>

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 \$83.3 million in 2018, \$79.3 million in 2017, and \$73.4 million in 2016. As of December 31, 2018, we had an accumulated deficit of \$535.5 million.

### *Sources of liquidity*

From our first institutional venture capital financing in 2006 through 2018, 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.

On December 6, 2018, we signed an amendment to the Second Amended and Restated Loan and Security Agreement with Hercules Technology Growth Capital Inc. (“Hercules”) that both refinanced our existing \$20 million credit facility and provided us with an additional commitment of \$30 million (of which \$15 million is subject to the discretion of Hercules) (the “Amended Facility”). At signing, we drew down an additional \$15 million, for a total outstanding amount of \$35 million. We have the right to draw another \$15 million through June 30, 2020 subject to the terms of the Amended Facility.

The Amended Facility extends the loan’s maturity date until June 1, 2023. This includes extending the interest-only period from November 2018 up to January 1, 2022, upon achieving certain specified conditions. As of December 31, 2018, \$35 million was outstanding (2017: \$20 million). We are required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. The variable interest rate is equal to the greater of (i) 8.85% or (ii) 8.85% plus the prime rate less 5.50%. Under the Amended Facility, we paid a facility fee equal to 0.50% of the \$35,000,000 loan outstanding and will owe a back-end fee of 4.95% of the outstanding debt.

On May 7, 2018, we completed a follow-on public offering of 5,175,000 ordinary shares at \$28.50 per ordinary share, resulting in gross proceeds to us of approximately \$147.5 million. The net proceeds to us from this offering were approximately \$138.4 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us. We capitalized \$0.2 million of expenses (which are presented as a reduction of additional paid-in capital) related to this 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 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.

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.

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 \$76.0 million for the year ended December 31, 2018, compared to \$64.3 million and \$72.2 million of cash used for the years ended December 31, 2017 and December 31, 2016, respectively.

The increase in net cash used in operating activities in 2018 compared to 2017 is primarily due to the decrease in collaboration revenue as well as changes in net working capital. In 2017, we collected \$4.6 million in Chiesi-related collaboration revenue, compared to \$0.0 million in 2018. 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.

**Net cash used in investing activities**

In 2018, we used \$4.2 million in our investing activities compared to \$5.6 million in 2017 and \$17.2 million in 2016.

	Years ended December 31,		
	2018	2017	2016
	in thousands		
Build out of Lexington site	\$ (1,596)	\$ (1,426)	\$ (1,837)
Build out of Amsterdam sites	(788)	(3,035)	(13,451)
Acquisition of licenses and patents	(1,861)	(1,122)	(1,884)
<b>Total investments</b>	<b>\$ (4,245)</b>	<b>\$ (5,583)</b>	<b>\$ (17,172)</b>

In 2018, we invested \$0.8 million in our facility in Amsterdam compared to \$3.0 million in 2017 and \$13.0 million (including a \$0.6 million deposit) in 2016.

In 2018, we invested \$1.6 million in our facility in Lexington compared to \$1.4 million in 2017 and \$1.8 million in 2016.

**Net cash generated from financing activities**

We received net proceeds of \$138.4 million associated with our follow-on offering in May 2018 and \$85.3 million associated with our follow-on offering in October 2017.

We received net proceeds of \$14.8 million associated with the refinancing of our loan facility in December 2018.

In 2018, we received \$4.8 million from the exercise of options to purchase ordinary shares issued in accordance with our share incentive plans, compared to \$4.0 million in 2017 and \$2.6 million in 2016.

In 2017, we paid \$0.6 million contingent consideration in relation to our 2014 acquisition of the InoCard business. No such disbursements were made in 2018 and 2016.

**Funding requirements**

We believe our cash and cash equivalents as of December 31, 2018 will enable us to fund our operating expenses including our debt repayment obligations as they become due and capital expenditure requirements into early 2021. Our future capital requirements will depend on many factors, including but not limited to:

- 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;

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- 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 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 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 January 2021 and will run through June 2023;
- the extent to which we acquire or in-license other businesses, products, product candidates or technologies; and
- the costs associated with maintaining quality compliance and optimizing our manufacturing processes, including the operating costs associated with our Lexington, Massachusetts manufacturing facility;

### **Contractual obligations and commitments**

The table below sets forth our contractual obligations and commercial commitments as of December 31, 2018.

	Undefined	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years	Total
	in thousands					
Debt obligations (including \$13.2 million interest payments)	\$ —	\$ 3,119	\$ 4,119	\$ 40,939	\$ —	\$ 48,177
Operating lease obligations	—	4,670	5,330	16,567	40,977	67,544
<b>Total</b>	<b>\$ —</b>	<b>\$ 7,789</b>	<b>\$ 9,449</b>	<b>\$ 57,506</b>	<b>\$ 40,977</b>	<b>\$ 115,721</b>

The contingent consideration related to our acquisition of InoCard (later renamed uniQure GmbH) amounted to \$15.5 million (€13.5 million). As the Joint Steering Committee for the collaboration has chosen to discontinue work on S100A1, we do not expect that any milestone obligations for the contingent consideration will become payable. We expect that BMS will replace the S100A1 collaboration target with another cardiovascular target. As of December 31, 2018, we recorded this obligation at a fair value of nil (December 31, 2017 \$4.0 million).

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.

### **Off-Balance Sheet Arrangements**

As of December 31, 2018, we did not have any off-balance sheet arrangement as defined 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 entities hold significant amounts of U.S. dollars in cash and cash equivalents, have debt and interest obligations to Hercules denominated in U.S. dollars, generate collaboration revenue denominated in U.S. dollars, receive services from vendors denominated in U.S. dollars and occasionally British Pounds and fund the operations of our U.S. operating entity in U.S. dollars. Foreign currency denominated account receivables and account payables are short-term in nature (generally 30 to 45 days).

Variations in exchange rates will impact earnings and other comprehensive income. At December 31, 2018, 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 \$12.9 million higher (December 31, 2017: \$1.8 million lower; December 31, 2016: \$4.7 million higher), and other comprehensive income would have been \$9.1 million lower (December 31, 2017: \$9.0 million higher, December 31, 2016: \$3.5 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 \$12.9 million lower (December 31, 2017: \$1.7 million higher, December 31, 2016: \$4.7 million lower), and other comprehensive income / (loss) would have been \$12.0 million higher (December 31, 2017: \$9.0 million lower, December 31, 2016: \$4.5 million higher). We strive to mitigate foreign exchange risk through holding sufficient funds in euro and dollars to finance budgeted cash flows for the next year.

The sensitivity in other comprehensive income to fluctuations in exchange rates is related to the funding by our Dutch entities of the investing and operating activities of our U.S. based entity as well as from translating the net assets of our Dutch entities from their functional currency euro into our reporting currency U.S. dollar.

### *Price risk*

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

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

We are not exposed to commodity price risk.

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

### *Interest rate risk*

Our interest rate risk arises from short- and long-term debt. In June 2013, we entered into the Hercules Agreement, which was amended from time to time, 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, 2018, the loan bore an interest rate of 8.85%.

As of December 31, 2018, 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 (2017: \$0.2 million; 2016: \$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.

Our cash and cash equivalents include bank balances, demand deposits and other short-term highly liquid investments (with maturities of less than three months at the time of purchase) that are readily convertible into a known amount of cash and are subject to an insignificant risk of fluctuation in value. Restricted cash includes deposits made in relation to facility leases. Cash, cash equivalents and restricted cash were placed at the following banks:

	As of December 31,			
	2018		2017	
	Amount	Credit rating	Amount	Credit rating
	in thousands			
<b>Bank</b>				
Rabobank	\$ 205,654	Aa3	\$ 76,745	Aa2
Bank of America	30,445	Aa3	83,743	Aa3
Commerzbank	—	A1	120	A2
Citizens Bank	1,243	A1	1,243	A1
<b>Total</b>	<b>\$ 237,342</b>		<b>\$ 161,851</b>	

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 into early 2021. 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	Between	Between	Over 5 years
		1 year	1 - 2 years	3 - 5 years	
	in thousands				
<b>At December 31, 2017</b>					
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	—	—	—	—
<b>Total</b>	<b>\$ 17,823</b>	<b>\$ 14,299</b>	<b>\$ 14,188</b>	<b>\$ 6,882</b>	<b>\$ —</b>
<b>At December 31, 2018</b>					
Long-term debt	\$ —	\$ 3,119	\$ 4,119	\$ 40,939	\$ —
Accounts payable, accrued expenses and other current liabilities	—	11,452	—	—	—
Derivative financial instruments	803	572	—	—	—
<b>Total</b>	<b>\$ 803</b>	<b>\$ 15,143</b>	<b>\$ 4,119</b>	<b>\$ 40,939</b>	<b>\$ —</b>

In connection with the Company's acquisition of the InoCard business ("InoCard") in 2014, the Company recorded contingent consideration related to amounts potentially payable to InoCard's former shareholders. The amounts payable in accordance with the sale and purchase agreement (as amended in August 2017) are contingent upon realization of milestones associated with our S100A1 protein research program and, as of December 2018, we do not expect to realize those milestones.

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

#### **Item 8. Financial Statements and Supplementary Data**

Our consolidated financial statements and the notes thereto, included in Part IV, Item 15, beginning on page 82, are 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 officer ("CEO"), who also serves as our chief financial officer, 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, 2018. Based on such evaluation, our CEO has concluded that as of December 31, 2018, 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, 2018. 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, 2018, based on criteria established in the COSO 2013 framework.

Our independent registered public accounting firm, which has audited the consolidated financial statements included in this Annual Report on Form 10-K, has also issued an audit report on the effectiveness of our internal control over financial reporting as of December 31, 2018. Their report is filed within this Annual Report on Form 10-K.

***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***

During the fourth quarter of 2018, there was no change in our internal control over financial reporting that materially affected, or are reasonably likely to materially affect, our internal control over 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 2019 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 2019 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 2019 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 2019 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 2019 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:

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<a href="#">Report of Independent Registered Public Accounting Firm</a>	84
<a href="#">Consolidated Balance Sheets as of December 31, 2018 and 2017</a>	86
<a href="#">Consolidated Statements of Operations and Comprehensive Loss for the Years Ended December 31, 2018, 2017 and 2016</a>	87
<a href="#">Consolidated Statements of Shareholders' Equity for the Years Ended December 31, 2018, 2017 and 2016</a>	88
<a href="#">Consolidated Statements of Cash Flows for the Years Ended December 31, 2018, 2017 and 2016</a>	89
<a href="#">Notes to Consolidated Financial Statements for the Years Ended December 31, 2018, 2017 and 2016</a>	90

- (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 is incorporated herein by reference.

**Item 16. Form 10-K Summary**

Not applicable.

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FOR THE YEARS ENDED DECEMBER 31, 2018, 2017 AND 2016

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<a href="#">Consolidated Statements of Cash Flows for the Years Ended December 31, 2018, 2017 and 2016</a>	89
<a href="#">Notes to Consolidated Financial Statements</a>	90

**Report of Independent Registered Public Accounting Firm**

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

***Opinions on the Financial Statements and Internal Control over Financial Reporting***

We have audited the accompanying consolidated balance sheets of uniQure N.V. and its subsidiaries (the “Company”) as of December 31, 2018 and 2017, 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, 2018, including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company’s internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

***Basis for Opinions***

The Company’s management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management’s Annual Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company’s consolidated financial statements and on the Company’s internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

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

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

***Definition and Limitations of Internal Control over Financial Reporting***

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

Amsterdam, The Netherlands, February 28, 2019  
PricewaterhouseCoopers Accountants N.V.

/s/ 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, 2018	December 31, 2017
	in thousands, except share and per share amounts	
<b>Current assets</b>		
Cash and cash equivalents	\$ 234,898	\$ 159,371
Accounts receivable and accrued income from related party	233	1,586
Prepaid expenses	1,116	1,139
Other current assets	329	687
<b>Total current assets</b>	<b>236,576</b>	<b>162,783</b>
<b>Non-current assets</b>		
Property, plant and equipment, net	29,179	34,281
Intangible assets, net	5,201	9,570
Goodwill	506	530
Restricted cash	2,444	2,480
<b>Total non-current assets</b>	<b>37,330</b>	<b>46,861</b>
<b>Total assets</b>	<b>\$ 273,906</b>	<b>\$ 209,644</b>
<b>Current liabilities</b>		
Accounts payable	\$ 3,792	\$ 2,908
Accrued expenses and other current liabilities	8,232	8,838
Current portion of long-term debt	—	1,050
Current portion of deferred rent	311	737
Current portion of deferred revenue	7,634	4,613
Current portion of contingent consideration	—	1,084
<b>Total current liabilities</b>	<b>19,969</b>	<b>19,230</b>
<b>Non-current liabilities</b>		
Long-term debt, net of current portion	35,471	19,741
Deferred rent, net of current portion	8,761	9,114
Deferred revenue, net of current portion	28,861	67,408
Contingent consideration, net of current portion	—	2,880
Derivative financial instruments related party	803	1,298
Other non-current liabilities	435	614
<b>Total non-current liabilities</b>	<b>74,331</b>	<b>101,055</b>
<b>Total liabilities</b>	<b>94,300</b>	<b>120,285</b>
Commitments and contingencies (see note 16)		
<b>Shareholders' equity</b>		
Ordinary shares, €0.05 par value: 60,000,000 shares authorized at December 31, 2018 and December 31, 2017 and 37,351,653 and 31,339,040 ordinary shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively.	2,299	1,947
Additional paid-in-capital	720,072	566,530
Accumulated other comprehensive loss	(7,259)	(3,800)
Accumulated deficit	(535,506)	(475,318)
<b>Total shareholders' equity</b>	<b>179,606</b>	<b>89,359</b>
<b>Total liabilities and shareholders' equity</b>	<b>\$ 273,906</b>	<b>\$ 209,644</b>

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,		
	2018	2017	2016
	in thousands, except share and per share amounts		
License revenues	\$ —	\$ 8	\$ 975
License revenues from related party	7,528	4,121	3,940
Collaboration revenues	—	4,638	7,164
Collaboration revenues from related party	3,756	4,340	13,019
<b>Total revenues</b>	<b>11,284</b>	<b>13,107</b>	<b>25,098</b>
<b>Operating expenses:</b>			
Research and development expenses	(74,809)	(72,172)	(72,510)
Selling, general and administrative expenses	(25,305)	(24,635)	(25,999)
<b>Total operating expenses</b>	<b>(100,114)</b>	<b>(96,807)</b>	<b>(98,509)</b>
Other income	2,146	15,430	1,465
Other expense	(1,548)	(3,073)	—
<b>Loss from operations</b>	<b>(88,232)</b>	<b>(71,343)</b>	<b>(71,946)</b>
Interest income	2,729	117	70
Interest expense	(2,160)	(2,232)	(2,172)
Foreign currency gains / (losses), net	4,382	(3,566)	1,034
Other non-operating income / (loss), net	208	(2,435)	785
<b>Loss before income tax expense</b>	<b>(83,073)</b>	<b>(79,459)</b>	<b>(72,229)</b>
Income tax (expense) / benefit	(231)	199	(1,145)
<b>Net loss</b>	<b>\$ (83,304)</b>	<b>\$ (79,260)</b>	<b>\$ (73,374)</b>
<b>Other comprehensive income / (loss), net of income tax:</b>			
Foreign currency translation adjustments net of tax impact of \$(0.2) million for the year ended December 31, 2018 (2017: \$0.2 million and 2016: \$(1.1) million)	(5,261)	2,757	271
<b>Total comprehensive loss</b>	<b>\$ (88,565)</b>	<b>\$ (76,503)</b>	<b>\$ (73,103)</b>
Basic and diluted net loss per ordinary share	\$ (2.34)	\$ (2.94)	\$ (2.93)
Weighted average shares used in computing basic and diluted net loss per ordinary share	35,639,745	26,984,183	25,036,465

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 (loss)/income	Accumulated deficit	Total shareholders' equity
	No. of shares	Amount				
in thousands, except share and per share amounts						
<b>Balance at December 31, 2015</b>	<b>24,327,944</b>	<b>\$ 1,542</b>	<b>\$ 455,897</b>	<b>\$ (6,828)</b>	<b>\$ (322,684)</b>	<b>\$ 127,927</b>
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
<b>Balance at December 31, 2016</b>	<b>25,257,420</b>	<b>\$ 1,593</b>	<b>\$ 464,653</b>	<b>\$ (6,557)</b>	<b>\$ (396,058)</b>	<b>\$ 63,631</b>
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
<b>Balance at December 31, 2017</b>	<b>31,339,040</b>	<b>\$ 1,947</b>	<b>\$ 566,530</b>	<b>\$ (3,800)</b>	<b>\$ (475,318)</b>	<b>\$ 89,359</b>
Cumulative effect of retroactive implementation of ASC 606						
Revenue recognition	—	—	—	1,802	23,116	24,918
Loss for the period	—	—	—	—	(83,304)	(83,304)
Other comprehensive loss	—	—	—	(5,261)	—	(5,261)
Follow-on public offering	5,175,000	309	138,052	—	—	138,361
Exercise of share options	425,074	19	4,741	—	—	4,760
Restricted and performance share units distributed during the period	409,948	24	(24)	—	—	—
Share-based compensation expense	—	—	10,708	—	—	10,708
Issuance of ordinary shares relating to employee stock purchase plan	2,591	—	65	—	—	65
<b>Balance at December 31, 2018</b>	<b>37,351,653</b>	<b>2,299</b>	<b>720,072</b>	<b>(7,259)</b>	<b>(535,506)</b>	<b>179,606</b>

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



uniQure N.V.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years ended December 31,		
	2018	2017	2016
	in thousands		
<b>Cash flows from operating activities</b>			
Net loss	\$ (83,304)	\$ (79,260)	\$ (73,374)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation, amortization and impairment losses	12,415	7,543	6,089
Share-based compensation expense	10,708	10,280	6,214
Change in fair value of derivative financial instruments and contingent consideration	(4,054)	5,194	(1,865)
Unrealized foreign exchange (gains) / losses	(5,502)	4,222	(755)
Change in deferred taxes	231	209	1,145
Change in lease incentives	(330)	2,215	649
Changes in operating assets and liabilities:			
Accounts receivable and accrued income, prepaid expenses and other current assets	1,578	9,715	(5,917)
Inventories	-	-	480
Accounts payable	1,065	(1,670)	344
Accrued expenses and other liabilities	(382)	(1,640)	499
Deferred revenue	(8,462)	(21,078)	(5,698)
Net cash used in operating activities	(76,037)	(64,270)	(72,189)
<b>Cash flows from investing activities</b>			
Purchases of intangible assets	(1,861)	(1,122)	(1,884)
Purchase of property, plant and equipment	(2,384)	(4,461)	(15,288)
Net cash used in investing activities	(4,245)	(5,583)	(17,172)
<b>Cash flows from financing activities</b>			
Proceeds from issuance of shares related to employee stock option and purchase plans	4,825	4,044	2,593
Proceeds from exercises of convertible loan warrants	-	1,322	-
Proceeds from public offering of shares, net of issuance costs	138,361	85,290	-
Proceeds from loan increment	14,775	-	-
Contingent consideration payment	-	(582)	-
Repayment of capital lease obligation	-	-	(148)
Net cash generated from financing activities	157,961	90,074	2,445
Currency effect cash, cash equivalents and restricted cash	(2,187)	7,306	(1,629)
Net increase (decrease) in cash, cash equivalents and restricted cash	75,491	27,527	(88,545)
Cash, cash equivalents and restricted cash at beginning of period	161,851	134,324	222,869
<b>Cash, cash equivalents and restricted cash at the end of period</b>	<b>\$ 237,342</b>	<b>\$ 161,851</b>	<b>\$ 134,324</b>
Supplemental cash flow disclosures:			
Cash and cash equivalents	\$ 234,898	\$ 159,371	\$ 132,496
Restricted cash related to leasehold and other deposits	\$ 2,444	\$ 2,480	\$ 1,828
<b>Total cash, cash equivalents and restricted cash</b>	<b>\$ 237,342</b>	<b>\$ 161,851</b>	<b>\$ 134,324</b>
Cash paid for interest	\$ 2,141	\$ 1,624	\$ 2,345
Non-cash (decreases) / increases in accounts payables related to purchases of intangible assets and property, plant and equipment	\$ (48)	\$ (1,557)	\$ 1,174

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

**uniQure N.V.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. General business information**

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

The Company is registered in the trade register of the 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](http://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, 2018 and the Company’s budgeted cash flows for the twelve months following the issuance date.

**2.2 Use of estimates**

The preparation of consolidated financial statements, in conformity with U.S. GAAP and 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 performance obligations and assessment of the performance period over which license 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.

See note 6, "Intangible assets," for additional information.

**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. 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. The Company performs the same quantitative analysis discussed above for long-lived assets and finite-lived intangible assets.

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

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

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

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

#### **2.3.12 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 and primarily relate to facility leases.

#### **2.3.13 Accounts receivable**

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.

#### Revenue recognition in accordance with ASC 606:

On January 1, 2018 the Company adopted new revenue recognition policies in accordance with ASC 606 using the modified retrospective approach. The new revenue recognition policies replace the revenue recognition standards under ASC 605. The Company elected to implement ASC 606 by applying it to active collaboration arrangements as of the Initial Application Date and to record a cumulative adjustment of revenue previously recognized to accumulated loss as of December 31, 2017. See note 2.3.23 "Recently Adopted Accounting Pronouncements" and note 4 "Collaboration" for additional information.

Revenue recognition for the years ended 2017 and 2016:

During the years ended December 31, 2017 and 2016 the Company applied ASC 605.

The Company recognized revenue when earned and realized or realizable. Accordingly, revenue was recognized for each unit of accounting when all of the following criteria were 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;
- 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.

Multiple element arrangements were 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 under ASC 605**

License revenues consisted 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 were initially reported as deferred revenue on the consolidated balance sheets and were 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 were recognized as revenues either on achievement of such milestones if the milestones were considered substantive or over the period the Company has continuing performance obligations, if the milestones were not considered substantive. When determining if a milestone is substantive, the Company considered 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 were recognized in earnings when earned.



**b. Collaboration revenue under ASC 605**

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 were reimbursed through the respective collaborative research and development program.

Collaboration revenues, which were related to reimbursements from collaborators for the Company's performance of research and development services under the respective agreements, were 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 was entitled under agreements were recognized as collaboration revenues in the same quarter of the recorded cost they were 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.

The Company's other income also consists of income from the subleasing of the Amsterdam facility while other expense consists of expenses incurred in relation to the subleasing income.

Income from releasing outstanding deferred revenue in relation to the termination of the collaboration with Chiesi in 2017 is presented as other income in 2017 with no such income in 2018.

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 with no such expenses in 2018.

**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, 2018, and 2017, the Company did not have any significant uncertain tax positions.

### 2.3.23 Recently Adopted Accounting Pronouncements

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

Effective January 1, 2018 the Company adopted new revenue recognition policies in accordance with ASC 606 using the modified retrospective approach. The new revenue recognition policies replace the revenue recognition standards under ASC 605. The Company elected to implement ASC 606 by applying it to active collaboration arrangements as of January 1, 2018 and to record a cumulative adjustment of revenue previously recognized to the accumulated loss as of December 31, 2017. The impact of implementing ASC 606 is summarized below:

- Recognized \$7.5 million of license revenue during the twelve months ended December 31, 2018, related to the collaboration with BMS compared to \$4.2 million that would have been recognized in accordance with the previous revenue recognition policies;
- Continued to present revenue recognized during the twelve months ended December 31, 2017 and December 31, 2016, in accordance with the previous revenue recognition policies;
- Decreased the accumulated loss by \$24.9 million as of January 1, 2018 and decreased deferred revenue as of the same date by \$24.9 million.

In accordance with the previous revenue recognition policies the Company had concluded that the BMS collaboration agreement consisted of three performance obligations, (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, and (iii) clinical and commercial manufacturing. The Company determined that these three performance obligations are substantially identical with the performance obligations in accordance with its new revenue recognition policies:

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

#### License Revenue

The Company previously recognized License Revenue over the expected performance period on a straight-line basis commencing on May 21, 2015. The Company now recognizes License Revenue over the expected performance period based on its progress toward the completion of its services (see note 4 for a detailed discussion).

#### Collaboration and Manufacturing Revenue

The adoption of the new revenue recognition policies did not materially impact the recognition of Collaboration or Manufacturing Revenue.

#### *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 was January 1, 2018. ASU 2016-01 did not have a material impact on our consolidated financial statements.

#### *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 was January 1, 2018. Neither ASU 2016-05 nor ASU 2016-06 had a material impact on our consolidated financial statements.

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### *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 was January 1, 2018. The new standard was to be applied prospectively. ASU 2017-09 did not have a material impact on our consolidated financial statements.

### *Recent Accounting Pronouncements Not Yet Effective*

#### *ASU 2016-02: Leases*

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). In July 2018, the FASB issued ASU No. 2018-10, “Codification Improvements to Topic 842, Leases” (ASU 2018-10), which provides narrow amendments to clarify how to apply certain aspects of the new lease standard, and ASU No. 2018-11, “Leases (Topic 842) - Targeted Improvements” (ASU 2018-11), which addresses implementation issues related to the new lease standard. Under the new guidance, lessees will be required to recognize the assets and liabilities that arise from operating leases. A lessee should recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. For leases with a term of 12 months or less, a lessee is permitted to make an accounting policy election by class of underlying asset not to recognize lease assets and lease liabilities. Lessees and lessors are required to recognize and measure leases at the beginning of the earliest period presented using a modified retrospective approach. ASU 2016-02 will be effective for the Company beginning in the first quarter of 2019 and early application is permitted. The Company is finalizing its evaluation of the impact of adopting this standard including finalizing the population of leases which mainly consist of the lease agreements for the buildings. The Company expects 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. The lease liability will be measured at the present value of the lease payments not yet paid discounted using the discount rate for the lease established at commencement date. The right-of-use asset will be valued at the amount of the lease liability adjusted for prepaid or accrued lease payments and the remaining balance of any lease incentives received. See Note 15, “Leases,” for current leases identified that will be impacted by the standard. Lease cost will continue to be recognized on a straight-line basis within income from continuing operations. Payments arising from operating leases will be classified within operating activities.

#### *ASU 2018-13: Fair Value Measurement*

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820) which modifies the disclosure requirements on fair value measurements. The effective date for the standard is fiscal years beginning after December 15, 2019, which for the Company is January 1, 2020. Early adoption is permitted. The new disclosure requirements for changes in unrealized gains and losses in other comprehensive income for recurring Level 3 measurements, the range and weighted average of significant unobservable inputs and the amended requirements for the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively. The Company does not expect ASU 2018-13 to have a material impact on our 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, 2018, 2017 and 2016 are as follows:

	Contingent consideration	Derivative financial instruments in thousands	Total
<b>Balance at December 31, 2015</b>	<b>\$ 2,926</b>	<b>\$ 837</b>	<b>\$ 3,763</b>
Gains recognized in profit or loss	(1,080)	(785)	(1,865)
Currency translation effects	(8)	10	2
<b>Balance at December 31, 2016</b>	<b>\$ 1,838</b>	<b>\$ 62</b>	<b>\$ 1,900</b>
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
<b>Balance at December 31, 2017</b>	<b>\$ 3,964</b>	<b>\$ 1,635</b>	<b>\$ 5,599</b>
Gains recognized in profit or loss	(3,846)	(208)	(4,054)
Currency translation effects	(118)	(52)	(170)
<b>Balance at December 31, 2018</b>	<b>\$ —</b>	<b>\$ 1,375</b>	<b>\$ 1,375</b>

#### *Contingent consideration*

In connection with the Company's acquisition of the InoCard business ("InoCard") in 2014, the Company recorded contingent consideration related to amounts potentially payable to InoCard's former shareholders. The amounts payable in accordance with the sale and purchase agreement (as amended in August 2017) are contingent upon realization of milestones associated with its S100A1 protein research program. As of December 31, 2018, the Company does not expect to realize those milestones and recorded a \$3.8 million gain within research and development expenses for the year ended December 31, 2018, to release the liability to profit and loss.

Accordingly, the fair value of the contingent liability as of December 31, 2018 amounted to nil (December 31, 2017: \$4.0 million and December 31, 2016: \$1.8 million).

The Company made \$1.2 million in milestone payments related to the liability 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. In addition, in 2017, the parties 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.

#### *Derivative financial instruments*

The Company issued derivative financial instruments related to its collaboration with 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, 2018, was \$1.4 million (December 31, 2017: \$1.6 million), and these derivative financial instruments are described in more detail below.

BMS collaboration

On April 6, 2015, the Company entered into several agreements with BMS (the “BMS Agreements”). Pursuant to the terms of the BMS Agreements the Company granted BMS 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.

The fair value of the warrants as of December 31, 2018 is \$0.8 million (December 31, 2017: \$1.3 million). During the year ended December 31, 2018, the Company recognized a \$0.5 million gain in non-operating income / expense (December 31, 2017: \$1.2 million loss; December 31, 2016: \$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 4 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 incorporates several inputs, 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, 2018.

	<u>Total warrants</u> <u>in thousands</u>
Base case	\$ 803
Increase volatility by 10% to 85%	236
Extend exercise dates by one year	55

Hercules loan facility

On June 14, 2013, the Company entered into a venture debt loan facility (the “Original Facility”) with 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 through profit or loss. The warrant included in the Original Facility remained in place following the 2014, 2016 and 2018 amendments of the loan. The fair value of this derivative, recorded in other current liabilities, as of December 31, 2018 is \$0.6 million (December 31, 2017: \$0.3 million). During the year ended December 31, 2018, uniQure recognized a \$0.3 million loss in other non-operating income / (expense) (December 31, 2017: \$0.3 million loss; December 31, 2016: \$0.3 million gain) related to fair value changes of the Hercules warrants.

**4. Collaboration arrangements and concentration of credit risk**

In the year ended December 31, 2018, the Company generated all collaboration and license revenues from its Collaboration and License Agreement with BMS.

The Company and Chiesi Farmaceutici S.p.A. (“Chiesi”) terminated their collaboration in 2017. As a result, the Company 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, 2018: 2.4 million ordinary shares or 6.4% 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,		
	2018	2017	2016
	in thousands		
Bristol Myers Squibb	\$ 11,284	\$ 8,461	\$ 16,959
Chiesi Farmaceutici S.p.A (terminated in 2017)	—	4,646	8,139
<b>Total</b>	<b>\$ 11,284</b>	<b>\$ 13,107</b>	<b>\$ 25,098</b>

Amounts owed by BMS in relation to the collaboration services are as follows:

	December 31, 2018	December 31, 2017
		in thousands
Bristol Myers Squibb	\$ 233	\$ 1,586
<b>Total</b>	<b>\$ 233</b>	<b>\$ 1,586</b>

***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. In total, the companies may collaborate on ten targets.

Upon BMS request the Company is conducting 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 its performance obligations in accordance with its adoption of ASC 606 on January 1, 2018, are as follows:

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

***License Revenue – BMS***

The Company recognized \$7.5 million of License Revenue for the year ended December 31, 2018 (December 31, 2017: \$4.1 million, December 31, 2016: \$3.9 million) in relation to a \$60.1 million upfront payment recorded on May 21, 2015, as well as \$15.0 million received in relation to the designation of the second, third and fourth collaboration target in August 2015 (together “Consideration”).

The Company will also be 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 a lead target and up to \$217.0 million for each of the other selected targets, if milestones are achieved. The Company will include the variable consideration related to the selection of the fifth to tenth collaboration target, or any of the milestones, in the transaction price once it is considered probable that including these payments in the transaction price would not result in the significant reversal of cumulative revenue recognized. The Company will recognize significant amounts of License Revenue for services performed in prior periods if and when the Company considers this probable. Due to the significant uncertainty surrounding the development of gene-therapy product candidates and the dependence on BMS's performance and decisions the Company does not currently consider this probable.

Additionally, the Company is eligible to receive net sales-based milestone payments and tiered mid-single to low double-digit royalties on product sales. The royalty term is determined on a licensed-product-by-licensed-product and country-by-country basis and begins on the first commercial sale of a licensed product in a country and ends on the expiration of the last to expire of specified patents or regulatory exclusivity covering such licensed product in such country or, with a customary royalty reduction, ten years after the first commercial sale if there is no such exclusivity. These revenues will be recognized when performance obligations are satisfied.

Under the previous revenue standard, the Company recognized License Revenue over the expected performance period on a straight-line basis commencing on May 21, 2015. In accordance with the new revenue recognition standards, the Company recognizes License Revenue over the expected performance period based on its measure of progress towards the completion of certain activities related to its services. The Company determines such progress by comparing activities performed at the end of each reporting period with total activities expected to be performed. The Company estimates total expected activities using a number of unobservable inputs, such as the probability of BMS designating additional targets, the probability of successfully completing each phase and estimated time required to provide services during the various development stages. If available, the Company uses product candidate-specific research and development plans. Alternatively, the Company assumes that completion of the pre-clinical phase requires an average of four years and that clinical development and commercial launch on average require 8.5 years.

The estimation of total services at the end of each reporting period involves considerable judgement. The estimated number of product candidates that BMS will pursue significantly impacts the amount of License Revenue the Company recognizes. For example, if the Company would increase the probability of all additional targets being designated by 10% then the revenue for the annual period ended December 31, 2018 would have decreased by approximately \$2.2 million to \$5.3 million, as the Company would be required to render more services in relation to the Consideration received.

#### *Collaboration Revenue – BMS*

The Company provides target-specific research and development services to BMS. Collaboration Revenue related to these contracted services is recognized when performance obligations are satisfied.

The Company generated \$3.8 million collaboration revenue for the year ended December 31, 2018 (December 31, 2017: \$4.3 million; December 31, 2016: \$13.0 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.

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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 no License Revenue for the year ended December 31, 2018 (December 31, 2017: \$0.0 million; December 31, 2016: \$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 no Collaboration Revenue for the year ended December 31, 2018 (December 31, 2017: \$4.6 million; December 31, 2016: \$7.2 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, 2018	December 31, 2017
	in thousands	
Leasehold improvements	\$ 32,462	\$ 32,297
Laboratory equipment	16,685	15,976
Office equipment	2,853	2,304
Construction-in-progress	73	745
Total property, plant, and equipment	52,073	51,322
Less accumulated depreciation	(22,894)	(17,041)
<b>Property, plant and equipment, net</b>	<b>\$ 29,179</b>	<b>\$ 34,281</b>

Total depreciation expense was \$6.5 million for the year ended December 31, 2018 (December 31, 2017: \$7.0 million, December 31, 2016: \$5.5 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.

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

	December 31, 2018	December 31, 2017
	in thousands	
Lexington, Massachusetts (United States of America)	\$ 14,598	\$ 17,177
Amsterdam (the Netherlands)	14,581	17,104
<b>Total</b>	<b>\$ 29,179</b>	<b>\$ 34,281</b>



**6. Intangible assets**

**a. Acquired licenses**

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

	December 31, 2018	December 31, 2017
	in thousands	
Licenses	\$ 7,528	\$ 9,551
Less accumulated amortization and impairment	(2,327)	(5,575)
<b>Licenses, net</b>	<b>\$ 5,201</b>	<b>\$ 3,976</b>
Acquired research and development	—	5,594
<b>Intangible assets, net</b>	<b>\$ 5,201</b>	<b>\$ 9,570</b>

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 12.6 years.

During the year ended December 31, 2018, the Company capitalized \$1.9 million of expenditures related to contractual milestone payments under existing license agreements as well as costs incurred in relation to entering into new license agreements. During the same period the Company disposed a number of fully amortized, expired licenses.

As of December 31, 2018, the estimated future amortization expense for each of the five succeeding years and the period thereafter is as follows:

Years	Amount
	in thousands
2019	\$ 471
2020	471
2021	462
2022	433
2023	433
Thereafter	2,931
<b>Total</b>	<b>\$ 5,201</b>

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

	December 31, 2018	December 31, 2017
	in thousands	
Protein Sciences Corporation	\$ 2,084	\$ 2,340
St. Jude Children's Hospital	633	707
Other	2,484	929
<b>Total</b>	<b>\$ 5,201</b>	<b>\$ 3,976</b>

The amortization expense related to licenses for the year ended December 31, 2018 was \$0.4 million (December 31, 2017: \$1.0 million; December 31, 2016: \$0.3 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.

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

The Company acquired research and development assets as part of its acquisition of InoCard in July 2014. Based on the review of pre-clinical data associated with those assets, the Company does not expect that it will pursue further research related to those assets. Accordingly, the Company recorded a \$5.4 million impairment loss within research and development expenses in the year ended December 31, 2018, to reduce the asset's carrying amount to its fair value of nil. The carrying amount as at December 31, 2017 was \$5.6 million.

**7. Accrued expenses and other (non) current liabilities**

Accrued expenses and other current liabilities include the following items:

	December 31, 2018	December 31, 2017
	in thousands	
Accruals for services provided by vendors-not yet billed	\$ 1,999	\$ 2,348
Personnel related accruals and liabilities	5,688	5,646
Other current liabilities	545	844
<b>Total</b>	<b>\$ 8,232</b>	<b>\$ 8,838</b>

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 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 February 2018, the Company entered into termination agreements with certain employees. 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, 2018, are detailed in the table below:

	Accrued termination benefits in thousands
<b>Balance at December 31, 2017</b>	<b>\$ 625</b>
Accrued through operations	96
Payments	(725)
Currency translation effects	4
<b>Balance at December 31, 2018</b>	<b>\$ —</b>

**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 of 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 initially was 8.25% per annum. 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.

On December 6, 2018, the Company signed an amendment to the Second Amended and Restated Loan and Security Agreement that both refinanced the existing \$20 million 2016 Amended Facility and provided an additional commitment of \$30 million (of which \$15 million is subject to the discretion of Hercules) (the “2018 Amended Facility”). At signing, the Company drew down an additional \$15 million for a total of \$35 million outstanding. The Company has the right to draw another \$15 million through June 30, 2020 subject to the terms of the 2018 Amended Facility. The 2018 Amended Facility extends the loan’s maturity date from May 1, 2020 until June 1, 2023. The interest-only period is extended from November 2018 to January 1, 2021, or in the event that specified conditions are met, the interest-only period may be extended to January 1, 2022. The Company is required to repay the facility in equal monthly installments of principal and interest between the end of the interest-only period and the maturity date. The interest rate continues to be adjustable and is the greater of (i) 8.85% or (ii) 8.85% plus the prime rate less 5.50% per annum.

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Under the 2018 Amended Facility, the Company paid a facility fee of 0.50% of the \$35,000,000 outstanding as of signing and will owe a back-end fee of 4.95% of the outstanding debt. In addition, in May 2020 the Company owes a back-end fee of 4.85% of \$20 million, which is the amount of debt raised under the 2016 Amended Facility.

The amortized cost was \$35.7 million as of December 31, 2018, compared to \$20.8 million as of December 31, 2017, and is recorded net of discount and debt issuance costs. The foreign currency loss on the loan was \$0.9 million in 2018 (December 31, 2017: gain of \$2.6 million; December 31, 2016: loss of \$0.9 million). The fair value of the loan approximates its carrying amount. Inputs to the fair value of the loan are considered Level 3 inputs.

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

<u>Years</u>	<u>Amount</u> <u>in millions</u>
2018	\$ 2.0
2017	2.2
2016	2.2

As a covenant in the 2018 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 65% balance of principal due and 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 2018 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 2018 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, 2018, the Company was in compliance with all covenants and provisions.

The aggregate maturities of the loan, including \$13.2 million of coupon interest payments and financing fees, for each of the 53 months subsequent to December 31, 2018, are as follows:

<u>Years</u>	<u>Amount</u> <u>in thousands</u>
2019	\$ 3,119
2020	4,119
2021	15,657
2022	15,657
2023	9,625
<b>Total</b>	<b>\$ 48,177</b>

## **9. Shareholders' equity**

As of December 31, 2018, the Company's authorized share capital is €3.0 million (exchange rate as of December 31, 2018, of 1.14449 \$ / €; \$3.4 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, 2018, and 2017 and 2016 the Company's reserves were restricted for payment of dividends for accumulated foreign currency translation losses of \$7.3 million, \$3.8 million and \$6.6 million, respectively.

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On May 7, 2018, the Company completed a follow-on public offering of 5,175,000 ordinary shares at \$28.50 per ordinary share, resulting in gross proceeds to the Company of approximately \$147.5 million. The net proceeds to the Company from this offering were approximately \$138.4 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company. The Company capitalized \$0.2 million of expenses related to this offering (which were deducted from additional paid-in capital in the accompanying consolidated balance sheet).

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).

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 Collier) continue to qualify as related parties to the Company.

On May 2, 2018, the Company and Leerink mutually terminated with immediate effect the September 2017 Sales Agreement with Leerink for an at-the-market offering program ("ATM program"). The ATM program allowed for the offer and sale of up to 5 million ordinary shares at prevailing market prices from time to time. The Company did not offer or sell any ordinary shares under the ATM program.

**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,		
	2018	2017	2016
Research and development - employees	\$ 3,994	\$ 3,945	\$ 3,302
Selling, general and administrative - employees	6,699	6,335	2,242
Research and development - non-employees	—	—	670
<b>Total</b>	<b>\$ 10,693</b>	<b>\$ 10,280</b>	<b>\$ 6,214</b>

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

Award type	Years ended December 31,		
	2018	2017	2016
Share options	\$ 4,766	\$ 3,246	\$ 5,187
Restricted share units ("RSUs")	3,020	2,588	528
Performance share units ("PSUs")	2,907	4,446	499
<b>Total</b>	<b>\$ 10,693</b>	<b>\$ 10,280</b>	<b>\$ 6,214</b>

As of December 31, 2018, 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	\$ 14,489	3.13
Restricted share units	4,055	2.12
Performance share units	4,934	1.62
<b>Total</b>	<b>\$ 23,478</b>	<b>2.64</b>

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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. The Company previously had a 2012 Equity Incentive Plan (the "2012 Plan"). As of December 31, 2018, 32,567 fully vested share options are outstanding (December 31, 2017: 72,818).

At the general meeting of shareholders on January 9, 2014, the Company's shareholders approved the adoption of the 2014 Plan. At the annual general meetings of shareholders in June 2015, 2016 and 2018, uniQure shareholders approved amendments of the 2014 Plan, increasing the shares authorized for issuance by 1,070,000 shares in 2015, 3,000,000 in 2016 and 3,000,000 shares in 2018, for a total of 8,601,471 shares.

*Share options*

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 over the remaining three years. 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, 2018:

	Options	Weighted average exercise price	Weighted average remaining contractual life in years	Aggregate intrinsic value in thousands
<b>Outstanding at December 31, 2017</b>	<b>2,456,433</b>	<b>\$ 10.06</b>	<b>7.98</b>	<b>\$ 24,213</b>
Granted	937,832	\$ 26.18		
Forfeited	(315,342)	\$ 13.27		
Expired	(17,008)	\$ 17.87		
Exercised	(388,203)	\$ 11.48		
<b>Outstanding at December 31, 2018</b>	<b>2,673,712</b>	<b>\$ 15.09</b>	<b>7.98</b>	<b>\$ 39,616</b>
Fully vested and exercisable at December 31, 2018	1,073,915	\$ 10.80	6.90	19,348
Outstanding and expected to vest at December 31, 2018	1,599,797	\$ 17.96	8.70	20,268
Outstanding and expected to vest at December 31, 2017	1,680,491	\$ 8.62		
Total weighted average grant date fair value of options issued during 2018 (in \$ millions)		\$ 14.9		
Granted to directors and officers during 2018 (options, \$ in millions)	315,156	\$ 4.7		
Proceeds from option sales during 2018 (in \$ millions)		\$ 4.5		

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, 2018	937,832	\$ 15.90
Granted, 2017	1,295,350	3.87
Granted, 2016	1,024,178	6.67
Vested, 2018	689,892	5.08
Forfeited, 2018	(315,342)	7.96

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

	<u>Options</u>	<u>Weighted average grant-date fair value</u>
Outstanding and expected to vest, 2018	1,599,797	\$ 10.83
Outstanding and expected to vest, 2017	1,680,491	5.06

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:

Assumptions	<u>Years ended December 31,</u>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
Expected volatility	75%-80%	75%-80%	75%
Expected terms (in years)	10 years	10 years	10 years
Risk free interest rate	2.67% - 3.20%	2.39% - 2.81%	0.16% - 2.67%
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:

	<u>Exercised during the year</u>	<u>Intrinsic value in thousands</u>
2018	388,203	\$ 7,515
2017	198,552	1,291
2016	239,861	3,039

*Restricted Share Units*

The following table summarizes the RSU activity for the year ended December 31, 2018:

	<u>RSU</u>	
	<u>Number of shares</u>	<u>Weighted average grant-date fair value</u>
<b>Non-vested at December 31, 2017</b>	<b>683,663</b>	<b>\$ 6.38</b>
Granted	262,599	\$ 23.61
Vested	(341,833)	\$ 6.43
Forfeited	(192,108)	\$ 8.15
<b>Non-vested at December 31, 2018</b>	<b>412,321</b>	<b>\$ 16.49</b>
Total weighted average grant date fair value of RSUs granted during 2018 (in millions)		\$ 6.2
Granted to directors and officers during 2018 (shares, \$ in millions)	133,808	\$ 3.3

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

	<u>Granted during the year</u>	<u>Weighted average grant-date fair value</u>
2018	262,599	\$ 23.61
2017	603,350	5.86
2016	358,678	9.05

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

	<u>Total fair value</u> <u>in thousands</u>
2018	\$ 8,546
2017	2,917
2016	2,296

*Performance Share Units (PSUs)*

The following table summarizes the PSU activity for the year ended December 31, 2018:

	<u>PSU</u>	
	<u>Number of shares</u>	<u>Weighted average grant-date fair value</u>
<b>Non-vested at December 31, 2017</b>	<b>511,074</b>	<b>\$ 16.73</b>
Granted	—	\$ —
Vested	(68,115)	\$ 15.79
Forfeited	(65,790)	\$ 17.44
<b>Non-vested at December 31, 2018</b>	<b>377,169</b>	<b>\$ 16.73</b>
PSUs awarded but not yet earned	136,982	\$ 28.82
Total non-vested and discretionary PSUs	514,151	\$ 19.95
Total weighted average grant date fair value of PSUs awarded during the period (in millions)		\$ 3.9

In January 2018, the Company awarded PSUs to its executives and other members of senior management. These PSUs were earned in February 2019 based on the Board's assessment of the level of achievement of agreed upon performance targets through December 31, 2018. The PSUs awarded for the year ended December 31, 2018 will vest on the third anniversary of the grant, subject to the grantee's continued employment.

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:

	<u>Granted during the year</u>	<u>Weighted average grant-date fair value</u>
2018	—	\$ —
2017	550,570	\$ 17.15
2016	111,564	\$ 5.76

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

	<u>Total fair value</u> <u>in thousands</u>
2018	\$ 1,350
2017	1,730
2016	N/A

*Employee Share Purchase Plan (“ESPP”)*

In June 2018 the Company’s shareholders adopted and approved an ESPP allowing the Company to issue up to 150,000 ordinary shares. The ESPP is intended to qualify under Section 423 of the Internal Revenue Code of 1986. Under the ESPP, employees are eligible to purchase ordinary shares through payroll deductions, subject to any plan limitations. The purchase price of the shares on each purchase date is equal to 85% of the lower of the closing market price on the offering date or the closing market price on the purchase date of each three-month offering period. For the current year ended December 31, 2018, 2,591 shares have been issued.

2012 Plan

The following table summarizes option activity under the Company’s 2012 Plan for the year ended December 31, 2018:

	2012 plan			
	Options	Weighted average exercise price	Weighted average remaining contractual life	Aggregate intrinsic value
			in years	in thousands
<b>Outstanding at December 31, 2017</b>	<b>72,818</b>	€ 5.77	3.00	\$ 922
Exercised	(40,251)	€ 6.21		
Forfeited	—	€ —		
Expired	—	€ —		
<b>Outstanding, fully vested and exercisable at December 31, 2018</b>	<b>32,567</b>	€ 5.23	3.62	939
Proceeds from option sales (in million)		\$ 0.3		

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

	Exercised during the year	Intrinsic value in thousands
2018	40,251	\$ 964
2017	405,188	1,176
2016	510,547	4,381

**11. Expenses by nature**

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

	Years ended December 31,		
	2018	2017	2016
	in thousands		
Employee-related expenses	\$ 46,254	\$ 46,373	\$ 42,260
Laboratory and development expenses	23,596	17,737	21,054
Office and housing expenses	7,281	9,327	10,384
Legal and advisory expenses	7,748	8,121	11,715
Depreciation, amortization and impairment expenses	12,415	6,779	6,089
Patent and license expenses	1,202	817	1,348
Non-employee share-based compensation expenses	—	—	670
Other operating expenses	1,618	7,653	4,989
<b>Total</b>	<b>\$ 100,114</b>	<b>\$ 96,807</b>	<b>\$ 98,509</b>



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

	Years ended December 31,		
	2018	2017	2016
	in thousands, except for employee numbers		
Wages and salaries	\$ 26,646	\$ 25,131	\$ 24,999
Share-based compensation expenses	10,708	10,280	5,544
Consultant expenses	2,974	4,758	5,873
Social security costs	2,231	2,077	1,824
Health insurance	1,750	1,536	1,099
Pension costs-defined contribution plans	628	802	1,088
Other employee expenses	1,317	1,789	1,833
<b>Total</b>	<b>\$ 46,254</b>	<b>\$ 46,373</b>	<b>\$ 42,260</b>
Number of employees at the end of the period	212	202	251

**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,		
	2018	2017	2016
	in thousands		
<b>Other non-operating income:</b>			
Derivative gains	\$ 208	\$ —	\$ 785
<b>Total other non-operating income:</b>	<b>208</b>	<b>—</b>	<b>785</b>
<b>Other non-operating expense:</b>			
Derivative losses	—	(2,192)	—
Finance expenses	—	(243)	—
<b>Total other non-operating expense:</b>	<b>—</b>	<b>(2,435)</b>	<b>—</b>
<b>Other non-operating income / (expense), net</b>	<b>\$ 208</b>	<b>\$ (2,435)</b>	<b>\$ 785</b>

The Company recorded a net gain of \$0.5 million for the year ended December 31, 2018, compared to a net loss of \$1.2 million and a net gain of \$0.5 million for the years ended December 31, 2017 and December 31, 2016, 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, 2018 (December 31, 2017: \$0.3 million net loss; December 31, 2016: \$0.3 million net gain) related to warrants issued to Hercules (see note 3, "Fair value measurement").

**13. Income taxes**

**a. Income tax benefit / (expense)**

No current tax charges or liabilities were recorded in 2018, 2017 and 2016 by the Company's 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, 2018, 2017 and 2016, loss before income taxes consists of the following:

	Years ended December 31,		
	2018	2017	2016
	in thousands		
Dutch operations	\$ (85,721)	\$ (60,966)	\$ (51,107)
U.S. operations	2,646	(18,493)	(21,221)
Foreign operations	3	—	99
<b>Total</b>	<b>\$ (83,073)</b>	<b>\$ (79,459)</b>	<b>\$ (72,229)</b>

The income tax benefit / (expense) for the years ended December 31, 2018, 2017 and 2016, consists of the following:

	Years ended December 31,		
	2018	2017	2016
	in thousands		
<b>Current benefit / (expense)</b>			
Dutch operations	\$ —	\$ —	\$ —
U.S. operations	—	—	—
Foreign operations	(22)	(10)	(51)
<b>Deferred benefit / (expense)</b>			
Dutch operations	(209)	209	(1,094)
U.S. operations	—	—	—
Foreign operations	—	—	—
<b>Total income tax benefit / (expense)</b>	<b>\$ (231)</b>	<b>\$ 199</b>	<b>\$ (1,145)</b>

**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, 2018, 2017 and 2016, is as follows:

	Years ended December 31,		
	2018	2017	2016
	in thousands		
Net loss before tax for the period	\$ (83,073)	\$ (79,459)	\$ (72,229)
Expected tax benefit / (expense) at the tax rate enacted in the Netherlands (25%)	20,768	19,865	18,057
Difference in tax rates between the Netherlands and foreign countries	(106)	1,664	1,905
Net change in valuation allowance	(19,207)	(17,358)	(20,054)
Non-deductible expenses	(2,648)	(3,248)	(1,323)
Change in fair value of contingent consideration	962	(724)	270
<b>Income tax benefit / (expense)</b>	<b>\$ (231)</b>	<b>\$ 199</b>	<b>\$ (1,145)</b>

Non-deductible expenses predominantly relate to share-based compensation expenses for an amount of \$2.7 million in 2018 (2017: \$2.5 million; 2016: \$1.6 million) and non-deductible results on derivative financial instruments of \$0.0 million (2017: \$0.5 million; 2016: \$0.0 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, 2018 and 2017 are as follows:

	Years ended December 31,	
	2018	2017
	in thousands	
<b>Deferred tax assets:</b>		
Net operating loss carryforwards	\$ 74,529	\$ 73,207
Intangible assets	847	924
Property, plant and equipment	561	173
Deferred revenue	7,481	17,930
Accrued expenses and other current liabilities	1,682	1,657
<b>Gross deferred tax asset</b>	<b>\$ 85,100</b>	<b>\$ 93,891</b>
Less valuation allowance	(85,100)	(93,682)
<b>Net deferred tax asset</b>	<b>\$ —</b>	<b>\$ 209</b>
Long-term loan to foreign operations	—	(209)
<b>Net deferred tax liability</b>	<b>\$ —</b>	<b>\$ (209)</b>
<b>Net deferred tax asset / (liability)</b>	<b>\$ —</b>	<b>\$ —</b>

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Changes in the valuation allowance were as follows:

	Years ended December 31,		
	2018	2017	2016
	in thousands		
<b>January 1,</b>	\$ 93,682	\$ 82,642	\$ 65,593
Changes related to reduction of deferred revenue recorded in equity upon implementation of ASC 606 Revenue recognition as of January 1, 2018	(6,229)	—	—
Changes recorded in profit and loss	19,207	19,080	20,054
Reduction related to 2018 Dutch tax reform	(15,670)	—	—
Reduction related to 2017 US tax reform	—	(1,722)	—
Other changes including currency translation effects	(5,890)	(6,318)	(3,005)
<b>December 31,</b>	<b>\$ 85,100</b>	<b>\$ 93,682</b>	<b>\$ 82,642</b>

The valuation allowance at December 31, 2018 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 Netherlands, changes to corporate taxes were enacted in December 2018. The changes reduce the corporate tax rate from 25% to 22.55% for the fiscal year 2020 and to 20.5%, effective January 1, 2021. The Company remeasured its temporary difference using a rate of 20.5% instead of the 25% rate effective in 2018 as it does not expect to utilize any of its loss carryforwards prior to 2021. This resulted in a \$15.6 million reduction of both the gross deferred tax asset and the valuation allowance in the year ended December 31, 2018. The December 2018 tax reform also limits the carryforward of tax losses arising from January 1, 2019, to six years after the end of the respective period. Tax losses incurred prior to this date continue to expire nine years after the end of the respective period.

The Dutch fiscal unity has as of December 31, 2018 an estimated \$311.7 million (2017: \$246.0 million; 2016: \$182.0 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, 2018 unused tax losses of \$20.0 million (December 31, 2017: \$24.5 million) expired.

	2019	2020	2021	2022	2023
	in thousands				
Loss expiring	\$ 20,746	18,857	14,189	24,148	23,518

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 reduced the corporate tax rate from 35% to 21%, effective January 1, 2018. As a foreign domiciled entity, the most significant impact of the Act related 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 in the year ended December 2017. In addition, the Act limits the utilization of tax losses incurred after January 1, 2018, to 80% of taxable income. The Company did not identify any further significant impacts related to the Act during 2018. The tax losses incurred prior to January 1, 2018 are approximately \$55.1 million. As of December 31, 2018, the estimated remaining tax losses available for carry forward are \$50.6 million. These losses will expire between 2034 and 2037.

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

There are no unrecognized tax benefits for the years ended December 31, 2018, 2017 and 2016.

#### 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 in the years presented, 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,		
	2018	2017	2016
	ordinary shares		
BMS warrants	8,575,000	6,800,000	3,587,333
Stock options under 2014 Plan and Nasdaq inducement rules	2,673,712	2,456,433	2,000,266
Non-vested RSUs and earned PSUs	789,490	1,194,737	418,627
Stock options under 2012 Plan	32,567	72,818	483,006
Warrants	37,175	37,175	37,175
Employee share purchase plan	1,012	—	—
<b>Total potential dilutive ordinary shares</b>	<b>12,108,956</b>	<b>10,561,163</b>	<b>6,526,407</b>

#### 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, was set for 10 years and is non-cancellable. Originally, the lease for this facility had a termination date of 2024. In November 2018, the term was expanded by five years to June 2029. The lease continues to be renewable for two subsequent five-year terms. Additionally, the lease was expanded to include an additional 30,655 square feet within the same facility and for the same term.

The original lease provides for annual minimum increases in rent through 2024, based on a consumer price index. The lease then resets to the same rate schedule as the expansion space.

##### *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 remaining nine-year term amount to \$9.5 million as of December 31, 2018.

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As of December 31, 2018, 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		
2019	\$ 2,707	\$ 1,963	\$ 4,670
2020	3,360	1,970	5,330
2021	3,455	1,970	5,425
2022	3,552	1,970	5,522
2023	3,650	1,970	5,620
Thereafter	24,892	16,085	40,977
<b>Total minimum lease payments</b>	<b>\$ 41,616</b>	<b>\$ 25,926</b>	<b>\$ 67,544</b>
Deferred rent related to lease incentives-non current	\$ 4,974	\$ 3,787	\$ 8,761
Deferred rent related to lease incentives-current	—	311	311

Rent expense is calculated on a straight-line basis over the term of the lease, and considers \$12.2 million of lease incentives received. Aggregate rent expense was as follows:

	Years ended December 31,		
	2018	2017	2016
Rent expense-Lexington	\$ 1,583	\$ 1,103	\$ 1,103
Rent expense-Amsterdam	1,667	2,503	2,871
<b>Total rent expense</b>	<b>\$ 3,250</b>	<b>\$ 3,606</b>	<b>\$ 3,974</b>

**16. Commitments and contingencies**

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.

**17. Related party transaction**

On June 13, 2018, the Company shareholders voted to approve the appointment of Robert Gut, M.D., Ph.D. as a non-executive director on our Board of Directors. On August 20, 2018, Dr. Gut was appointed as the Company's Chief Medical Officer following his resignation as a non-executive director. On October 24, 2018, at an extraordinary general meeting, the Company's shareholders voted to approve the appointment of Dr. Gut as executive director on the Board of Directors. Dr. Gut's annual base salary will be \$425,000 and he will be eligible for an annual bonus of 40% of his base salary. Dr. Gut was granted 35,000 restricted stock units vesting in equal installments over three years as well as an option to purchase 70,000 ordinary shares of the Company that will vest over a period of four years. In addition, Dr. Gut retains his option to purchase 10,000 ordinary shares vesting over three years, which he was granted upon his appointment as a non-executive director in June 2018.

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 of Directors until September 14, 2017. Dr. van Deventer has resigned as Managing Partner of Forbion Capital Partners, and became 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 of Directors. 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**

<b>Exhibit No.</b>	<b>Description</b>
3.1*	<a href="#">Amended Articles of Association of the Company.</a>
10.1t	<a href="#">2014 Share Incentive Plan (incorporated by reference to Exhibit 4.3 of the Company's registration statement on Form S-8 (file no. 333-225629) filed with the Securities and Exchange Commission).</a>
10.2t	<a href="#">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).</a>
10.3t	<a href="#">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).</a>
10.4t	<a href="#">Form of Restricted Stock Unit Award under the 2014 Share Incentive (incorporated by reference to Exhibit 10.4 of the Company's annual report on Form 10-K (file no. 001-36294) for the period ending December 31, 2017 filed with the Securities and Exchange Commission).</a>
10.5t	<a href="#">Form of Performance Stock Unit Award under the 2014 Share Incentive Plan (incorporated by reference to Exhibit 10.4 of the Company's annual report on Form 10-K (file no. 001-36294) for the period ending December 31, 2017 filed with the Securities and Exchange Commission).</a>
10.6t	<a href="#">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).</a>
10.7t	<a href="#">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).</a>
10.8t	<a href="#">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).</a>
10.10	<a href="#">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 filed with the Securities and Exchange Commission).</a>
10.11	<a href="#">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).</a>
10.15	<a href="#">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).</a>
10.18	<a href="#">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).</a>
10.19	<a href="#">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).</a>

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10.20	<a href="#">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).</a>
10.21	<a href="#">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).</a>
10.22†	<a href="#">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).</a>
10.26	<a href="#">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).</a>
10.27†	<a href="#">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).</a>
10.28†	<a href="#">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).</a>
10.29†	<a href="#">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).</a>
10.30†	<a href="#">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).</a>
10.31†	<a href="#">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).</a>
10.32	<a href="#">Lease relating to Paasheuvelweg 25, dated as of March 7, 2016, by and between 52 IFH GmbH &amp; 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).</a>
10.34t	<a href="#">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).</a>
10.35t	<a href="#">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).</a>
10.36t	<a href="#">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).</a>
10.37†	<a href="#">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).</a>
10.38t*	<a href="#">Employment Agreement dated August 20, 2018 by and between uniQure, Inc. and Dr. Robert Gut</a>

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10.39	<a href="#">Amendment No. 1 to Second Amended and Restated Loan and Security Agreement dates as of December 6, 2018 by and among uniQure Biopharma B.V., uniQure, Inc., uniQure IP B.V., the Company, and Hercules Technology Growth Capital, Inc (incorporated by reference to Exhibit 10.1 of the Company's current report on Form 8-K (file no. 001-36294) filed with the Securities and Exchange Commission) filed on December 10, 2018.</a>
10.40	<a href="#">First Amendment Lease relating to 113 Hartwell Avenue, Lexington, Massachusetts, dated as of July 24, 2013, by and between the Company and King113 Hartwell LLC (incorporated by reference to Exhibit 10.1 of the Company's current report on form 8-K (file no. 001-36294) filed with the Securities and Exchange Commission) filed on November 15, 2018.</a>
10.41t	<a href="#">Employee Share Purchase Plan (incorporated by reference to Exhibit 4.2 of the Company's registration statement on Form S-8 (file no. 333-225629) filed with the Securities and Exchange Commission) filed on June 14, 2018.</a>
14.1	<a href="#">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).</a>
21.1*	<a href="#">Subsidiaries of the Company</a>
23.1*	<a href="#">Consent of Independent Registered Public Accounting Firm</a>
24.1*	<a href="#">Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K)</a>
31.1*	<a href="#">Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer</a>
31.2*	<a href="#">Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer</a>
32.1*	<a href="#">Section 1350 Certification</a>
101*	The following materials from the Company's Annual Report on Form 10-K for the year ended December 31, 2018, formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Income (Loss), (iii) Consolidated Statements of Shareholders' 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.

### UNIQUE, 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.

<u>Signatures</u>	<u>Title</u>	<u>Date</u>
<u>/s/ MATHEW KAPUSTA</u> Matthew Kapusta	Chief Executive Officer, Chief Financial Officer and Director (Principal Executive and Financial Officer)	February 28, 2019
<u>/s/ ROBERT GUT</u> Robert Gut	Executive Director	February 28, 2019
<u>/s/ CHRISTIAN KLEMT</u> Christian Klemt	Chief Accounting Officer	February 28, 2019
<u>/s/ PHILIP ASTLEY SPARKE</u> Philip Astley Sparke	Director	February 28, 2019
<u>/s/ JACK KAYE</u> Jack Kaye	Director	February 28, 2019
<u>/s/ DAVID SCHAFFER</u> David Schaffer	Director	February 28, 2019
<u>/s/ PAULA SOTEROPOULOS</u> Paula Soteropoulos	Director	February 28, 2019
<u>/s/ MADHAVAN BALACHANDRAN</u> Madhavan Balachandran	Director	February 28, 2019
<u>/s/ JEREMY P. SPRINGHORN</u> Jeremy P. Springhorn	Director	February 28, 2019
<u>/s/ DAVID MEEK</u> David Meek	Director	February 28, 2019

**NOTE ABOUT TRANSLATION:**

*This document is an English translation of a document prepared in Dutch. In preparing this document, an attempt has been made to translate as literally as possible without jeopardizing the overall continuity of the text. Inevitably, however, differences may occur in translation and if they do, the Dutch text will govern by law.*

*In this translation, Dutch legal concepts are expressed in English terms and not in their original Dutch terms. The concepts concerned may not be identical to concepts described by the English terms as such terms may be understood under the laws of other jurisdictions.*

**ARTICLES OF ASSOCIATION OF**

*"uniQure N.V."*

as these read after the execution of the deed of amendment of the articles of association executed on 15 June 2017 before C. Holdinga, civil-law notary in Amsterdam.

**1. DEFINITIONS.**

In the articles of association the following terms shall have the meaning as defined below:

- **Annual Accounts:** the annual accounts referred to in section 2:361 DCC;
  - **Annual Statement of Accounts:** the Annual Accounts and, if applicable, the Annual Report as well as the additional information referred to in section 2:392 DCC;
  - **Board:** the corporate body of the Company consisting of the Executive Directors of the board in office and the Non-Executive Directors of the board in office;
  - **Board Members:** the Executive Directors of the Board in office and the Non-Executive Directors of the Board in office;
  - **Chief Executive Officer:** the Executive Director appointed as chief executive officer as referred to in article 7.3.;
  - **Company:** the public limited company which organisation is laid down in these articles of association;
  - **Executive Director:** a Board member appointed as executive director;
  - **DCC:** the Dutch Civil Code;
  - **General Meeting:** the corporate body that consists of Shareholders entitled to vote and all other persons entitled to vote / the meeting in which Shareholders and all other persons entitled to attend general meetings assemble;
  - **Management Report:** the annual report referred to in section 2:391 DCC;
  - **Meeting Rights:** the right to, either in person or by proxy authorised in writing, attend the General Meeting and to address such meeting;
  - **Non-Executive Director:** a Board member appointed as non-executive director;
  - **Persons entitled to attend General Meetings:** Shareholders as well as holders of a right of use and enjoyment (*vruchtgebruik*) and holders of a right of pledge with Meeting Rights;
  - **Persons entitled to vote:** Shareholders with voting rights as well as holders of a right of use and enjoyment (*vruchtgebruik*) and holders of a right of pledge with voting rights;
  - **Secretary:** the secretary of the Company as referred to in article 7.8.;
  - **Share:** a share in the share capital of the Company;
  - **Shareholder:** a holder of a Share;
  - **Subsidiary:** a subsidiary as referred to in section 2:24a DCC.
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## **2. NAME. CORPORATE SEAT.**

2.1. The name of the Company is: **uniQure N.V.**

Its corporate seat is in Amsterdam, the Netherlands, and it may establish branch offices elsewhere.

### **2.2. Objects.**

The objects of the Company are:

- (a) to research, develop, produce and commercialise products, services and technology in the (bio-) pharmaceutical sphere;
- (b) to incorporate, participate in, conduct the management of and take any other financial interest in other companies and enterprises;
- (c) to render administrative, technical, financial, economic or managerial services to other companies, persons or enterprises;
- (d) to acquire, dispose of manage and exploit real and personal property, including patents, marks, licenses, permits and other intellectual property rights;
- (e) to borrow and/or lend moneys, act as surety or guarantor in any other manner, and bind itself jointly and severally or otherwise in addition to or on behalf of others,

the foregoing, whether or not in collaboration with third parties, and inclusive of the performance and promotion of all activities which directly and indirectly relate to those objects, all this in the broadest sense.

## **3. SHARE STRUCTURE.**

### **3.1. Authorised share capital**

3.1.1. The authorised share capital of the Company amounts to three million euro (EUR 3.000.000,00) and is divided into sixty million (60,000,000) shares, each with a nominal value of five cent (€ 0.05).

3.1.2. The Shares shall be in registered form and shall be consecutively numbered from 1 onwards.

3.1.3. No share certificates shall be issued.

### **3.2. Issue of Shares.**

3.2.1. Shares shall be issued pursuant to a resolution of the Board if by resolution of the General Meeting the Board has been authorised for a specific period not exceeding five (5) years to issue Shares. The resolution granting the aforesaid authorisation must determine the number and class of the Shares that may be issued. The authorisation may from time to time be extended for a period not exceeding five (5) years. Unless otherwise stipulated at its grant, the authorisation cannot be withdrawn.

3.2.2. If and insofar as an authorisation as referred to in article 3.2.1 is not in force, the General Meeting shall have the power, upon the proposal of the Board to resolve to issue Shares.

3.2.3. Article 3.2.1 and 3.2.2 shall equally apply to a grant of rights to subscribe for Shares, but shall not apply to an issue of Shares to a person who exercises a previously acquired right to subscribe for Shares.

3.2.4. Save for the provisions of section 2:80 DCC, the issue price may not be below nominal value of the Shares.

3.2.5. Shares shall be issued by deed in accordance with the provisions of sections 2:86c and 2:96 DCC.

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3.3. **Payment for Shares.**

- 3.3.1. Shares may only be issued against payment in full of the amount at which such Shares are issued and with due observance of the provisions of sections 2:80a and 2:80b DCC.
- 3.3.2. Payment must be made in cash, unless an alternative contribution has been agreed. Payment other than in cash is made with due observance of the provisions of section 2:94b DCC.
- 3.3.3. Payment in cash may be made in a foreign currency if the Company agrees to this. In that case, the payment obligation shall be fulfilled for the amount up to which the amount paid up can be freely exchanged into euro. This rate of exchange shall be determined by the rate of exchange prevailing on the day of payment or, after application of the provisions of the next sentence, on the day referred to there. The Company may demand payment at the rate of exchange prevailing on a specific day within two (2) months prior to the last day on which payment must have been made, provided that the Shares shall be included on the official list of any stock exchange immediately following the issue.
- 3.3.4. The Company may grant loans for the purpose of a subscription for or an acquisition of Shares in its share capital subject to any applicable statutory provisions.
- 3.3.5. The Board may perform legal acts as referred to in section 2:94 DCC without the prior approval of the General Meeting.

3.4. **Pre-emptive rights.**

- 3.4.1. Upon the issue of Shares, each Shareholder shall have a pre-emptive right to acquire such newly issued Shares in proportion to the aggregate amount of his Shares, it being understood that this pre-emptive right shall not apply to:
  - (a) any issue of Shares to employees of the Company or employees of a group Company;
  - (b) Shares which are issued against payment in kind.
- 3.4.2. Pre-emptive rights may be limited or excluded by resolution of the General Meeting upon proposal of the Board. The Board shall have the power to resolve upon the limitation or exclusion of the pre-emptive right, if and to the extent the Board has been designated by the General Meeting. Such designation shall only be valid for a specific period of not more than five (5) years and may from time to time be extended with a period of not more than five (5) years. Unless provided otherwise in the designation, the designation cannot be cancelled.

A resolution of the General Meeting to limit or exclude the pre-emptive rights as well as a resolution to designate the Board as referred to in this article 3.4.2 requires a two thirds majority of the votes cast if less than half the issued share capital is represented at a meeting.
- 3.4.3. Without prejudice to section 2:96a DCC, the General Meeting or the Board, as the case may be, shall, when adopting a resolution to issue Shares, determine the manner in which and the period within which such pre-emptive rights may be exercised.
- 3.4.4. The Company shall announce the issue with pre-emptive rights and the period within which such rights can be exercised in such manner as shall be prescribed by applicable law and applicable stock exchange regulations, including, but not limited to, an announcement published by electronic means of communication.
- 3.4.5. This article 3.4 shall equally apply to a grant of rights to subscribe for Shares, but shall not apply to an issue of Shares to a person who exercises a previously acquired right to subscribe for Shares.

3.5. **Depositary receipts for shares**

The Company is not authorised to cooperate in the issue of depositary receipts for Shares.

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#### **4. OWN SHARES. CAPITAL REDUCTION.**

##### **4.1. Acquisition of Shares.**

4.1.1. Subject to authorisation by the General Meeting and with due observance of the applicable relevant statutory provisions, the Board may resolve on the acquisition by the Company of fully paid-up Shares. Such authorisation shall only be valid for a specific period of not more than eighteen (18) months and may from time to time be extended with a period of not more than eighteen (18) months. Acquisition by the Company of non-paid up Shares is null and void.

4.1.2. The authorisation of the General Meeting as referred to in article 4.1.1 shall not be required if the Company acquires fully paid-up Shares for the purpose of transferring such Shares, by virtue of an applicable employee stock purchase plan, to persons employed by the Company or by a group Company, provided such Shares are quoted on the official list of any stock exchange.

##### **4.2. Capital reduction.**

4.2.1. With due observance of the statutory requirements the General Meeting may resolve at the proposal of the Board to reduce the issued share capital by (i) reducing the nominal value of Shares by amending the articles of association, or (ii) cancelling:

(a) Shares in its own share capital which the Company holds itself in the Company's share capital, or

(b) all issued Shares against repayment of the amount paid-up on those Shares;

4.2.2. Partial repayment on Shares pursuant to a resolution to reduce their nominal value will be made proportionally.

#### **5. TRANSFER.**

##### **5.1. Form of transfer of Shares.**

5.1.1. The transfer of a Share shall require a deed executed for that purpose and, save in the event that the Company itself is a party to the transaction, written acknowledgement by the Company of the transfer. The acknowledgement is to be made either in the transfer deed, or by a dated statement endorsed upon the transfer deed or upon a copy of or extract from that deed certified by a notary (notaris) or bailiff (deurwaarder), or in the manner as referred to in article 5.1.2. Service of notice of the transfer deed or of the aforesaid copy or extract upon the Company shall be the equivalent of acknowledgement as stated in this paragraph.

5.1.2. The preceding paragraph shall apply mutatis mutandis to the transfer of any limited right to a Share, provided that a pledge may also be created without acknowledgement by or service of notice upon the Company and that section 3:239 DCC applies, in which case acknowledgement by or service of notice upon the Company shall replace the announcement referred to section 3:239, subsection 3 DCC.

#### **6. REGISTERS. PLEDGE. USE AND ENJOYMENT (*vruchtgebruik*)**

##### **6.1. Shareholders register.**

6.1.1. With due observance of the applicable statutory provisions in respect of registered shares, a shareholders register shall be kept by or on behalf of the Company, which register shall be regularly updated and, at the discretion of the Board, may, in whole or in part, be kept in more than one copy and at more than one address. Part of the shareholders register may be kept abroad in order to comply with applicable foreign statutory provisions or applicable listing rules.

6.1.2. Each Shareholder's name, his address and such further information as required by law or considered appropriate by the Board, shall be recorded in the shareholders register.

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- 6.1.3. The form and the contents of the shareholders register shall be determined by the Board with due observance of the articles 6.1.1 and 6.1.2.
- 6.1.4. Upon his request a Shareholder shall be provided free of charge with written evidence of the contents of the shareholders register with regard to the Shares registered in his name, and the statement so issued may be validly signed on behalf of the Company by a person to be designated for that purpose by the Board.
- 6.1.5. The provisions of the articles 6.1.3 and article 6.1.4 shall equally apply to persons who hold a right of use and enjoyment (*vruchtgebruik*) or a right of pledge on one or more Shares.

6.2. **Joint holding.**

If through any cause whatsoever one or more Shares are jointly held by two or more persons, such persons may jointly exercise the rights arising from those Shares, provided that these persons be represented for that purpose by one from their midst or by a third party authorised by them for that purpose by a written power of attorney.

The Board may, whether or not subject to certain conditions, grant an exemption for the provision of the previous sentence.

6.3. **Right of pledge.**

- 6.3.1. Shares may be encumbered with a pledge as security for a debt.
- 6.3.2. If a Share is encumbered with a pledge, the voting right attached to that Share shall vest in the Shareholder, unless at the creation of the pledge the voting right has been granted to the pledgee.
- 6.3.3. Shareholders who as a result of a right of pledge do not have voting rights, have Meeting Rights.

6.4. **Right of use and enjoyment (*vruchtgebruik*).**

- 6.4.1. Shares may be encumbered with a right of use and enjoyment.
- 6.4.2. If a Share is encumbered with a right of use and enjoyment, the voting right attached to that Share shall vest in the Shareholder, unless at the creation of the right of use and enjoyment the voting right has been granted to the holder of the right of use and enjoyment.
- 6.4.3. Shareholders who as a result of a right of use and enjoyment do not have voting rights, have Meeting Rights.

**7. BOARD.**

7.1. **Board: composition.**

- 7.1.1. The Company shall be managed by the Board.
- 7.1.2. The Board shall consist of one or more Executive Directors and one or more Non-Executive Directors. The board shall determine the number of Executive Directors and the number of Non-Executive Directors, provided that the number of Executive Directors shall at all times be less than the number of Non-Executive Directors.  
  
Only natural persons can be Non-Executive Director.

7.2. **Board: appointment, suspension and dismissal.**

- 7.2.1. The Executive Directors and the Non-Executive Directors shall be appointed as such by the General Meeting at the binding nomination of the Non-Executive Directors.
  - 7.2.2. If an Executive Director or Non-Executive Director is to be appointed, the Non-Executive Directors shall make a binding nomination of at least the number of persons as prescribed by law.  
  
The General Meeting may at all times overrule the binding nomination by a resolution adopted by at least a two thirds majority of the votes cast, provided such majority represents more than half
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the issued share capital. If the General Meeting overruled the binding nomination, the Non-Executive Directors shall make a new nomination.

The nomination shall be included in the notice of the General Meeting at which the appointment shall be considered.

If a nomination has not been made or has not been made in due time, this shall be stated in the notice and the General Meeting shall be free to appoint a Board Member at its discretion.

7.2.3. A resolution to appoint a Board Member that was not nominated by the Non-Executive Directors may only be adopted by at least a two thirds majority of the votes cast, provided such majority represents more than half the issued share capital.

7.2.4. When a proposal for appointment of a person as Executive Director is made, the following particulars shall be stated: his age and the position he holds or has held, insofar as these are relevant for the performance of the duties of an Executive Director. The proposal must state the reasons on which it is based.

7.2.5. When a proposal for appointment of a person as Non-Executive Director is made, the following particulars shall be stated: his age, his profession, the number of shares he holds and the positions he holds or has held, insofar as these are relevant for the performance of the duties of a Non-Executive Director. Furthermore, the names of the legal entities of which he is already a non-executive director shall be indicated; if those include legal entities which belong to the same group, reference of that group will be sufficient. The proposal must state the reasons on which it is based.

7.2.6. Board Members are appointed for a maximum term of four (4) years, provided that, unless a Board Member resigns earlier, his term of appointment shall end at the close of the annual General Meeting to be held in the fourth year after the year of his appointment.

A Board Member may be reappointed with due observance of the preceding sentence. The Board shall draw up a retirement schedule for the Board Members.

7.2.7. The General Meeting shall at all times be entitled to suspend or dismiss a Board Member. The General Meeting may only adopt a resolution to suspend or dismiss a Board Member by at least a two thirds majority of the votes cast, provided such majority represents more than half the issued share capital.

A second General Meeting as referred to in section 2:120, subsection 3 DCC may not be convened.

The Board shall also at all times be entitled to suspend (but not to dismiss) an Executive Director. Within three (3) months after a suspension of a Board Member has taken effect, the General Meeting or the Board if the Board resolves to suspend the Board Member, will resolve to either terminate or extend the suspension for a maximum period of another three (3) months. The suspended Board Member shall be given the opportunity to account for his actions at that meeting.

7.2.8. If neither such resolution is adopted or the General Meeting has resolved to dismiss the Board Member, the suspension shall terminate after the period of suspension has expired.

7.2.9. In the event of the absence or inability to act of one or more Board Members, the powers of the Board remain intact, provided that:

(i) the Non-Executive Directors shall be authorised to temporarily fill the vacant position for a period up to the first General Meeting or, in case of a Board Member unable to act, up to the moment he is no longer unable to act;

(ii) in the event of the absence or inability to act of all members of the Board, the Secretary shall temporarily be responsible for the management of the Company until the vacancies have been filled.

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In the event of the absence or inability to act of all members of the Board, the Secretary shall as soon as possible take the necessary measures to make a definitive arrangement.

The term prevented from acting means:

- (i) suspension;
- (ii) illness;
- (iii) inaccessibility,

in the events referred to under sub (ii) and (iii) without the possibility of contact between the Board Member concerned and the Company for a period of five (5) days, unless the Board or the Secretary sets a different term in the case at hand.

7.3. **Chief Executive Officer. Chairman of the Board.**

- 7.3.1. The Board shall appoint an Executive Director as Chief Executive Officer for such period as the Board may decide. In addition, the Board may grant other titles to an Executive Director.
- 7.3.2. The Board shall appoint a Non-Executive Director to be chairman of the Board for such period as the board may decide.
- 7.3.3. The Board may appoint one or more of the Non-Executive Directors as vice-chairman of the Board for such period as the Board may decide. If the chairman is absent or unwilling to take the chair, a vice-chairman shall be entrusted with such duties of the chairman as the Board may decide.
- 7.3.4. If no chairman has been appointed or if the chairman is absent or unwilling to take the chair, a meeting of the Board shall be presided over by a vice-chairman or in the event of his absence or unwillingness to take the chair, by a Board Member or another person present designated for such purpose by the meeting.

7.4 **Board: remuneration.**

- 7.4.1. The Company must establish a policy in respect of the remuneration of the Board. The remuneration policy is adopted by the General Meeting upon the proposal of the Non-Executive Directors.  
The remuneration of the Executive Directors shall be determined by the Non-Executive Directors with due observance of the remuneration policy adopted by the General Meeting. The remuneration of the Non-Executive Directors shall be determined by the Board with due observance of the remuneration policy adopted by the General Meeting.
- 7.4.2. A proposal with respect to remuneration schemes in the form of Shares or rights to Shares is submitted by the Non-Executive Directors to the General Meeting for its approval.  
This proposal must set out at least the maximum number of Shares or rights to Shares to be granted to members of the Board and the criteria for granting or amendment.

7.5. **Board: meetings.**

- 7.5.1. Meetings of the Board may be called at any time, either by one or more Board Members or, on his or their instructions, by the Secretary.
  - 7.5.2. The Secretary may attend the meetings of the Board. The board may decide to permit others to attend a meeting as well.
  - 7.5.3. Each Board Member will have the right to cast one (1) vote. The Board shall adopt its resolutions by an absolute majority of votes cast. In the event of a tie, the proposal shall be considered rejected.
  - 7.5.4. A Board Member will not participate in deliberations and the adoption of resolutions in respect of which he has a personal direct or indirect conflict of interest with the company or its enterprise. If all Board Members have a conflict of interest, the resolution concerned will be adopted by the General Meeting.
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7.5.5. The minutes of meetings of the Board shall be kept by the Secretary. The minutes shall be adopted by the Board at the same meeting or at a subsequent meeting.

If the Board has adopted resolutions without holding a meeting, the Secretary shall keep a record of each resolution adopted without holding a meeting. Such record shall be signed by the chairman and the Secretary.

7.6. **Board: powers, division of duties, restrictions.**

7.6.2. The Board shall be entrusted with the management of the Company and shall for such purpose have all the powers within the limits of the law that are not granted by the articles of association to others. The day to day management of the Company shall be entrusted to the Executive Directors. The task to supervise the performance by the Directors of their duties cannot be taken away from the Non-Executive Directors.

7.6.2. With due observance of the articles of association the Board shall adopt one or more sets of regulations dealing with such matters as its internal organisation, the manner in which decisions are taken, the composition, the duties and organisation of committees as referred to in article 7.6.4. and any other matters concerning the Board, the Chief Executive Officer, the Executive Directors, the Non-Executive Directors and the committees established by the Board.

7.6.3. The Executive Directors may adopt legally valid resolutions with respect to matters that fall within the scope of their duties referred to in article 7.6.1. and 7.6.2. The Non-Executive Directors may also adopt legally valid resolutions with respect to matters that fall within the scope of their duties referred to in article 7.6.1. and 7.6.2.

7.6.4. The Board may establish such committees as it may deem necessary which committees may consist of one or more Board Members or of other persons.

7.6.5. The Executive Directors shall timely provide the Non-Executive Directors with all information required for the exercise of their duties.

7.6.6. Without prejudice to any other applicable provisions of these articles of association, the Board shall require the approval of the General Meeting for resolutions of the Board regarding a significant change in the identity or nature of the Company or the enterprise, including in any event:

- (a) the transfer of the enterprise or practically the entire enterprise to a third party;
- (b) the entry into or termination of any long-lasting cooperation by the Company or a Subsidiary with any other legal person or company or as a fully liable general partner of a limited partnership or a general partnership, provided that such cooperation or the termination thereof is of significant importance to the Company; and
- (c) the acquisition or disposal of a participating interest in the capital of a Company with a value of at least one-third of the sum of the assets according to the consolidated balance sheet with explanatory notes thereto according to the last adopted Annual Accounts of the Company, by the Company or a Subsidiary.

7.7. **Representation.**

7.7.1. The Board as well as two (2) Executive Directors acting jointly are authorised to represent the Company. In case only one Executive Director is in office, such Executive Director is authorised to represent the Company acting independently

7.7.2. The Board may grant one or more persons, whether or not employed by the Company, the power to represent the Company (procuratie) or grant the power to represent the Company on a continuing basis in a different manner.

7.8. **Secretary.**

7.8.1. The Board shall appoint a Secretary from outside its members.

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7.8.2. The Secretary shall participate in the meetings of the Board, as well as the meetings of the committees established by the Board, this in conformity with the regulations to be decided upon.

7.8.3. The Secretary shall further have such powers as are assigned to him by the articles of association and, subject to the articles of association, by the Board on or after his appointment.

7.8.4. The Secretary may be removed from office at any time by the Board.

7.9. **Indemnification Board Members.**

7.9.1. Unless Dutch law provides otherwise, the following shall be reimbursed to current and former members of the Board:

- (a) the reasonable costs of conducting a defence against claims based on acts or failures to act in the exercise of their duties or any other duties currently or previously performed by them at the Company's request;
- (b) any damages or fines payable by them as a result of an act or failure to act as referred to under a;
- (c) the reasonable costs of appearing in other legal proceedings in which they are involved as current or former members of the Board, with the exception of proceedings primarily aimed at pursuing a claim on their own behalf.

There shall be no entitlement to reimbursement as referred to above if and to the extent that:

- (d) a Dutch court or, in the event of arbitration, an arbitrator has established in a final and conclusive decision that the act or failure to act of the person concerned can be characterised as wilful (opzettelijk), intentionally reckless (bewust roekeloos) or seriously culpable (ernstig verwijtbaar) conduct, unless Dutch law provides otherwise or this would, in view of the circumstances of the case, be unacceptable according to standards of reasonableness and fairness; or
- (e) the costs or financial loss of the person concerned are covered by an insurance and the insurer has paid out the costs or financial loss.

If and to the extent that it has been established by a Dutch court or, in the event of arbitration, an arbitrator in a final and conclusive decision that the person concerned is not entitled to reimbursement as referred to above, he shall immediately repay the amount reimbursed by the Company.

7.9.2. The Company may take out liability insurance for the benefit of the persons concerned.

7.9.3. The Board may by agreement give further implementation to the above.

**8. GENERAL MEETINGS.**

8.1. **General Meetings.**

8.1.1. General Meetings shall be held in Amsterdam or in the municipality of Haarlemmermeer (Schiphol Airport).

8.1.2. A General Meeting shall be held once a year, no later than six (6) months after the end of the financial year of the Company.

8.1.3. The Board shall provide the General Meeting with all requested information, unless this would be contrary to an overriding interest of the Company. If the Board invokes an overriding interest, it must give reasons.

8.2. **Extraordinary General Meetings.**

Extraordinary General Meetings shall be convened by the Board or by those who are authorised by law or pursuant to these articles of association to do so.

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8.3. **General Meetings: notice and agenda.**

- 8.3.1. Notice of the General Meeting shall be given by the Board or by those who are authorised by law or pursuant to these articles of association to do so upon a term of at least such number of days prior to the day of the meeting as required by law, in accordance with law and the regulations of the stock exchange where the Shares in the share capital of the Company at the Company's request are officially listed.
- 8.3.2. The Board or the person who is authorised by law or pursuant to these articles of association to convene the meeting may decide that the convocation letter in respect of a person authorised to attend a General Meeting who agrees thereto, is replaced by a legible and reproducible message sent by electronic mail to the address indicated by him to the Company for such purpose.
- 8.3.3. The notice shall state the subjects on the agenda or shall inform the persons authorised to attend a General Meeting that they may inspect the agenda at the office of the Company and that copies thereof are obtainable at such places as are specified in the notice.
- 8.3.4. The agenda for the annual General Meeting shall in any case include the following items:
- (a) the consideration of Annual Statement of Accounts;
  - (b) the adoption of the Annual Accounts;
  - (c) the appropriation of profits;
  - (d) proposals relating to the composition of the Board, including the filling of any vacancies in the Board;
  - (e) the proposals placed on the agenda by the Board together with proposals made by Shareholders in accordance with provisions of the law and the provisions of the articles of association.
- 8.3.5. A matter, the consideration of which has been requested in writing by one or more Shareholders, representing solely or jointly at least the percentage prescribed by law of the issued share capital, will be placed on the notice or will be announced in the same manner if the Company has received the request not later than on the date as prescribed by law.
- 8.3.6. The Board shall inform the General Meeting by means of a shareholders' circular or explanatory notes to the agenda of all facts and circumstances relevant to the proposals on the agenda.

8.4. **General Meetings: attendance of meetings.**

- 8.4.1. The persons who are entitled to attend the General Meeting are persons who:
- (i) are a Shareholder or a person who is otherwise entitled to attend the General Meeting as per a certain date, determined by the Board, such date hereinafter referred to as: the "record date";
  - (ii) are as such registered in a register (or one or more parts thereof) designated thereto by the Board, hereinafter referred to as: the "register"; and
  - (iii) have given notice in writing to the Company prior to a date set in the notice that they will attend a General Meeting,
- regardless of who will be Shareholder at the time of the meeting. The notice will contain the name and the number of Shares the person will represent in the meeting. The provision above under (iii) concerning the notice to the Company also applies to the proxy holder of a person authorised to attend a General Meeting.
- 8.4.2. The Board may decide that Persons entitled to attend General Meetings and vote thereat may, within a period prior to the General Meeting to be set by the Board, which period cannot begin prior to the record date as meant in article 8.4.1, cast their votes electronically in a manner to be decided by the Board. Votes cast in accordance with the previous sentence are equal to votes cast at the meeting.
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- 8.4.3. The Board may decide that the business transacted at a General Meeting can be taken note of by electronic means of communication.
- 8.4.4. The Board may decide that each person entitled to attend General Meetings and vote thereat may, either in person or by written proxy, vote at that meeting by electronic means of communication, provided that such person can be identified via the electronic means of communication and furthermore provided that such person can directly take note of the business transacted at the General Meeting concerned. The Board may attach conditions to the use of the electronic means of communication, which conditions shall be announced at the convocation of the General Meeting and shall be posted on the Company's website.
- 8.4.5. Board Members shall have admission to the General Meetings. They shall have an advisory vote at the General Meetings.
- 8.4.6. Furthermore, admission shall be given to the persons whose attendance at the General Meeting is approved by the chairman of the meeting.
- 8.4.7. All issues concerning the admittance to the General Meeting shall be decided by the chairman of the meeting.

8.5. **General Meetings: order of the meeting, minutes.**

- 8.5.1. The General Meeting will be chaired by the chairman of the Board or in his absence by one of the other Non-Executive Directors designated by the Board; if none of the Non-Executive Directors is present at the meeting, the meeting will be chaired by one of the Executive Directors designated by the Board. The chairman shall designate the secretary.
- 8.5.2. The chairman of the meeting shall determine the order of proceedings at the meeting with due observance of the agenda and he may restrict the allotted speaking time or take other measures to ensure orderly progress of the meeting.
- 8.5.3. All issues concerning the proceedings at the meeting, shall be decided by the chairman of the meeting.
- 8.5.4. Minutes shall be kept of the business transacted at the meeting unless a notarial record is prepared thereof. Minutes shall be adopted and in evidence of such adoption be signed by the chairman and the secretary of the meeting concerned.
- 8.5.5. A certificate signed by the chairman and the secretary of the meeting confirming that the General Meeting has adopted a particular resolution, shall constitute evidence of such resolution vis-à-vis third parties.

8.6. **General Meetings: adoption of resolutions.**

- 8.6.1. Unless another majority of votes or quorum is required by virtue of the law, all resolutions of the General Meeting shall be adopted by at least a simple majority of the votes cast, in a meeting where more than one-third of the issued share capital is represented.  
A second meeting referred to in article 2:120, subsection 3 DCC cannot be convened.
  - 8.6.2. Each Share confers the right to cast one (1) vote at the General Meeting.  
Blank votes and invalid votes shall be regarded as not having been cast.
  - 8.6.3. No votes may be cast at the General Meeting in respect of Shares which are held by the Company or any of its Subsidiaries.  
Holders of a right of use and enjoyment (vruchtgebruik) and pledgees of Shares which belong to the Company or its Subsidiaries shall not be excluded from the right to vote if the right of use and enjoyment or pledge was created before the Shares concerned were held by the Company or a Subsidiary of the Company and at the creation of the right of pledge or the right of use and enjoyment, the voting rights were granted to the pledgee or holder of the right of use and enjoyment.
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- 8.6.4. The chairman of the General Meeting determines the method of voting.
- 8.6.5. The ruling pronounced by the chairman of the General Meeting in respect of the outcome of any vote taken at a General Meeting shall be decisive. The same shall apply to the contents of any resolution passed.
- 8.6.6. Any and all disputes with regard to voting for which neither the law nor the articles of association provide shall be decided by the chairman of the General Meeting.

## **9. FINANCIAL YEAR. AUDITOR.**

### **9.1. Financial year; Annual Statement of Accounts.**

9.1.1. The financial year of the Company shall be the calendar year.

9.1.2. Annually, within the term set by law, the Board shall prepare Annual Accounts.

The Annual Accounts shall be accompanied by the auditor's statement referred to in article 9.2.1, if the instruction referred to in that article has been given, by the Report of the Board of Directors, unless section 2:391 DCC does not apply to the Company, as well as by the other particulars to be added to those documents by virtue of applicable statutory provisions.

The Annual Accounts shall be signed by all Board Members; if the signature of one or more of them is lacking, this shall be disclosed, stating the reasons therefor.

9.1.3. The Company shall ensure that the Annual Accounts as prepared, the Report of the Board of Directors (if applicable) and the other particulars referred to in article 9.1.2 shall be made available at the office of the Company as of the date of the notice of the General Meeting at which they are to be discussed.

The Shareholders and other Persons entitled to attend General Meetings may inspect the above documents at the office of the Company and obtain a copy thereof free of charge.

### **9.2. Auditor.**

9.2.1. The General Meeting shall instruct a registered accountant or another expert, as referred to in section 2:393, subsection 1 DCC, both hereinafter called: the "auditor", to audit the Annual Accounts prepared by the Board, in accordance with the provisions of section 2:393, subsection 3 DCC. The auditor shall report on his audit to the Board and shall present the results of his examination regarding the accuracy of the Annual Accounts in an auditor's statement.

9.2.2. If the General Meeting fails to give such instructions, then the Board shall be so authorised.

9.2.3. The instruction given to the auditor may be revoked by the General Meeting and by the corporate body which has given such instruction.

The instruction may only be revoked for good reasons with due observance of section 2:393, subsection 2 DCC.

9.2.4. The Board may give instructions to the auditor or any other auditor at the expense of the Company.

## **10. PROFITS.**

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

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

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

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- 10.1.3 Distributions of profit, meaning the net earnings after taxes shown by the adopted Annual Accounts, shall be made after the adoption of the Annual Accounts from which it appears that they are permitted, without prejudice to any of the other provisions of these articles of association.
- 10.1.4 The Board may determine that any amount out of the profit shall be added to the reserves.
- 10.1.5 The profit remaining after application of article 10.1.4 shall be at the disposal of the General Meeting, which may resolve to carry it to the reserves or to distribute it among the Shareholders.
- 10.1.6 On a proposal of the Board the General Meeting may resolve to distribute to the Shareholders a dividend in the form of Shares in the share capital of the Company.
- 10.1.7 Subject to the other provisions of this article 10.1 the General Meeting may, on a proposal made by the Board resolve to make distributions to the Shareholders to the debit of one (1) or several reserves which the Company is not prohibited from distributing by virtue of the law.
- 10.1.8 No dividends shall be paid on Shares held by the Company in its own share capital, unless such Shares are encumbered with a right of use and enjoyment (vruchtgebruik) or pledge.

10.2. **Interim distributions.**

- 10.2.1 The Board may resolve to make interim distributions to the Shareholders if an interim statement of assets and liabilities shows that the requirement of article 10.1.2 has been met.
- 10.2.2 The interim statement of assets and liabilities shall relate to the condition of the assets and liabilities on a date no earlier than the first day of the third month preceding the month in which the resolution to distribute is published. It shall be prepared on the basis of generally acceptable valuation methods. The amounts to be reserved under the law and these articles of association shall be included in the statement of assets and liabilities. It shall be signed by the Board Members. If the signature of one or more of them is lacking, this shall be disclosed, stating the reasons therefor.
- 10.2.3 Any proposal for distribution of dividend on Shares and any resolution to distribute an interim dividend on Shares shall immediately be published by the Board in accordance with the regulations of the stock exchange where the Shares at the Company's request are officially listed. The notification shall specify the date when and the place where the dividend shall be payable or - in the case of a proposal for distribution of dividend - is expected to be made payable.
- 10.2.4 Dividends shall be payable no later than thirty (30) days after the date they were declared, unless the body declaring the dividend determines a different date.
- 10.2.5 Dividends which have not been claimed upon the expiry of five (5) years and one (1) day after the date when they became payable shall be forfeited to the Company and shall be carried to the reserves.
- 10.2.6 The Board may determine that distributions on Shares shall be made payable either in euro or in another currency.

**11. AMENDMENT OF THE ARTICLES OF ASSOCIATION, DISSOLUTION OF THE COMPANY.**

- 11.1. A resolution to amend the articles of association or to dissolve the Company may only be adopted at the proposal of the Board.

11.2. **Liquidation.**

- 11.2.1 On the dissolution of the Company, the liquidation shall be carried out by the Board, unless otherwise resolved by the General Meeting.
  - 11.2.2 Pending the liquidation, the provisions of these articles of association shall remain in force to the fullest extent possible.
  - 11.2.3 The surplus assets of the Company remaining after satisfaction of its debts shall, in accordance with the provisions of section 2:23b DCC, be for the benefit of the Shareholders in proportion to the nominal value amount of the Shares held by each of them.
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**EMPLOYMENT AGREEMENT**

THIS EMPLOYMENT AGREEMENT (this "Agreement") is made and entered into as of August 20, 2018 (the "Effective Date"), by and between uniQure, Inc., 113 Hartwell Avenue, Lexington, MA 02421 (the "Company") and Dr. Robert Gut (the "Executive"), \_\_\_\_\_.

**WITNESSETH:**

WHEREAS, the Company desires to employ Executive, and Executive desires to be employed by the Company, each upon the terms set forth herein.

NOW, THEREFORE, in consideration of the mutual promises and covenants contained herein and intending to be legally bound hereby, the Company and Executive agree as follows.

1. Employment. The Company hereby agrees to employ Executive, and Executive hereby accepts employment by the Company, as a full-time employee for the period and upon the terms and conditions contained in this Agreement.

2. Term. Executive's term of employment with the Company under this Agreement shall begin on August 20, 2018 (the "Start Date") and shall continue in force and effect from year to year unless terminated earlier in accordance with Section 19 (the "Term").

3. Position and Duties. During the Term, Executive shall serve the Company as its Chief Medical Officer, reporting directly to the uniQure Chief Executive Officer (the "CEO").

The initial primary focus of the Chief Medical Officer will be:

- Responsible for leading the strategy and development of the medical function consisting of Clinical Operations, Medical Affairs, Global Drug Safety, Global Quality Management, Medical Information and External Medical Relations.
- Ensuring that uniQure is equipped to develop and market pharmaceutical products according to all applicable medical scientific, regulatory, ethical and legal standards
- Support uniQure's value proposition of marketing and pipeline products to design of the clinical and regulatory strategy in the context of the corporate strategy. Portfolio selection is conducted together with management.
- Develop and recommend the clinical development strategy for new drug candidates from research to regulatory approval and beyond taking into account the constraints of a small and creative biotechnology firm
- Provide leadership in being the key uniQure spokesperson to external and internal bodies on medical and scientific issues related to uniQure's products
- Manage the Global Drug Safety according to all local and international requirements
- Ensure GCP compliance of all clinical trials
- Responsible for scientific publication strategy
- Actively partner with the commercial organization to promote the scientific and medical value of uniQure's products

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- Develop budget plans for all functions under the CMO and ensure program expenses in line with approved budget.
- Communicate effectively all medical objectives and activities with the company's management and other functional areas

4. Commencing on the Start Date and during the Term, Executive shall devote full business time, best efforts, skill, knowledge, attention and energies to the advancement of the Company's business and interests and to the performance of Executive's duties and responsibilities as an employee of the Company. Executive shall abide by the rules, regulations, instructions, personnel practices and policies of the Company and any changes therein that may be adopted from time to time by the Company.

This Agreement will not affect Executive's existing role as a Director of the Company, except that Executive understands that he likely will be considered a non-independent, executive-director and that his compensation as a member of the Board of Directors of the Company (the "Board") will likely change. Executive agrees to at all times abide by the policies and decisions of the Board with respect to this Agreement, any conflicts of interest, determinations of independence, compositions of committees of the Board, compensation as a member of the Board, and any other issues related to his role as a member of the Board, and Executive agrees to take any reasonable and appropriate actions required to resolve such issues. Executive agrees to resign any existing appointments to Committees of the Board, if requested by the Board.

5. Notwithstanding the foregoing, Executive may engage in civic and charitable organizations and manage his personal and business affairs during normal business hours provided that such activities do not, individually or collectively, interfere with the performance of his duties hereunder. Commencing on the Start Date and during the Term, and subject to the provisions of Paragraph 4 above, Executive shall not be engaged in any business activity which, in the judgment of the Company, conflicts with Executive's duties hereunder, whether or not such activity is pursued for pecuniary advantage. Should Executive wish to provide any services to any other person or entity other than the Company or to serve on the board of directors of any other entity or organization, Executive shall submit a written request to the Company for consideration and approval by the Company, which approval shall not unreasonably be withheld. If the Company later makes a reasonable, good faith determination that Executive's continued service on another entity's board would be detrimental to the Company, it will give Executive thirty (30) days' written notice that it is revoking the original approval, and Executive will resign from the applicable board within thirty (30) days after receipt of such notice.

6. Location. Executive shall perform the services hereunder from the Company's USA headquarters at 113 Hartwell Avenue, Lexington MA, USA; provided, however, that Executive shall be required to travel from time to time for business purposes.

7. Compensation and Benefits.

- (a) *Base Salary*. For all services rendered by Executive under this Agreement, the Company will pay him a base salary at the annual rate of US\$425,000 (four hundred and twenty-five thousand dollars), which shall be reviewed annually by the CEO for adjustment (the base salary in effect at any time, the "Base Salary"). In order to be eligible for an

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increase in Base Salary applicable to the year following the year in which the Start Date falls, Executive's Start Date must be before October 1st in any given year. Any merit increase would be pro-rated for the 2018 calendar year. Executive's Base Salary shall be paid in bi-weekly installments, less withholdings as required by law and deductions authorized by Executive, and payable pursuant to the Company's regular payroll practices in effect at the time.

- (b) *Discretionary Bonus.* Following the end of each calendar year and subject to the approval of the Company, Executive shall be eligible for a retention and performance bonus of forty percent (40%) of the annual Base Salary based on performance and the Company's performance and financial condition during the applicable calendar year, as determined by the Company in its sole discretion. In any event, Executive must be an active employee of the Company on the date the bonus is distributed in order to be eligible for and to earn any bonus, as it also serves as an incentive to remain employed by the Company. In order to be eligible for a bonus which is paid in the year following the year in which the Start Date falls, Executive's Start Date must be before October 1st in any given year. Any bonus would be pro-rated for the 2018 calendar year.
- (a) *Expenses Related to Relocation.* The Company will reimburse executive for the expenses associated with Executive's relocation of himself and his family to the Boston area ("Relocation Expenses") to a maximum net amount (i.e., grossed-up to be net of taxes) of Seventy-Five Thousand Dollars and No Cents (US \$75,000.00). The Relocation Expenses include the following:
  - (b) a) monthly local temporary housing costs (which may include furnished housing and/or rental furniture/housewares), for a maximum of 12 months, if required;
  - (c) c) the expenses associated with Executive's (and his partner) 'house hunting' visits to the Boston area;
  - (d) d) travel and lodging expenses incurred in Executive's weekly commutes to his current residence;
  - (e) e) moving expenses;
  - (f) f) other expenses associated with Executive's and his family's move to the Boston area that are not expressly set forth above, provided that for any expense greater than \$1,000 Executive shall obtain prior written approval from SVP Human Resources prior to incurring the expense.
  - (g) Executive agrees that he shall forfeit and be obligated to re-pay the full amount of the Relocation Expenses if, prior to the one-year anniversary of the Start Date: (a) Executive resigns without Good Reason as defined in Section 19 (f); or (b) Executive is terminated for

Cause as defined in Section 19(c). If Executive's employment terminated between the one-year anniversary of the Start Date and 180 days after the one-year anniversary of the Start Date, Executives obligation to re-pay the Relocation Expenses shall be pro-rated according to the following formula: repayment obligation = RE x (1 – D/180) (RE represents the full amount of Relocation Expenses Executive received; D represents the number of days elapsed after the one-year anniversary of the Start Date). Executive expressly authorizes the Company to deduct this amount from a subsequent or wages that the Company pays to Executive if his employment terminates pursuant to subsection (a) above or if his termination under subsection (b) above is undisputed.

8. Equity. Subject to Board of Directors approval at the next regularly scheduled uniQure N.V. Board meeting after execution of this Agreement, Executive shall be granted 35,000 (thirty-five thousand) restricted stock units of the Company and 70,000 (Seventy Thousand) stock option units, the terms of which shall reflect the standard vesting and other terms and conditions contained in the uniQure N.V.'s Amended and Restated 2014 Share Incentive Plan. Such restricted stock units will be approved by the Board of Directors of uniQure N.V. not later than at its next regularly scheduled meeting and the exercise price will be the closing share price on the grant date. If the Board fails to make the grant at such regularly scheduled meeting, it shall be deemed a Good Reason event under Section 19(f) hereof. The Executive will be eligible for future equity grants pursuant to the Company's policies and procedures. The Executive will be eligible for future equity grants pursuant to the Company's policies and procedures. First year grants will be prorated based on hire date.

9. Benefits. Executive is eligible to participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided that Executive is eligible under (and subject to all provisions of) the plan documents that govern those programs. These include medical, dental and disability insurances. Benefits are subject to change at any time in the Company's sole discretion.

10. Paid Time Off and Holidays. Executive is eligible for four (4) weeks of paid vacation per calendar year (pro-rated for 2018) to be taken at such times as may be approved in advance by the Company. Executive is also entitled to all paid holidays observed by the Company in the United States. Executive shall have all rights, including the right to potentially earn more than four (4) weeks of paid vacation per year, and be subject to all obligations and responsibilities with respect to paid time off and holidays as are set forth in the Company's employee manual or other applicable policies and procedures.

11. 401(k) Plan. Subject to Section 9 (benefits).

12. Expense Reimbursement. During the Term, Executive shall be reimbursed by the Company for all necessary and reasonable expenses incurred by Executive in connection with the performance of Executive's duties hereunder (including business trips to the uniQure Amsterdam headquarters). Executive shall keep an itemized account of such expenses, together with vouchers and/or receipts verifying the same, and submit for reimbursement on a monthly basis. Any such expense reimbursement will be made in accordance with the Company's travel and expense policies governing reimbursement of expenses as are in effect from time to time.

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13. Withholding. All amounts set forth in this Agreement are on a gross, pre-tax basis and shall be subject to all applicable federal, state, local and foreign withholding, payroll and other taxes, and the Company may withhold from any amounts payable to Executive (including any amounts payable pursuant to this Agreement) in order to comply with such withholding obligations.

14. IP and Restrictive Covenants. Executive's employment is contingent upon Executive's execution of the Company's Confidentiality, Developments, and Restrictive Covenants Agreement, attached as Exhibit A to this Agreement.

15. At-Will Employment. This Agreement shall not be construed as an agreement, either express or implied, to employ Executive for any stated term, and shall in no way alter the Company's policy of employment at-will, under which both the Company and Executive remain free to end the employment relationship for any reason, at any time, with or without cause or notice. Similarly, nothing in this Agreement shall be construed as an agreement, either express or implied, to pay Executive any compensation or grant Executive any benefit beyond the end of employment with the Company, other than as set out elsewhere in this Agreement.

16. Conflicting Agreements. Executive acknowledges and represents that by executing this Agreement and performing Executive's obligations under it, Executive has disclosed and provided copies to the Company of any and all confidentiality or restrictive covenant agreements that Executive is a party or is bound, to that could limit or prohibit the full performance of Executive's duties to the Company.

17. No Prior Representations. This Agreement and its exhibits constitute all the terms of Executive's hire and supersede all prior representations or understandings, whether written or oral, relating to the terms and conditions of Executive's employment.

18. Change of Control. In the event of a Change of Control as defined below, the vesting conditions that may apply to any equity held by Executive pursuant to this Agreement and the Company's Amended and Restated 2014 Share Incentive Plan will be automatically waived and all the equity will be deemed to be fully exercisable commencing on the date of the Change of Control and ending on the eighteen (18) month anniversary of the Change of Control. For purposes of this Agreement, "Change of Control" shall mean the date on which any of the following events occurs:

- (a) any "person," as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Act") (other than the Company, any of its subsidiaries, or any trustee, fiduciary or other person or entity holding securities under any employee benefit plan or trust of the Company or any of its subsidiaries), together with all "affiliates" and "associates" (as such terms are defined in Rule 12b-2 under the Act) of such person, shall become the "beneficial owner" (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, of securities of the Company representing forty (40) percent or more of the combined voting power of the Company's then outstanding securities having the right to vote in an election of the Board ("Voting Securities") (in such case other than as a result of an acquisition of securities directly from the Company); or

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- (b) a majority of the members of the Board is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of the Board before the date of the appointment or election; or
- (c) the consummation of (i) any consolidation or merger of the Company where the stockholders of the Company, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, shares representing in the aggregate more than fifty (50) percent of the voting shares of the Company issuing cash or securities in the consolidation or merger (or of its ultimate parent corporation, if any), or (ii) any sale or other transfer (in one transaction or a series of transactions contemplated or arranged by any party as a single plan) of all or substantially all of the assets of the Company.

19. Termination. The Term shall continue until the termination of Executive's employment with the Company as provided below.

- (a) *Events of Termination.* Executive's employment, Base Salary and any and all other rights of Executive under this Agreement or otherwise as an employee of the Company will terminate:
  - (i) upon the death of Executive;
  - (ii) upon the Disability of Executive (immediately upon notice from either party to the other). For purposes hereof, the term "Disability" shall mean an incapacity by accident, illness or other circumstances which renders Executive mentally or physically incapable of performing the duties and services required of Executive hereunder on a full-time basis for a period of at least 120 consecutive days.
  - (iii) upon termination of Executive for Cause;
  - (iv) upon the resignation of employment by Executive without Good Reason (upon thirty (30) days' prior written notice);
  - (v) upon termination by the Company for any reason other than those set forth in Sections 19(a)(i) through 19(a)(iv) above;
  - (vi) upon voluntary resignation of employment by Executive for Good Reason as described in Section 19(f), below;
  - (vii) upon a Change of Control Termination as described in Section 19(g), below.
- (b) In the event Executive's termination occurs pursuant to Sections 19(a)(i) - (iv) above, Executive will be entitled only to the Accrued Benefits through the termination date. The Company will have no further obligation to pay any compensation of any kind (including,

without limitation, any bonus or portion of a bonus that otherwise may have become due and payable to Executive with respect to the year in which such termination date occurs), or severance payment of any kind, unless otherwise provided herein. For purposes of this agreement, Accrued Benefits shall mean (i) payment of Base Salary through the termination date, (ii) any payments or benefits under the Company's benefit plans that are vested, earned or accrued prior to the termination date (including, without limitation, earned but unused vacation); and (iii) payment of unreimbursed business expenses incurred by Executive.

- (c) For purposes of this Agreement, "Cause" shall mean the good faith determination by the Company (which determination shall be conclusive), after written notice from the Company to Executive that one or more of the following events has occurred and stating with reasonable specificity the actions that constitute Cause and the specific reasonable cure (related to subsections (i) and (viii) below):
- (i) Executive has willfully or repeatedly failed to perform Executive's material duties and such failure has not been cured after a period of thirty (30) days' written notice;
  - (ii) any reckless or grossly negligent act by Executive having the foreseeable effect of injuring the interest, business or reputation of the Company, or any of its parents, subsidiaries or affiliates in any material respect;
  - (iii) Executive's evidenced use of any illegal drug, or illegal narcotic, or excessive amounts of alcohol (as determined by the Company in its reasonable discretion) on Company property or at a function where Executive is working on behalf of the Company;
  - (iv) the indictment on charges or conviction for (or the procedural equivalent of conviction for), or entering of a guilty plea or plea of no contest with respect to a felony;
  - (v) the conviction for (or the procedural equivalent of conviction for), or entering of a guilty plea or plea of no contest with respect to a misdemeanor which, in the Company's reasonable judgment, involves moral turpitude deceit, dishonesty or fraud, except that, in the event that Executive is indicted on charges for a misdemeanor, the Company may elect, in its sole discretion, to place Executive on administrative garden leave with or without continuation of full compensation and benefits under this Agreement during the pendency of the proceedings;
  - (vi) conduct by or at the direction of Executive constituting misappropriation or embezzlement of the property of the Company, or any of its parents or affiliates (other than the

- occasional, customary and *de minimis* use of Company property for personal purposes);
- (vii) a material breach by Executive of a fiduciary duty owing to the Company, including the misappropriation of (or attempted misappropriation of) a corporate opportunity or undisclosed self-dealing;
  - (viii) a material breach by Executive of any material provision of this Agreement, any of the Company's written employment policies or Executive's fiduciary duties to the Company, which breach, if curable, remains uncured for a period of thirty (30) days after receipt by Executive of written notice of such breach from the Company, which notice shall contain a reasonably specific description of such breach and the specific reasonable cure requested by the Board; and
  - (ix) any material breach of Executive's Confidentiality, Developments, and Restrictive Covenants Agreement.
- (d) The definition of Cause set forth in this Agreement shall govern for purposes of Executive's equity compensation and any other compensation containing such a concept.
- (e) *Notice Period for Termination Under Section 19(a)(iv).* Upon a termination of Executive under Section 19(a)(iv), during the notice period the Company may, in its sole discretion, relieve Executive of all of Executive's duties, responsibilities, and authority, may restrict Executive's access to Company property, and may take other appropriate measures deemed necessary under the circumstances.
- (f) *Termination by Executive for Good Reason.* During the Term, Executive may terminate this Agreement at any time upon thirty (30) days' written notice to the Company for "Good Reason." For purposes of this Agreement, "Good Reason" shall mean that Executive has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following actions undertaken by the Company without Executive's express prior written consent: (i) the material diminution in Executive's responsibilities, authority and function; (ii) a material reduction in Executive's Base Salary, provided, however, that Good Reason shall not be deemed to have occurred in the event of a reduction in Executive's Base Salary which is pursuant to a salary reduction program affecting the CEO and all or substantially all other senior management employees of the Company and that does not adversely affect Executive to a greater extent than other similarly situated employees; provided, however that such reduction may not exceed twenty (20%) percent; (iii) a material change in the geographic location at which Executive provides services to the Company (i.e., outside a radius of fifty (50) miles from Lexington, Massachusetts) (each a "Good Reason Condition").

"Good Reason Process" shall mean that: (i) Executive has reasonably determined in good faith that a Good Reason Condition has occurred; (ii) Executive has notified the Company in writing of the first occurrence of the Good Reason Condition within 60 days of the first occurrence of such condition; (iii) Executive has cooperated in good faith with the Company's efforts, for a period not less than thirty (30) days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason Condition continues to exist; and (v) Executive terminates employment within sixty (60) days after the end of the Cure Period. If the Company cures to Executive's satisfaction (not unreasonably withheld) the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

- (g) *Termination As A Result of a Change Of Control.* For purposes of this Agreement, "Change of Control Termination" shall mean any of the following:
- (i) Any termination by the Company of Executive's employment, other than for Cause (as defined in Section 19(c), above), that occurs within twelve (12) months after the Change of Control; or
  - (ii) Any resignation by Executive for Good Reason (as defined in Section 19(f), above), that occurs within twelve (12) months after the Change of Control.
  - (iii) For purposes of this Section 19(g), "Change of Control" shall have the same meaning as defined above in Section 18.
- (h) *Separation Benefits.* Should Executive experience a termination of employment during the Term pursuant to Section 19(a)(v), (vi), or (vii) above, in addition to the Accrued Benefits Executive shall also be entitled to a lump sum severance payment equal to 100% of the annual Base Salary. To avoid duplication of severance payments, any amount paid under this subsection shall be offset against any severance amounts that may be owed by the Company to Executive pursuant to the Company's Change of Control guidelines.

20. General Release of Claims. Notwithstanding any provision of this agreement, all severance payments and benefits described in Section 19 of this Agreement (except for payment of the Accrued Benefits) are conditioned upon the execution, delivery to the Company, and expiration of any applicable revocation period without a notice of revocation having been given by Executive, all by the 30th day following the termination date of a General Release of Claims by and between Executive (or Executive's estate) and the Company in the form attached as Exhibit B to this Agreement. (In the event of Executive's death or incapacity due to Disability, the release will be revised for signature accordingly.) Provided any applicable timing requirements set forth above have been met, the payments and benefits will be paid or provided to Executive as soon as administratively practicable (but not later than forty-five (45) days) following the date Executive signs and delivers the General Release to the Company and any applicable revocation period has expired without a

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notice of revocation having been given. Any severance or termination pay will be the sole and exclusive remedy, compensation or benefit due to Executive or Executive's estate upon any termination of Executive's employment (without limiting Executive's rights under any disability, life insurance, or deferred compensation arrangement in which Executive participates or at the time of such termination of employment or any Option Agreements or any other equity agreements to which Executive is a party). If such 45-day period spans two calendar years, payment will be paid after such 45-day period and revocation period have expired.

21. Certain Company Remedies. Executive acknowledges that Executive's promised services and covenants are of a special and unique character, which give them peculiar value, the loss of which cannot be reasonably or adequately compensated for in an action at law, and that, in the event there is a breach hereof by Executive, the Company will suffer irreparable harm, the amount of which will be impossible to ascertain. Accordingly, the Company shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either at law or in equity, to obtain damages for any breach of this Agreement, or to enjoin Executive from committing any act in breach of this Agreement. The remedies granted to the Company in this Agreement are cumulative and are in addition to remedies otherwise available to the Company at law or in equity.

22. Indemnification.

- (a) The Company agrees that Executive shall be entitled to indemnification to the fullest extent permitted by Delaware law and under the Company's articles of incorporation, bylaws and any other corporate-related plan, program or policy. In addition, as soon as reasonably practicable following the Start Date and for a period of at least three (3) years after Executive's termination of employment, the Company shall maintain a directors and officers liability insurance policy under which Executive shall be included as a "Covered Person."
- (b) In addition, and for the sake of clarity, the Company hereby specifically agrees that (i) if Executive is made a party, or is threatened to be made a party, to any "Proceeding" (defined as any threatened or actual action, suit or proceeding whether civil, criminal, administrative, investigative, appellate or other) by reason of the fact that (1) Executive is or was an employee, officer, director, agent, consultant or representative of the Company, or (2) is or was serving at the request of the Company or any of its affiliates as employee, officer, director, agent, consultant or representative of another person, or (ii) if any "Claim" (defined as any claim, demand, request, investigation, dispute, controversy, threat, discovery request or request for testimony or information) is made, or threatened to be made, that arises out of or relates to Executive's service in any of the foregoing capacity or to the Company, then Executive shall be indemnified and held harmless by the Company to the fullest extent permitted by applicable law, against any and all costs, expenses, liabilities and losses (including, without limitation, attorney's fees, judgments, interest, expenses of investigation, penalties, fines, taxes or penalties and amounts paid or to be paid in settlement) incurred or suffered by Executive in connection therewith, except with respect to any costs, expenses, liabilities or



losses (A) that were incurred or suffered as a result of Executive's willful misconduct, gross negligence or knowing violation of any written agreement between Executive and the Company, or (B) that a court of competent jurisdiction determines to have resulted from Executive's knowing and fraudulent acts; provided, however, that the Company shall provide such indemnification only if (I) notice of any such Proceeding is given promptly to the Company, by Executive; (II) the Company is permitted to participate in and assume the defense of any such Proceeding; (III) such cost, expense, liability or loss results from the final judgment of a court of competent jurisdiction or as a result of a settlement entered into with the prior written consent of the Company; and (IV) in the case of any such Proceeding (or part thereof) initiated by Executive, such Proceeding (or part thereof) was authorized in advance in writing by the Company. Such indemnification shall continue even if Executive has ceased to be an employee, officer, director, agent, consultant or representative of the Company or an affiliate thereof until all applicable statute of limitations have expired, and shall inure to the benefit of Executive's heirs, executors and administrators. The Company shall pay directly or advance to Executive all costs and expenses incurred by Executive in connection with any such Proceeding or Claim (except for Proceedings brought by the Company against Executive for claims other than shareholder derivative actions) within 30 days after receiving written notice requesting such an advance. Such notice shall include, to the extent required by applicable law, an undertaking by Executive to repay the amount advanced if Executive was ultimately determined not to be entitled to indemnification against such costs and expenses

23. Miscellaneous.

- (a) *Right to Offset.* The Company may offset any undisputed amounts Executive owes the Company or its affiliates at the time of Executive's termination of employment (including any payment of Accrued Benefits or separation pay), except for secured or unsecured loans, against any amounts the Company owes Executive hereunder including, but not limited to, any wages, accrued vacation and bonuses, which Executive acknowledges and agrees would constitute a valid offset pursuant to any state or federal law (including the Massachusetts Payment of Wages Statute, M.G.L. c. 149 § 148 et. seq.).
- (b) *Cooperation.* Executive agrees that, during and after Executive's employment with the Company, subject to reimbursement of Executive's reasonable expenses, Executive will cooperate fully with the Company and its counsel with respect to any matter (including, without limitation, litigation, investigations, or governmental proceedings) in which Executive was in any way involved during Executive's employment with the Company. Executive shall render such cooperation in a timely manner on reasonable notice from the Company, and at such times and places as reasonably acceptable to Executive and the Company. The Company, following Executive's termination of employment, exercises commercially reasonable efforts

to schedule and limit its need for Executive's cooperation under this paragraph so as not to interfere with Executive's other personal and professional commitments.

- (c) *Company Documents and Property.* Upon termination of Executive's employment with the Company, or at any other time upon the request of Company, Executive shall forthwith deliver to Company any and all documents, notes, notebooks, letters, manuals, prints, drawings, block diagrams, photocopies of documents, devices, equipment, keys, security passes, credit cards, hardware, data, databases, source code, object code, and data or computer programming code stored on an optical or electronic medium, and any copies thereof, in the possession of or under the control of Executive that embodies any confidential information of the Company. Executive agrees to refrain from purging or deleting data from any Company-owned equipment, including email systems, in connection with Executive's termination. To the extent that Executive possesses any data belonging to Company on any storage media owned by Executive (for example, a home computer's hard disk drive, portable data storage device, etc.), Executive agrees that Executive will work cooperatively with the Company to return such data and ensure it is removed from Executive's devices in a manner that does not adversely impact any personal data. Executive agrees not to take any steps to delete any Company data from any device without first obtaining Company's written approval. Executive agrees to cooperate with Company if Company requests written or other positive confirmation of the return or destruction of such data from any personal storage media. Nothing herein shall be deemed to prohibit Executive from retaining (and making copies of): (i) Executive's personal non-business-related correspondence files; or (ii) documents relating to Executive's personal compensation, benefits, and obligations and documents reasonably necessary to prepare personal income tax returns.
- (d) *Waivers.* No waiver of any provision will be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement does not prevent subsequent enforcement of that term or obligation. The waiver by any party of any breach of this Agreement does not waive any subsequent breach.
- (e) *Governing Law; Consent to Exclusive Jurisdiction and Venue/Jury Waiver.* This Agreement and all questions relating to its validity, interpretation, performance and enforcement (including, without limitation, provisions concerning limitations of actions), shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (notwithstanding any conflict-of-laws doctrines of such state or other jurisdiction to the contrary), and without the aid of any canon, custom or rule of law requiring construction against the draftsman. The parties hereby consent and submit to the exclusive jurisdiction of the federal and state courts in the Commonwealth of Massachusetts, and to exclusive venue in any

Massachusetts federal court and/or Massachusetts state court located in Suffolk County, for any dispute arising from this Agreement. The parties further acknowledge and agree that any such dispute shall be tried by a Judge alone, and both parties hereby waive and forever renounce the right to a trial before a civil jury. Executive hereby agrees that he will neither commence or prosecute, nor assist in any way another person or entity to commence or prosecute, any legal action or other proceeding (including but not limited to a declaratory judgment action) against the Company concerning a dispute arising from or relating to this Section in any forum or jurisdiction other than the state and federal courts in the Commonwealth of Massachusetts. Executive further agrees that, in the event Executive disregards this clause, the Company shall be entitled to recover its reasonable attorneys' fees and other costs incurred in staying, transferring, dismissing or otherwise defending such out-of-state action or proceeding, regardless of whether such fees and costs are incurred in the forum where Executive (or another person or entity, as applicable), commenced the action or in a Massachusetts forum, and without regard to whether the Company prevails in its efforts to enforce this covenant.

- (f) *Notices.* Any notices, requests, demands, and other communications described in this Agreement are sufficient if in writing and delivered in person or sent postage prepaid, by certified or registered U.S. mail or by FedEx/UPS to Executive at Executive's last known home address and a copy by e-mail to Executive, or in the case of the Company, to the attention of the General Counsel, copy to the CEO, at the main office of uniQure, Inc. Any notice sent by U.S. mail shall be deemed given for all purposes 72 hours from its deposit in the U.S. mail, or the next day if sent by overnight delivery.
- (g) *Successors and Assigns.* Executive may not assign this Agreement, by operation of law or otherwise, without the Company's prior written consent. Without the Company's consent, any attempted transfer or assignment will be void and of no effect. The Company may assign its rights under this Agreement if the Company consolidates with or merges into any other entity, or transfers substantially all of its properties or assets to any other entity, provided that such entity expressly agrees to be bound by the provisions hereof. This Agreement will inure to the benefit of and be binding upon the Company and Executive, their respective successors, executors, administrators, heirs, and permitted assigns.
- (h) *Counterparts; Facsimile.* This Agreement may be executed in two or more counterparts, each of which shall be an original and all of which together shall constitute one and the same instrument. This Agreement may be executed by facsimile transmission, PDF, electronic signature or other similar electronic means with the same force and effect as if such signature page were an original thereof.

**Dr. Robert Gut**

Employment Agreement

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Initials: \_\_\_\_\_

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- (i) *Severability.* The provisions of this Agreement are independent of and separable from each other, and no provision shall be affected or rendered invalid or unenforceable by virtue of the fact that for any reason any other provision or provisions may be invalid or unenforceable in whole or in part.
- (j) *Enforceability.* If any portion or provision of the Agreement is declared illegal or unenforceable by a court of competent jurisdiction, the remainder of the Agreement will not be affected, and each remaining portion and provision of this Agreement will be valid and enforceable to the fullest extent permitted by law.
- (k) *Survival.* Sections 14, 20, 21, and the Company's Confidentiality, Developments, and Restrictive Covenants Agreement (Exhibit A) and all other provisions necessary to give effect thereto, shall survive the termination of Executive's employment for any reason.
- (l) *Entire Agreement; Amendment.* This Agreement contains the entire understanding among the parties hereto with respect to the subject matter hereof, and supersedes all prior and contemporaneous agreements and understandings, inducements or conditions, express or implied, oral or written, between the parties hereto (including without limitation any prior employment agreements between the parties hereto); provided, however, that any agreements referenced in this Agreement or executed herewith are not superseded. The express terms hereof control and supersede any course of performance and/or usage of the trade inconsistent with any of the terms hereof. This Agreement may be amended or modified only by a written instrument signed by Executive and by a duly authorized representative of the Company.
- (m) *Section Headings.* The section headings in this Agreement are for convenience only, form no part of this Agreement and shall not affect its interpretation.

[This space intentionally left blank.]

IN WITNESS WHEREOF, the parties have executed and delivered this Agreement as of the date first above written.

uniQure, Inc.

By: /s/ Matt Kapusta

Name: Matt Kapusta  
Title: Chief Executive Officer

EXECUTIVE

/s/ Dr. Robert Gut

Dr. Robert Gut

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February 28, 2019

Exhibit 21.1

SUBSIDIARIES OF UNIQUE N.V.

<u>Name of Subsidiary</u>	<u>Jurisdiction of Organization</u>
uniQure biopharma B.V.	The Netherlands
uniQure IP B.V.	The Netherlands
uniQure Inc.	Delaware
uniQure GmbH	Germany

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**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-225636) and Form S-8 (No. 333-225629, No. 333-222051, No. 333-218005 and No. 333-197887) of uniQure N.V. of our report dated February 28, 2019 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

Amsterdam, The Netherlands, February 28, 2019  
PricewaterhouseCoopers Accountants N.V.

/s/ R.M.N. Admiraal RA

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**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 control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; 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*  
February 28, 2019

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**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 control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; 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*  
February 28, 2019

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**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, 2018, 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*  
February 28, 2019

*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.*

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