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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-202456

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has become effective by rule of the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED APRIL 7, 2015

Preliminary Prospectus Supplement
(To Prospectus Dated March 3, 2015)

3,000,000 Shares

uniQure

Ordinary Shares

We are offering 3,000,000 of our ordinary shares in this offering. Our ordinary shares are listed on the NASDAQ Global Select Market under the symbol "QURE". uniQure N.V. is a public company with limited liability *(naamloze vennootschap)* incorporated under the laws of the Netherlands. On April 6, 2015, the last reported sale price for our ordinary shares on the NASDAQ Global Select Market was $33.61 per share.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and are subject to reduced public company reporting requirements.

Investing in our ordinary shares involves a high degree of risk. Please read "Risk Factors" on page S-7 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if this prospectus supplement or the accompanying prospectus is accurate or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to uniQure N.V.	$	$

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to an additional 450,000 of our ordinary shares. See "Underwriting" for more information.

The underwriters expect to deliver the ordinary shares to the purchasers on or about April , 2015.

Joint Book-Running Managers

Leerink Partners **Cowen and Company** **Piper Jaffray & Co.**

Co-Managers

Oppenheimer & Co. **H.C. Wainwright & Co.**

April , 2015

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We have not, and the underwriters have not, authorized anyone to provide you with information different than that which is contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents

incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled "Where You Can Find Additional Information" and "Incorporation of Certain Information by Reference."

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of ordinary shares, and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein, is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our ordinary shares. Unless the context otherwise indicates, references in this prospectus to "we," "our," and "us" refer to uniQure N.V., a company organized under the laws of the Netherlands, and its consolidated subsidiaries. As adjusted financial numbers presented in this prospectus supplement have been converted from Euro to US dollars at a rate of €0.8237 to $1.00, the official exchange rate quoted by the European Central Bank at the close of business on December 31, 2014.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, and the documents incorporated herein and therein by reference contain forward-looking statements based on beliefs of our management. Any statements contained in this prospectus supplement, the accompanying prospectus, and the documents incorporated herein and therein by reference that are not historical facts are forward-looking statements as defined in Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934 (the "Exchange Act"). We have based these forward-looking statements on our current expectations and projections about future events, including:

- the timing of commencement of and receipt of data from our planned clinical trials;
- the timing of the ongoing and planned clinical trials conducted by our collaborators and other third parties;
- our ongoing and planned discovery and development of product candidates;
- our expectations regarding the timing or likelihood of regulatory filings and approvals for our product candidates;
- our ability to expand our sales, marketing and medical affairs infrastructure;
- our ability to close our recently announced collaboration with Bristol-Myers Squibb and the ultimate success of this collaboration;
- our ability to successfully commercialize Glybera and our product candidates;
- the potential advantages of Glybera and our product candidates;
- our estimates regarding the market opportunities for our product candidates;
- the rate and degree of market acceptance and clinical benefit of Glybera and our product candidates;
- our expectations regarding milestone, royalty and expense reimbursement payments under our licensing arrangements;
- our estimates of the net amount will we retain from sales of Glybera;
- the operating costs of our manufacturing facility in Lexington, Massachusetts;
- our ability to establish and maintain collaborations, including our recently announced collaboration with Bristol-Myers Squibb;
- our ability to develop, acquire or in-license additional product candidates and other key intellectual property;
- our future intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and
- other factors discussed in the section entitled "Risk Factors" in this prospectus supplement.

The words "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "predict," "potential," "should" and "will" and similar expressions as they relate to us are intended to identify such forward-looking statements. These forward-looking statements are not statements of historical fact and represent only our management's belief as of the date of such statement, and involve risks and uncertainties that could cause actual results to differ materially and from expectations expressed in or indicated by the forward-looking statements. Assumptions, expectations, projections, intentions and beliefs about future events may, and often do, vary from actual

results and these differences can be material. There are a variety of factors, many of which are beyond our control, which affect our operations, performance, business strategy and results and could cause actual reported results and performance to differ materially from the performance and expectations expressed in these forward-looking statements. We caution readers of this prospectus supplement and the accompanying prospectus not to place undue reliance on these forward-looking statements, which speak only as of their dates. We undertake no obligation to publicly update or revise any forward-looking statements.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all the information you should consider before investing in our ordinary shares. You should carefully read this entire prospectus supplement and accompanying prospectus, including the documents incorporated by reference, particularly the risks and discussion of risks in the "Risk Factors" section of this prospectus supplement and the "Operating and Financial Review and Prospects" sections and our consolidated financial statements and related notes contained in our Annual Report on Form 20-F for the year ended December 31, 2014, filed with the SEC on April 7, 2015, as well as the informatio included in any free writing prospectus that we have authorized for use in connection with this offering. This summary contains forward-looking statements that involve risks and uncertainties. Our actual results may differ significantly from the results stated in or suggested by such forward-looking statements due to a variety of factors, including those set forth in the "Risk Factors" and "Special Note Regarding Forward-Looking Statements" sections.

uniQure N.V.

We are a leader in the field of gene therapy and have a technology platform that we use as the basis for our proprietary and collaborative product lines across multiple therapeutic areas. Our core gene therapies include AMT-060 for the treatment of hemophilia B, in which we initiated a Phase I/II clinical trial in the first quarter of 2015; our preclinical S100A1 therapeutic for the treatment of congestive heart failure; and Glybera, the first and currently the only gene therapy product to receive regulatory approval in the European Union.

Our aim is to make gene therapy a mainstay of modern medicine by:

- using our technology platform to develop our own programs in liver-based diseases, cardio/metabolic diseases and central nervous system, or CNS, diseases. Our focus is on areas in which we believe the modular nature of our approach offers the potential to reduce development risk, cost and time-to-market by allowing us to advance multiple programs using validated components of our technology and relying on safety and efficacy data from earlier clinical studies.
- sponsoring and acquiring additional early-stage programs in these areas from other biopharmaceutical companies and academic investigators;
- enhancing and accelerating these programs through our modularized research and development platform and our experience with the EU and FDA regulatory environments for gene therapies;
- applying our proprietary, commercial-scale manufacturing process to produce high-quality material for our own and our collaborators' programs; and
- collaborating with pharmaceutical companies with the necessary expertise to enhance our late-stage therapy development and maximize the value of our therapies at the commercialization stage.

We believe that our technology platform and strategic collaborations place us at the forefront of gene therapy within our chosen therapeutic areas. Our transgene delivery system is based on common, adeno-associated viruses, or AAV, which we believe are safe and effective delivery methods for efficient expression of transgenes. We have the exclusive or non-exclusive rights to natural AAV serotypes for lipoprotein lipase deficiency, or LPLD, liver and CNS applications and the capability to identify and develop synthetic AAV vectors that are designed to optimize the expression of a particular transgene in specific tissue types. We produce ou AAV-based vectors in our own facilities with a proprietary, commercial-scale, consistent manufacturing process using insect cells and baculoviruses, a common

family of viruses found in invertebrates. We believe our Lexington, Massachusetts-based facility, which is currently being qualified, is one of the world's leading, mos versatile, gene therapy manufacturing facilities. We believe this technology platform, combined with our know-how derived from achieving the first regulatory approval of a gene therapy in the European Union, provides us a significant advantage in bringing our gene therapy products to the market ahead of our competitors.

We seek to develop gene therapies targeting a range of liver-based, cardio/metabolic and CNS indications, from ultra-orphan diseases, such as LPLD (for which Glybera is designated), to orphan diseases such as hemophilia B and Sanfilippo B syndrome, to common diseases that affect far larger populations, such as congestive heart failure and Parkinson's disease. The core of our approach is our modular technology backbone, which allows us to advance our programs in multiple therapeutic areas using validated components of our technology and safety and efficacy data from earlier clinical studies, with the potential to reduce development risk, cost and time to market. As part of our strategy, we are accessing important medical expertise for our therapeutic focuses through strong ties with academic thought leaders an clinical institutions. For cardio/metabolic diseases we are building a center of expertise in our German subsidiary, uniQure GmbH, in close cooperation with leading academic clinicians and surgeons at the university hospital and heart center in Heidelberg, Germany. Our CNS activities are based on collaborations with the University of California at San Francisco, the National Institutes of Health, and the Institut Pasteur, Paris, France. Our hemophilia B product originates from St. Jude Children's research Hospital in Memphis, Tennessee. We also seek to collaborate with or acquire emerging companies within our chosen therapeutic areas that are conducting or sponsoring early-stage clinical trials. Our collaborations allow us to cost-effectively obtain access to pre-clinical and early-stage programs without expending significant resources of our own. We generally have the rights to the data generated in these collaborator-sponsored programs, but do not control their design or timing. Our collaboration programs include gene therapy candidates for Parkinson's disease, Sanfilippo B syndrome, Acute Intermittent Porphyria and amyotrophic lateral sclerosis.

Bristol-Myers Squibb Collaboration

On April 6, 2015, we entered into an agreement with Bristol-Myers Squibb, or BMS, that provides BMS exclusive access to uniQure's gene therapy technology platform for multiple targets in cardiovascular and other target-specific disease areas. The collaboration includes our proprietary congestive heart failure gene therapy candidate, which has demonstrated in advanced preclinical models that it can restore the ability to synthesize S100A1, a calcium sensor and master regulator of heart function, and increase survival rates after myocardial infarction. In addition, we will collaborate with BMS on up to nine additional gene therapy targets addressing a broad range of heart conditions and other target-specific disease areas. We will be responsible for discovery, preclinical development, and CMC, and will provide BM our vector technologies and access to our industrial, proprietary insect-cell based manufacturing platform. uniQure will be responsible for CMC portions of regulatory filings and will co-operate with BMS in the preparation of all regulatory materials and interactions with regulatory authorities. BMS will be responsible for clinical development and all commercial activities across all programs.

The financial terms include guaranteed, near-term payments to us of at least $97 million, including an upfront payment of $50 million to be made at the closing o the transaction. The closing of the transaction is expected to occur in the second quarter of 2015 subject to Hart-Scott-Rodino clearance and customary closing conditions. An additional $15 million payment is to be received within three months of the closing for the selection of three additional collaboration targets, in additio to the S100A1 program. An initial equity investment in uniQure will be made for a number of shares that will equal 4.9% of the total number of shares outstanding following such issuance, at a purchase price of $33.84 per share, or at least $32 million in total. This investment is expected to be completed in the second quarter of 2015. BMS is also obligated to make an additional equity investment in uniQure for

a number of shares that will equal 5.0% of the total number of shares outstanding following such issuance by December 31, 2015 and will be granted two warrants to acquire at its option up to an additional 10% equity interest, at a premium to market, based on additional targets being introduced into the collaboration. The parties have also agreed to enter into a supply contract, under which uniQure will undertake the manufacturing of all gene therapy products under the collaboration.

uniQure will be eligible to receive research, development and regulatory milestone payments, including up to $254 million for the lead S100A1 therapeutic and up to $217 million for each other gene therapy product potentially developed under the collaboration, assuming designation of all targets by BMS and achievement of all milestones. uniQure is also eligible to receive target designation fees, net sales based milestone payments and tiered single to double-digit royalties on product sales.

Company Information

Our company is registered with the Dutch Trade Register of the Chamber of Commerce (*handelsregister van de Kamer van Koophandel en Fabrieken*) in Amsterdam, the Netherlands under number 54385229. Our corporate seat is in Amsterdam, the Netherlands, and our registered office is located at Meibergdreef 61, 1105 BA Amsterdam, the Netherlands, and our telephone number is +31 20 240 6000. Our website address is www.uniqure.com. Information on our website is not incorporated by reference into this prospectus supplement or any other report we file with or furnish to the SEC. Our ordinary shares are traded on the NASDAQ Global Select Market under the symbol "QURE".

THE OFFERING

Ordinary shares offered by us	3,000,000 ordinary shares
Ordinary shares to be outstanding immediately after this offering	21,430,066 ordinary shares
Option to purchase additional ordinary shares	We have granted the underwriters an option to purchase up to an additional 450,000 ordinary shares from us. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Use of Proceeds	We estimate that the net proceeds to us from this offering, based on an assumed offering price of $33.61, the last reported sale price of our ordinary shares on the NASDAQ Global Select Market on April 6, 2015, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $94.0 million, or $108.2 million if the underwriters exercise their option to purchase additional shares from us in full. We intend to use the net proceeds from this offering to fund research and development to build our product platform and advance our pipeline of preclinical product candidates and for working capital and general corporate purposes. See "Use of Proceeds".
Risk factors	Investing in our ordinary shares involves a high degree of risk. See "Risk Factors" in this prospectus supplement.
NASDAQ Global Select Market Symbol	QURE

The total number of ordinary shares that will be outstanding immediately after this offering includes:

- 18,430,066 ordinary shares outstanding as of April 7, 2015; and
- 3,000,000 ordinary shares to be issued and sold by us in this offering;

and excludes:

- 2,762,032 shares issuable upon the exercise of options and other equity awards outstanding as of April 7, 2015 at a weighted average exercise price of $7.51 per share; and
- up to 461,283 ordinary shares reserved for future issuance under our equity incentive plans as of April 7, 2015;
- 152,436 ordinary shares issuable as of April 7, 2015 upon exercise of options granted on January 17, 2014 in connection with our collaboration and license agreement with 4D Molecular Therapeutics, at an exercise price of €0.05 per share;
- 170,802 ordinary shares issuable upon the exercise of warrants outstanding as of April 7, 2015, at a weighted average exercise price of €10.31 per ordinary share; and
- 179,068 restricted share units outstanding as of April 7, 2015.

Except as otherwise indicated, we have presented the information in this prospectus supplement assuming:

- no exercise by the underwriters in this offering of their option to purchase additional ordinary shares; and
- no exercise of outstanding options or warrants described above.

SUMMARY FINANCIAL DATA

The summary consolidated financial data as of December 31, 2014 and for each of the years ended December 31, 2012, 2013 and 2014 have been derived from our audited consolidated financial statements and notes thereto incorporated by reference in this prospectus supplement. The following summary consolidated financi data should be read in conjunction with our "Operating and Financial Review and Prospects" and our consolidated financial statements and the related notes thereto incorporated by reference in this prospectus supplement. Our financial statements are prepared in accordance with IFRS.

Consolidated Statements of Comprehensive Income Data:

	Year ended December 31,		
€ in thousands (except share and per share data)	**2012**	**2013**	**2014**
Revenues:			
License revenues	—	440	883
Collaboration revenues	—	2,503	3,802
Total revenues	—	2,943	4,685
Cost of goods sold	—	(800)	—
Other income	649	585	773
Research and development expenses	(10,231)	(13,182)	(33,932)
Selling, general and administrative expenses	(4,564)	(11,628)	(11,167)
Other gains/(losses)—net	(45)	(453)	5,807
Total operating costs	(14,840)	(25,263)	(39,292)
Operating result	(14,191)	(22,535)	(33,834)
Finance income	22	102	254
Finance expense	(547)	(4,387)	(3,460)
Finance income/(expense)—net	(525)	(4,285)	(3,206)
Net loss	(14,716)	(26,820)	(37,040)
Items that may be subsequently reclassified to profit or loss	—	12	1,149
Other comprehensive income	—	12	1,149
Total comprehensive loss	(14,716)	(26,808)	(35,891)
Loss per share attributable to the equity holders of the company during the year			
Basic and diluted loss per share	(1.70)	(2.48)	(2.16)
Weighted average shares outstanding used in computing per share amounts (in thousands):			
Basic and diluted	9,653,495	12,194,906	18,092,194

The following table summarizes our balance sheet data as of December 31, 2014:

- on an actual basis; and
- on an as adjusted basis to give effect to the issue and sale of 3,000,000 ordinary shares by us in this offering at an assumed public offering price of $33.61 per ordinary share, which is the last reported sale price of our ordinary shares on the NASDAQ Global Select Market on April 6, 2015, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Consolidated Balance Sheet Data:

(€ in thousands)	As of December 31, 2014 Actual	As Adjusted
Cash and cash equivalents	53,219	130,672
Total assets	95,786	173,239
Total debt	17,270	17,270
Accumulated deficit	(181,081)	(181,699)
Total shareholders' equity (deficit)	43,084	120,537

(1) Each $1.00 increase or decrease in the assumed public offering price of $33.61 per ordinary share would increase or decrease, respectively, the amount of cash and cash equivalents, working capital, total assets and total shareholders' equity by $2.9 million, assuming the number of ordinary shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We may also decrease the number of ordinary shares we are offering. A decrease of 1,000,000 in the number of ordinary shares we are offering would decrease the amount of cash, cash equivalents and short-term investments, working capital, total assets and shareholders' equity by approximately $31.6 million, assuming the assumed public offering price per ordinary share remains the same. The as adjusted information is illustrative only, and we will adjust this information based on the actual public offering price and other terms of this offering determined at pricing.

RISK FACTORS

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 €37.0 million in 2014, €26.8 million in 2013 and €14.7 million in 2012. As of December 31, 2014, we had an accumulated deficit of €181.1 million. To date, we have financed our operations primarily through the sale of equity securities and convertible debt and, to a lesser extent, through milestone payments, subsidies and grants from governmental agencies and fees for services. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. Although our recently signed agreement with Bristol-Myers Squibb Company, or BMS, will, following closing, provide us with substantial near-term collaboration and equity financing, a significant portion of the potential consideration 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:

- conduct our Phase I/II clinical trial of AMT-060 for hemophilia B in collaboration with Chiesi;
- complete our EMA-mandated post-approval clinical trials of Glybera;
- conduct a clinical trial of Glybera, either as part of the EMA-mandated post-approval clinical trials or separately, to obtain data needed to file a BLA for Glybera with the FDA, and seek marketing approval for Glybera in the United States and other countries;
- advance the preclinical and clinical development of our other product candidates, most of which are at relatively early stages of development, and seek to discover and develop additional product candidates;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and medical affairs infrastructure in the United States;
- complete validation of and commence commercial manufacturing at our facility in Lexington, Massachusetts;
- maintain, expand and protect our intellectual property portfolio, including in-licensing additional intellectual property rights from third parties;
- hire additional personnel, particularly in our manufacturing, research, clinical development, medical affairs, commercial and quality groups;
- continue to add operational, financial and management information systems and related compliance personnel; and
- continue to operate as a public company.

We and our collaborators 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 ongoing activities. Although our recently signed agreement with BMS will, following closing, provide us with substantial near-term collaboration and equity financing, a significant portion of the potential consideration is contingent on achieving research, development, regulatory and sales milestones. We expect 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., or Hercules, and our pledge to Hercules of substantially all of 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. See also "—Risks Related to Our Dependence on Third Parties—If our collaboration with BMS does not close or is not successful, our development plans, financial position and opportunities for growth may be adversely affected."

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

As of December 31, 2014, we had €16.4 million of outstanding borrowings under our Loan and Security Agreement with Hercules, which we are required to repay in monthly principal installments from January 2016 through June 2018. 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 of our assets.

Our revenues will depend in part on the commercial success of sales of Glybera.

We anticipate that the first patient will be treated with Glybera in the European Union in mid-2015, although such revenues are initially likely to be modest. A number of factors, some of which are out of our control, may adversely affect the commercial success of Glybera, including the following:

- our collaborator Chiesi may not successfully commercialize Glybera in the European Union and other countries in the Chiesi territory;
- the post-approval requirements imposed by the EMA in connection with Glybera's approval under exceptional circumstances may be costly or may eventually lead to withdrawal of approval;
- we may never be able to obtain marketing approval for Glybera in the United States or other countries;
- Glybera may fail to achieve market acceptance by physicians, patients, third-party payors and others in the medical community;
- other alternative treatments for LPLD may be developed and gain commercial acceptance, eroding Glybera's market share;
- the limited label we have received for Glybera in the European Union may limit our addressable market, and other regulatory agencies may approve Glybera only with a similarly limited label;
- we may be unable to establish or maintain sales, marketing and medical affairs capabilities for the commercialization of Glybera in the United States, even if we receive FDA approval;
- we may be unable to manufacture Glybera to the quality specifications required in a required time frame or in quantities necessary to timely satisfy demand for Glybera;
- we may be unable to maintain our marketing approval for Glybera in the European Union if it is determined by the EMA that there are safety, quality, efficacy or other material concerns associated with Glybera; and
- coverage, pricing and reimbursement levels may be lower than we expect.

If we fail to achieve anticipated revenues from this product, it may have an adverse effect on our results of operations and cause the value of our ordinary shares to decline.

Even if our commercialization of Glybera or other product candidates for which we obtain marketing approval is successful, we may not be financially successful due to our obligations to third parties.

We have obtained exclusive or non-exclusive rights from third parties under a number of patents and other technology that we are exploiting in Glybera and our development programs. 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 portion of amounts we receive from our sublicensees and payments upon the achievement of specified development, regulatory or commercial milestones. For example, we are contractually obligated to pay royalties and other obligations to third parties on net sales of Glybera by us, Chiesi or other sublicensees or on other amounts we receive,

including from Chiesi or other sublicensees for their sales of Glybera. We also received a technical development loan from the Dutch government, which requires repayment based on the timing and amount of revenues we receive from the sale of Glybera. These financial obligations to third parties are an expense to us, which could adversely affect our financial position.

Risks Related to the Development of Our Product Candidates

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

A key 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 collaborators. 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 collaborators may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. If we do not continue to successfully develop and commercialize product candidates based upon our technology, we may face difficulty in obtaining product revenues in future periods, which could result in significant harm to our financial position and adversely affect our share price.

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

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

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 development is expensive, time-consuming and uncertain as to outcome. Our product candidates are in early clinical or preclinical development, and there is a significant risk of failure or delay in each of these programs. In several of our programs, we intend to transition a collaborator's program to a different viral vector or to our insect cell-based manufacturing process, which could result in additional development challenges and delays. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more 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, or CROs, and clinical trial sites;
- delays in obtaining required Institutional Review Board, or 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 the retention of proper case files;
- failure to perform in accordance with the FDA's good clinical practices, or GCP, or applicable regulatory guidelines in other countries;
- delays 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.

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. 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 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 or clinical efficacy, which may require longer clinical trial

periods or longer patient follow-up than we currently expect or is typically required in the case of other therapies.

Our ability to recruit patients for our trials is often reliant on third parties, such as the pharmacies at our clinical trial sites. These third parties may not have the adequate infrastructure established to handle gene therapy products to support certain gene therapy product formulations, in order for them to agree to recruit patients on our behalf. To the extent that the infrastructure cannot be established at the pharmacies we may experience delays in recruiting patients for our studies. For example, we deliver clinical supplies for our hemophilia B trial in vials, which must be combined into infusion bags, and we have been informed that certain pharmacies at some prospective clinical trial sites are not able to undertake this procedure.

In addition, we or our collaborators may not be able to locate and enroll a sufficient number of 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. In particular, because several of our programs are focused on the treatment of patients with orphan or ultra-orphan diseases, our ability to enroll eligible patients in these trials may be limited or slower than we anticipate in light of the small patient populations involved. For example, we reduced the number of patients enrolled in our second Phase II/III clinical trial of Glybera from the 16 patients originally planned to five patients due to slow recruitment. In addition, our potential competitors, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, may seek to develop competing therapies, which would further limit the small patient pool available for our studies.

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

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

With the exception of Glybera, 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 desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage clinical trials. If a larger population of patients does not experience positive results, if these results are not reproducible, or if our products show diminishing activity over time, our products may not receive approval from the EMA or FDA. 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 as a result of many factors, including changes in regulatory

policy during the period of product development. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our products in late-stage clinical trials with larger patient populations could have a material adverse effect on our business that would cause our share price to decline.

Progress in trials of Glybera and its approval in the European Union do not indicate that we will make similar progress in additional trials for Glybera or in trials for our other product candidates. While Glybera uses an AAV1 vector for gene delivery, the rest of the product candidates in our pipeline use other AAV serotypes, such as AAV5 or AAV2. Also, while Glybera is injected directly into the muscles of the leg, the rest of the products in our pipeline target other tissues. Due to these variations, trials for our other product candidates may be less successful than the trials for Glybera.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of Glybera and our product candidates or adversely affect our ability to conduct our business or obtain further marketing approvals for Glybera and 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. For example, a generalized public backlash developed against gene therapy following the death in September 1999 of an 18-year-old who had volunteered for a gene therapy experiment at the University of Pennsylvania. In addition, two gene therapy studies in 2003 were terminated after five subjects developed leukemia.

Although none of our current product candidates utilize the retroviruses used in the 2003 studies, our product candidates do use a viral vector delivery system. 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.

Glybera or our product candidates may prove to have undesirable or unintended side effects, toxicities or other characteristics that may require us to abandon or limit their development, preclude our obtaining additional marketing approval or prevent or limit commercial use. In our clinical trials for Glybera, there were, as at March 20, 2015, a total of 55 serious adverse event reports in Glybera-treated patients, two of which were assessed as potentially related to Glybera, one incidence of pulmonary embolism and one incidence of fever. In our partner's clinical development program for AIP, there were four serious adverse events, none of which was determined by the investigator to be treatment-related.

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 such adverse events occur, commercialization of Glybera or further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations.

Risks Related to Regulatory Approval

We cannot predict when or if we will obtain marketing approval to commercialize a product candidate or, in the case of Glybera, further marketing approval in jurisdictions outside the European Union, and any approval we receive may be for a more narrow indication than we expect.

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.

We have not received approval to market any of our products or product candidates from regulatory authorities in the United States. We received marketing authorization for Glybera from the European Commission in October 2012 under exceptional circumstances for a subset of LPLD patients, after our initial application was rejected in June 2011. The FDA does not maintain a regulatory approval process similar to the EMA's marketing authorization under exceptional circumstances, which may make it more difficult to obtain marketing authorization for Glybera or other product candidates in the United States. Given the differences between the regulatory schemes for approval of new products in Europe and the United States, approval of Glybera in the European Union does not assure or increase the likelihood of approval of the product in the United States. The results of our prior clinical trials of Glybera will not be sufficient to obtain FDA approval, and the FDA may not ultimately approve Glybera for marketing in the United States. Based on our meetings with the FDA in August and December 2013 and December 2014, we believe that, to obtain marketing approval for Glybera in the United States, we will need to successfully conduct an adequate and appropriately controlled clinical trial. We have not yet completed the design of this trial or submitted a protocol for this trial to the FDA. We are seeking to amend the protocol for our EU post-approval trial of Glybera so that it could also serve as a clinical program with a design that addresses the FDA's requirements and are in preliminary discussions with EU regulatory authorities regarding the acceptability of the amended protocol. We intend to file a special protocol assessment with the FDA in first half of 2015 in respect of this trial design. The FDA may require preclinical testing or clinical trials beyond this clinical trial as a basis for marketing approval of Glybera, which would be expensive and time-consuming. If we fail to obtain marketing approval of Glybera in the United States in our anticipated timeframe, or obtain only limited approval for a specific patient population, our business could be materially adversely affected.

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. For example, we received marketing authorization for Glybera in the European Union only for a restricted patient population, and other regulatory agencies may approve Glybera only with a similarly limited label, which limits our addressable market. Further, Glybera received marketing approval subject to post-approval restrictions including the requirement to conduct a post-approval clinical study, and if we fail to adequately satisfy these post-approval requirements the EMA may withdraw its approval.

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

The European Commission authorized marketing of Glybera under exceptional circumstances, and only after the relevant committees had initially reached negative decisions on the use of Glybera for the treatment of all patients with LPLD.

The process for obtaining approval of Glybera in the European Union was protracted and complicated by initial decisions against approval by the committees charged with review of our marketing authorization application. In their initial decision in June 2011, both the Committee for Advanced Therapeutics, or CAT, and the Committee for Human Medicinal Products, or CHMP, determined that the benefit-risk balance for Glybera was negative for the treatment of all patients with LPLD.

Following our further submissions, in June 2012 the CAT gave a positive opinion and the CHMP then reassessed Glybera and recommended approval for adult patients diagnosed with familial LPLD and suffering from severe or multiple pancreatitis attacks despite dietary fat restrictions. This was a more restricted patient population than we had sought in our original application. The European Commission granted this approval in October 2012, subject to certain conditions including additional post-marketing studies for efficacy. If these post-approval studies do not produce data that support the results of our original development program for Glybera, the marketing authorization for Glybera in the European Union could be withdrawn.

Our receipt of marketing authorization under exceptional circumstances in the European Union does not provide any assurance that we will be able to obtain marketing authorization for Glybera elsewhere, including in the United States, or for our other gene therapies in any country.

The FDA will require us to conduct comparability studies evaluating the products manufactured at our Amsterdam facility with those to be manufactured at our new Lexington, Massachusetts facility. Those studies and their results could substantially delay or preclude our ability to commercialize Glybera and our product candidates in the United States.

The FDA maintains strict requirements governing the manufacturing process for biologics. When a manufacturer seeks to modify or change that process, or begin manufacturing at a new facility, the FDA typically requires the applicant to conduct non-clinical and, depending on the magnitude of the changes, potentially clinical comparability studies that evaluate the potential differences in the product resulting from the change in the manufacturing process or facility. In connection with any application for marketing approval in the United States, we will be required to conduct comparability studies assessing product manufactured at our facility in Amsterdam with product to be manufactured at our new facility in Lexington, Massachusetts. The FDA may be especially concerned about the need for such a comparability study for Glybera if the clinical studies on which we rely for approval of our application only involved product manufactured at our facility in the Netherlands and if we intend to market only product manufactured in Lexington in the United States.

Delays in designing and completing a comparability study to the satisfaction of the FDA could delay or preclude our development and commercialization plans and, thereby, limit our revenues and growth. For example, for Glybera, we may attempt to show comparability of the product manufactured at the different facilities through the use of non-clinical data, such as potency assays and animal studies. In the event that the FDA does not accept such non-clinical comparability data, we may need

to conduct a study involving dosing of patients with product from our Lexington facility. That potential study may result in a delay of the approval or launch of Glybera in the United States.

We are subject to potentially costly post-approval obligations, review and other regulatory requirements for Glybera in the European Union, and any of our product candidates for which we obtain marketing approval in the future could be subject to similar requirements, which may restrict or eliminate the commercial success of Glybera or our other product candidates.

Glybera and any of our product candidates for which we obtain marketing approval in the future, as well as the manufacturing process, post-approval studies and measures, labeling, advertising and promotional activities for such products, will be subject to continued requirements of and review by the FDA, EMA and other regulatory authorities.

As part of our marketing approval under exceptional circumstances in the European Union, the EMA has imposed ongoing requirements for a potentially costly post-approval study and market surveillance activities. Specifically, as a condition to approval of Glybera we are required to complete a post-approval clinical trial and implement a disease registry for long-term surveillance of patients, as well as implement risk management procedures, distribute educational materials to healthcare professionals and patients, implement an additional manufacturing process step, comply with certain notification obligations and undergo annual reassessment, any negative outcome of which could potentially lead to a withdrawal of marketing approval for Glybera. The expense and uncertain result of these post-approval requirements may delay, limit or terminate our commercialization plan for Glybera and adversely affect our financial position, particularly in light of the relatively small market for this orphan indication. Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties.

In addition, we have submitted several Type II variations to the EMA, which seek to update the summary product of characteristics, SmPC, of Glybera to include additional six-year follow-up and other clinical data. Following our submission of the Type II variations, and a voluntary disclosure of accidental destruction of some historical source data at a site in Canada, the EMA requested a good clinical practices, or GCP, inspection of our Glybera trial program. The Dutch and UK regulatory authorites conducted the inspection on behalf of the EMA in early 2015. The inspectors reported to the EMA on the quality control mechanisms that were in place in our company during data acquisition and processing in 2009 and 2010 with respect to maintaining patient and trial data obtained prior to approval of Glybera, and the integrity of the historical trial data as a whole. We have already implemented corrective quality control actions to rectify the oversight issues identified by the inspection and continue to refine our quality system. We believe that the events in the past do not materially affect the previously reported results of our historical trials. The inspection team also concluded "that the quality of the data and the level of GCP compliance both are acceptable" and that the trial data can be used for the submitted Type II variations.

As part of the ongoing variation procedure, the EMA is currently reviewing the risk/benefit analysis of Glybera in light of the additional six-year follow-up data we provided and the findings of the GCP inspection. Although we believe that these data support the conclusions that led to the original approval of Glybera under exceptional circumstances, there can be no assurance that the EMA or its committees will not reach a different conclusion. We anticipate that the CAT and CHMP will review this matter during its meetings in April 2015, and expect to receive a response setting out the EMA's preliminary position around April 23, 2015. We anticipate this response will include requests for additional information as part of the variation procedure, which may require a further response from us to support our position. Any adverse outcome of this review could require us to expend significant further resources to support our conclusions, including potentially conducting further post-approval studies, or could potentially result in revocation of the marketing approval for Glybera in the European Union.

Should we receive FDA approval of Glybera or any of our other product candidates in the future, the FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, also closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved label.

Any government investigation of alleged violations of law could require us to expend significant time and resources and could generate negative publicity. The occurrence of any event or penalty may inhibit our ability or that of our collaborators to commercialize Glybera and any other products and generate revenues or may lead to withdrawal of marketing approval, which would have a material adverse effect on our business.

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

We believe that all of our current product candidates, including Glybera, will be viewed as gene therapy products by the applicable regulatory authorities. Gene therapies are relatively new treatments for which regulators do not have extensive experience or standard review and approval processes. The FDA has never approved a gene therapy product as safe and effective and, unlike the EMA, does not have an exceptional circumstances approval pathway. The EMA has approved only one gene therapy, Glybera, for a subset of LPLD patients, under exceptional circumstances, and only did so by a vote of 17 to 15 and after twice denying approval.

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. For example, in 2003, the FDA suspended 27 gene therapy trials involving several hundred patients after learning that a child treated in France had developed a condition resembling leukemia. The FDA and the EMA have issued various guidance documents pertaining to gene therapy products, with which we likely must comply to gain regulatory approval of any of our product candidates in the United States or European Union, respectively. The close regulatory scrutiny of gene therapy products may result in delays and increased costs, and may ultimately lead to the failure to obtain approval for any gene therapy product.

Regulatory requirements affecting gene therapy have changed frequently and may continue to change. For example, the European Commission conducted a public consultation in early 2013 on the application of EU legislation that governs advanced therapy medicinal products, including gene therapy products, which could result in changes in the data we need to submit to the EMA in order 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. For further discussion about the regulation we face in Europe and the United States, please see "Information on the Company—Business Overview—Government Regulation and Reimbursement."

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. The FDA has established the Office of Cellular, Tissue and Gene Therapies within the Agency's Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH are also subject to review by the NIH Office of Biotechnology Activities' Recombinant

DNA Advisory Committee, or the RAC. Also, before a clinical trial can begin at an NIH-funded institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will review the proposed clinical trial to assess the safety of the study.

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 of time.

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 time period. The EMA, however, may subsequently approve a similar drug for the same indication during the first product's market exclusivity if the EMA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may be lost if the EMA or FDA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if the incidence and prevalence of patients who are eligible to receive the drug in these markets materially increase.

We have obtained orphan designation for Glybera in the European Union and the United States. If we lose orphan drug exclusivity for Glybera or if our competitors obtain orphan drug exclusivity in indications related to our other product candidates before we do, we may lose out on the potential benefits of market exclusivity or be precluded from obtaining marketing authorization for our product candidate.

Risks Related to Commercialization

If we or our collaborators are unable to commercialize Glybera or our other 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 and, in the mid-term, the successful commercialization of Glybera. The success of our product candidates will depend on a number of 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;
- launching commercial sales of our products, if and when 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 sale of Glybera or other product candidates;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement; and
- complying with post-approval requirements of the EMA and maintaining a continued acceptable overall safety profile based on the EMA's risk-benefit analysis.

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

The affected populations for our gene therapies, including Glybera, 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 a number of 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, or new patients may become increasingly difficult to identify or access, any of which would adversely affect our results of operations and our business.

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

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

- the efficacy and potential advantages of our therapies compared with alternative treatments;
- our ability to convince payors of the long-term cost-effectiveness of our therapies and, consequently, the availability of third-party coverage and adequate reimbursement;

- the limitations on use and label requirements imposed by regulators;
- the convenience and ease of administration of our gene therapies compared with alternative treatments;
- the willingness of the target patient population to try new therapies, especially a gene therapy, and of physicians to administer these therapies;
- the strength of marketing and distribution support;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products.

In the case of Glybera in the European Union, we are required to put in place a restricted access program to ensure that the product is used appropriately when the diagnosis is confirmed, mandating that the product only be supplied to doctors who have received the appropriate educational materials and only be used to treat patients participating in a registry to monitor outcomes. If Glybera does not achieve an adequate level of acceptance, we may not generate significant revenues from this product and we may never achieve profitability.

If our collaboration with Chiesi is not successful, we may not effectively commercialize Glybera in the European Union and other covered countries.

We have entered into a collaboration with Chiesi for the commercialization of Glybera in the European Union, China, Russia and other specified countries. As a result, we are dependent on the efforts of Chiesi to successfully commercialize Glybera in these countries. There is a risk that Chiesi:

- may not perform its obligations as expected;
- may have difficulties gaining acceptance of the use of Glybera in the clinical community and achieving or maintaining satisfactory pricing and reimbursement of Glybera;
- may terminate, or may elect not to continue or renew, our commercialization arrangements based on changes in its strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities; and
- may not commit sufficient resources to the marketing and distribution of Glybera.

In addition, we are required to manufacture Glybera for sale by Chiesi. Should we encounter manufacturing problems, we may fail to adequately supply Glybera to Chiesi. For example, in the second half of 2014 we encountered problems with the consistency and stability of the manufacturing process for Glybera. We have developed an improved manufacturing process for Glybera, which addresses also our post-approval commitment, and will conduct consistency and comparability studies in respect of this process, which we expect to submit to the EMA in mid-2015. Although these manufacturing issues are specific to Glybera and do not affect the manufacturing of our other product candidates, any failure to introduce and receive approval for our improved Glybera manufacturing process on schedule could adversely affect our ability to meet our obligations under our agreement with Chiesi, which could result in modest financial penalties and potential reputational harm.

If any of these circumstances related to our collaboration with Chiesi are realized, they may adversely affect the commercial success of Glybera in the European Union and other countries covered by our partnership with Chiesi.

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

The development and commercialization of new biotechnology and biopharmaceutical products, including gene therapies, is highly competitive. We may face competition with respect to Glybera and our current 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 several companies focused on developing gene therapies in various indications, including AGTC, Asklepios, Audentes Therapeutics, Avalanche, Baxter, BioMarin, bluebird bio, Celladon, Dimension/Regen X, Isis, Oxford BioSciences, Sangamo BioScience, Spark 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 pharmaceuticals under development at pharmaceutical and biotechnology companies, including Amgen, Baxter, Bayer, Biogen Idec, BioMarin, Genzyme, Novartis, Novo Nordisk, Pfizer and Shire. We must 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.

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 EMA, FDA 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

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, our business could be adversely affected.

We have entered into collaborations with other companies and academic research institutions with respect to important elements of our commercial and development programs. For example, we have collaboration agreements with BMS for the development and commercialization of gene therapies for cardiovascular and potentially other diseases, with Chiesi, for both co-development and commercialization of our hemophilia B program and commercialization of Glybera in the European Union and certain other countries, and development programs with Institut Pasteur and UCSF for our development programs in Sanfilippo B syndrome and Parkinson's disease, respectively.

Our existing collaborations, and any future collaborations we enter into, may pose a number of 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;
- if our collaborators do not conduct the clinical trials they sponsor in accordance with regulatory requirements or stated protocols, we will not be able to rely on the data produced in such trials in our further development efforts;
- collaborators may not perform their obligations as expected;
- collaborators may also have relationships with other entities, some of which may be our competitors;
- collaborators may not pursue development and commercialization of any product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could develop, independently or with third parties, products that compete directly or indirectly with our products or product candidates, if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- our collaboration arrangements may impose restrictions on our ability to undertake other development efforts that may appear to be attractive to us;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to Glybera or one or more of our product candidates 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, 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 of the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of our development collaborators.

If our collaboration with BMS does not close or is not successful, our development plans, financial position and opportunities for growth may be adversely affected.

Our recently signed collaboration with BMS for the development and commercialization of gene therapies for cardiovascular and potentially other diseases is subject to customary closing conditions, including clearance under the Hart-Scott-Rodino Antitrust Improvements Act. We also must obtain shareholder approval of our proposed equity issuances to BMS. If HSR clearance is not received, we would not be able to close this collaboration. In addition, if our shareholders do not approve the issuance of all shares issuable under our agreements with BMS, we would issue to BMS a lower number of our ordinary shares and would therefore receive lower proceeds from these equity arrangements than anticipated, which may limit our ability to advance our other development programs in the manner we intend.

In order to earn all milestone payments and royalties potentially due under this collaboration, we are dependent on BMS electing to designate and actively pursue target indications covered by the collaboration and we achieve meet all development, clinical and regulatory milestones under the collaboration. If BMS designates or actively pursues fewer development targets, or if we fail to achieve a significant number of the applicable milestones, the total payments we receive under this collaboration will be materially lower than are potentially payable. See also "Item 3—Key Information—Collaborations—Bristol-Myers Squibb Collaboration."

If we are unable to enter into additional collaborations in the future, or if our new collaborations are not successful, we may not be able to develop or market our product candidates or obtain a strategic position in the development of new gene therapies.

We believe collaborations enable us to gain access to early-stage clinical programs and related data, as well as to promising transgenes and other intellectual property, with limited financial investment by us. Collaborations also allow us to share the costs of larger development and commercialization efforts with partners with greater resources. Part of our strategy is to leverage our experience and expertise in gene therapy research and development, as well as our proprietary manufacturing capabilities, to be an attractive collaborator for academic research institutions and

biotechnology and pharmaceutical companies seeking to advance their programs into larger, late-stage clinical trials that require commercial-scale manufacturing. We face significant competition and we may be unable to attract suitable collaborators or reach agreements with them on acceptable terms, which could limit our access to attractive development programs.

Many of our agreements with our licensors, including our agreements with the NIH, require us to obtain consent from the licensor before we can enter into arrangements involving the sublicensing of technology we have licensed from such licensors. Our licensors may withhold such consent, or may provide such consent only if we agree to reduce our rights or increase our financial or other obligations to them. Obtaining such consent may also hamper our ability to enter into collaboration arrangements on a timely basis.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

We do not currently have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. We may not be successful in entering into arrangements with third parties in the future to sell, market and distribute our product candidates, including Glybera in territories outside the European Union and certain other countries, or we may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

Risks Related to Our Manufacturing

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

We manufacture Glybera and clinical supplies of our product candidates ourselves in our facility in Amsterdam and plan to commence production of Glybera and of our hemophilia B and other product candidates in our new facility in Lexington, Massachusetts. The insect-cell based manufacturing process we use to produce Glybera and our other product candidates is highly complex and in the normal course is subject to production difficulties. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and insufficient inventory. We may encounter problems achieving adequate or clinical-grade materials that meet EMA, FDA or other applicable standards or specifications with consistent and acceptable production yields and costs. For example, in the second half of 2014 we encountered problems with the consistency and stability of the manufacturing process for Glybera. We have developed an improved manufacturing process for Glybera, which addresses also our post-approval commitment, and will conduct consistency and comparability studies in respect of this process, which we expect to submit to the EMA in mid-2015. Although these manufacturing issues are specific to Glybera and do not affect the manufacturing of our other product candidates, any failure to introduce and receive approval for our improved Glybera manufacturing process on schedule could adversely affect our ability to meet our obligations under our agreement with Chiesi, which could result in modest financial penalties and potential reputational harm.

A number of factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including equipment malfunctions, facility contamination, labor problems, raw

materials shortages or contamination, natural disasters, disruption in utility services, terrorist activities, human error or disruptions in the operations of our suppliers. We also may encounter problems in hiring and retaining the experienced specialist personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

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

Delays in receiving regulatory approvals for our new U.S. manufacturing facility could delay our development and commercialization plans and thereby limit our revenues and growth.

Our manufacturing facility in Lexington, Massachusetts of approximately 53,000 square feet, will require regulatory approval. If regulatory approval is delayed, we may not be able to manufacture sufficient quantities of Glybera or our product candidates, which would limit our commercialization and development activities and our opportunities for growth. Cost overruns associated with this facility could also require us to raise additional funds from external sources, which may be unavailable on favorable terms or at all.

Our manufacturing facilities are 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 facilities in Amsterdam and Lexington are subject to ongoing regulation and periodic inspection by the EMA, FDA and other regulatory bodies to ensure compliance with current Good Manufacturing Practices, or 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.

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 and other hazardous materials, and produce waste products. Accordingly, we are subject to national, federal, state and local laws and regulations in the United States and the Netherlands governing the use, manufacture, distribution, storage, handling, treatment and disposal of these materials. In addition to ensuring the safe handling of these materials, applicable requirements require increased safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and

safety and export control laws and regulations, we could be held liable for damages that result, and any such liability could exceed our assets and resources.

Risks Related to 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. For example, we have an exclusive license from the NIH for "the development and sale of AAV5 based therapeutic products to be delivered to the brain or liver for treatment of human diseases originating in the brain or liver," other than arthritis-related diseases. We also have a non-exclusive license from the NIH for the development and sale of AAV5 based therapeutic products to treat human diseases other than those covered by our exclusive license.

We believe that our exclusive license from the NIH includes the systemic administration of AAV5-based therapeutic products so long as such therapeutic products are "to be delivered to the brain or liver for treatment of human diseases originating in the brain or liver." However, Sangamo BioSciences, Inc., or Sangamo, has announced that it has broad worldwide licenses to use AAV vectors, including AAV5 and AAV6, for research, development and commercialization of therapies for hemophilia A and B, Huntington's disease and other targets. We believe Sangamo's view may be that our exclusive license excludes systemic administration because Sangamo interprets the phrase "to be delivered to" to require direct administration into the brain or liver. Our view is that the phrase "to be delivered to"

indicates the ultimate destination of the therapy and not the location where it is first introduced into the body. Although we think our interpretation is correct, there can be no assurance that a court would agree with our interpretation regarding the meaning of this phrase. If our interpretation of the phrase "to be delivered to" is incorrect, then others may obtain licenses from the NIH that may enable them to compete with us in the systemic administration of AAV5-based therapeutics for treatment of human diseases originating in the brain or liver, which could harm our business.

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

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

We rely upon a combination of in-licensed and owned patents, trade secret protection and confidentiality agreements to protect our intellectual property. Our success depends in 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 behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after their priority date, or in some cases at all. Therefore, we cannot know with certainty whether we were the first to make the inventions or that we were the first to file for patent protection of the inventions claimed in our owned or licensed patents or pending patent applications. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the European Union, the United States or other countries may diminish the value of our patents or narrow the scope of our patent protection.

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

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

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

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

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

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

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

In addition, these agreements typically restrict the ability of our collaborators, advisors and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that 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 Glybera and any product candidates for which we may receive marketing approval.

We anticipate that the cost of treatment using Glybera or our other 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 Glybera or our other product candidates without reimbursement from third-party payors, such as government health administration authorities, private health insurers and other organizations. Even if there is a commercially viable market, if the level of third-party reimbursement is below our expectations, our revenues and gross margins will be adversely affected and our business will be harmed.

Government authorities and other third party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Reimbursement systems vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. Government authorities and third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and procedures. Increasingly, third party payors require drug companies to provide them with predetermined discounts from list prices, are exerting influence on decisions regarding the use of particular treatments and are limiting covered indications. Additionally, in the United States and some foreign jurisdictions, legislative and regulatory changes regarding the

healthcare system and insurance coverage 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 often 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. As a result of these restrictions, Glybera, as well as any product candidates for which we may obtain marketing approval in the future, 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 in order to increase the likelihood of obtaining reimbursement approvals. In the event that 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 payors, 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 particular challenges to pricing review and negotiation for Glybera and our product candidates for which we may obtain marketing authorization. The patient populations for Glybera and our product candidates targeted at orphan and ultra-orphan diseases are relatively small. If we are unable to obtain adequate levels of reimbursement relative to the small market size in our target orphan and ultra-orphan indications, our ability to support our development and commercial infrastructure and to successfully market and sell Glybera and other product candidates for which we may obtain marketing approval will be adversely affected.

We also anticipate that Glybera and 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 payors 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 we anticipate that Glybera will need to be administered only once, there may be situations in which we may need to re-administer Glybera, which may further complicate the pricing and reimbursement for Glybera. In addition, in light of the anticipated cost of these therapies, governments and other payors may be particularly restrictive in making coverage decisions. These factors could limit our commercial success and harm our business.

Risks Related to Other Legal Compliance Matters

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

Healthcare providers, physicians and third-party payors 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 payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval.

Within the European Union, the control of unlawful marketing activities is a matter of national law in each of the member states. Industry associations also closely monitor the activities of member companies. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

If we market a product in the United States in the future, we will be subject to various federal and state laws and regulations including, the federal Anti-Kickback Statute, the federal False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996, federal law that requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals and certain state and local laws applicable to pharmaceutical companies. We are also subject to the U.S. Foreign Corrupt Practices Act.

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

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. 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 in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of Glybera and any products that we may develop in the future.

We face an inherent risk of product liability related to the testing of our product candidates in human clinical trials and will face an even greater risk when we commercially sell Glybera and any other products that we may develop. 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.

We currently hold €9,500,000 in clinical trial insurance coverage in the aggregate, with a per incident limit of €400,000 to €450,000, with respect to the clinical studies we conduct. Such coverage may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials. In addition, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the research and development, clinical and business development expertise of our Chief Executive Officer, Jörn Aldag, our Chief Medical Officer, Christian Meyer, M.D., and our Chief Scientific Officer, Harald Petry, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our senior management, each of them may terminate their employment on relatively short notice. We do not maintain "key person" insurance for any of our senior management or employees.

The loss of the services of our senior management or other key employees could impede the achievement of our research, development and commercialization 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 of time because of the limited number of individuals in our industry with the breadth and depth of skills and experience required to successfully develop, gain regulatory approval of and commercialize 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.

We are expanding our key capabilities and, as a result, may encounter difficulties in managing our growth, which could disrupt our operations.

If we receive marketing approval, we intend to build a sales, marketing and medical affairs infrastructure to market Glybera and potentially other product candidates in the United States and other countries. We currently have no experience building and training an internal sales force. We have experienced and expect in the future to continue to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of manufacturing, clinical development, regulatory affairs and sales, marketing and distribution. To manage our current and anticipated future growth, we will be required to implement and improve our managerial, operational and financial systems, expand our facilities and recruit and train additional qualified personnel. Recruiting and training a sales force is expensive and time-consuming and could delay any ultimate launch of Glybera or other product candidates for which we are able to obtain marketing approval in the United States and other markets. Due to our limited financial resources and the limited experience of our management team in running a company with this level of anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel.

If the commercial launch of Glybera or any other product candidate for which we recruit additional sales force, marketing, manufacturing or other personnel is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition such personnel. If we do not successfully establish sales, marketing and medical affairs capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing Glybera or other product candidates in the United States or other countries in which we may receive marketing approval.

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, 2013 through March 31, 2015, the sale price of our ordinary shares ranged from a high of $28.00 to a low of $8.29. The closing price on April 6, 2015 was $33.61 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. We have no plans to list our ordinary shares in any other jurisdiction. As a result, a holder of our ordinary shares outside the United States may not be able to effect transactions in our ordinary shares as readily as the holder may if our securities were listed on an exchange in that holder's home jurisdiction.

Our senior managers, directors 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 management board and supervisory board members, senior management, and our shareholders and their affiliates who own more than 5% of our outstanding ordinary shares, in the aggregate, beneficially own approximately 63.7% of our share capital. As a result, if these shareholders were to choose to act together, they would be able to control all matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of supervisory board directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

Provisions of our articles of association or Dutch corporate law might deter acquisition bids for us that might be considered favorable and prevent or frustrate any attempt to replace or remove the management board and supervisory 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 management board or supervisory board. These provisions include:

- staggered three-year terms of our supervisory directors;
- a provision that our managing directors and supervisory 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 (unless the removal was proposed by the supervisory board); 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 management board that has been approved by our supervisory 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. Under Dutch law, we may only pay dividends if our shareholders' equity exceeds the sum of the paid-up and called-up share capital plus the reserves required to be maintained by Dutch law or by our articles of association. In addition, our loan agreement with Hercules contains, and any other loan facilities that we may enter into may contain, restrictions on our ability, or that of our subsidiaries, to pay dividends. Subject to such restrictions, a proposal for the payment of cash dividends in the future, if any, will be at the discretion of our management board, subject to the approval of our supervisory board, and will depend upon such factors as earnings levels, capital requirements, contractual restrictions, our overall financial condition and any other factors deemed relevant by our management board. Accordingly, shareholders cannot rely on dividend income from our ordinary shares and any returns on an investment in our ordinary shares will likely depend entirely upon any future appreciation in the price of our ordinary shares.

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

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

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

We cannot predict whether investors will find our ordinary shares less attractive if we rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may be more volatile.

We are a foreign private issuer and, as a result, we are not subject to U.S. proxy rules and are subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

We report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act and although we are subject to Dutch laws and regulations with regard to such matters and intend to furnish quarterly financial information to the SEC, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and

- the rules under the Exchange Act requiring the filing with the Securities and Exchange Commission of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events.

In addition, foreign private issuers are not be required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, our shareholders may not have the same protections afforded to shareholders of companies that are not foreign private issuers. We cannot predict whether investors will find our ordinary shares less attractive if we rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may be more volatile.

We may lose our foreign private issuer status which would then require us to comply with the Exchange Act's domestic reporting regime and cause us to incur significant legal, accounting and other expenses.

If we lose foreign private issuer status we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and NASDAQ rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that any loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities more time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our supervisory board.

We will continue to incur significant costs as a result of operating as a public company, and our management will be required to continue to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. We currently estimate that we will incur incremental annual costs of approximately $1.5 million associated with operating as a public company, although it is possible that our actual incremental annual costs will be higher than we currently estimate. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives.

These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices and control environment process improvements.

If we fail to implement and 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.

Prior to our initial public offering in February 2014, we were a private company with limited accounting personnel and other resources with which to address our internal controls and procedures. In connection with the preparation and external audit of our consolidated financial statements as of and for the year ended December 31, 2014 and our management's assessment of our internal control over financial reporting, we and our auditors, an independent registered public accounting firm, noted three material weaknesses in our internal control over financial reporting. We and our independent registered public accounting firm had identified the same three material weaknesses in our internal control over financial reporting in connection with the audit of our consolidated financial statements as of and for year ended December 31, 2013. Our independent registered public accounting firm has not conducted an audit of our internal control over financial reporting. Had our independent registered public accounting firm conducted an audit of our internal control over financial reporting, such firm might have identified additional material weaknesses and deficiencies.

A significant deficiency is a control deficiency, or a combination of control deficiencies, that adversely affects our ability to initiate, authorize, record, process, or report external financial data reliably in accordance with IFRS such that there is more than a remote likelihood that a misstatement of our annual or interim financial statements that is more than inconsequential will not be prevented or detected by our employees. A material weakness is a control deficiency, or combination of control deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statement will not be prevented or detected. In response, we are implementing several remedial actions to address these material weaknesses though we cannot guarantee when these material weaknesses will be fully remediated. For details, see "Item 15—Controls and Procedures."

If we fail to achieve and maintain the adequacy of our internal control over financial reporting, as the applicable standards are modified, supplemented or amended from time to time, we may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting. If we fail to achieve and maintain an effective internal control environment, 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. We may also be required to restate our financial statements for prior periods. Our reporting and compliance obligations may place a significant strain on our management, operational and financial resources and systems for the foreseeable future. We may be unable to timely complete the required remediation efforts.

We rely on NASDAQ Stock Market rules that permit us to comply with applicable Dutch corporate governance practices, rather than the corresponding domestic U.S. corporate governance practices, and therefore the rights of our shareholders will differ from the rights of shareholders of a domestic U.S. issuer.

As a foreign private issuer whose ordinary shares are listed on The NASDAQ Global Select Market, we are permitted in certain cases to follow Dutch corporate governance practices instead of the corresponding requirements of the NASDAQ Marketplace Rules. A foreign private issuer that elects to follow a home country practice instead of NASDAQ requirements must submit to NASDAQ in advance a written statement from an independent counsel in such issuer's home country certifying that the issuer's practices are not prohibited by the home country's laws. In addition, a foreign private

issuer must disclose in its annual reports filed with the Securities and Exchange Commission each such requirement that it does not follow and describe the home country practice followed instead of any such requirement. We follow Dutch corporate governance practices with regard to the quorum requirements applicable to meetings of shareholders and the provision of proxy statements for general meetings of shareholders, rather than the corresponding domestic U.S. corporate governance practices. In accordance with Dutch law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. Although we do provide shareholders with an agenda and other relevant documents for the general meeting of shareholders, Dutch law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in the Netherlands. Accordingly, our shareholders may not be afforded the same protection as provided under NASDAQ's corporate governance rules.

We do not comply with all the provisions of the Dutch Corporate Governance Code.

As a Dutch company we are subject to the Dutch Corporate Governance Code, or DCGC. The DCGC contains both principles and best practice provisions for management boards, supervisory boards, shareholders and general meetings of shareholders, financial reporting, auditors, disclosure, compliance and enforcement standards. The DCGC applies to all Dutch companies listed on a government-recognized stock exchange, whether in the Netherlands or elsewhere, including The NASDAQ Global Select Market. The principles and best practice provisions apply to our management board and supervisory board, in relation to their role and composition, conflicts of interest and independence requirements, board committees and remuneration, shareholders and the general meeting of shareholders, for example, regarding anti-takeover protection and obligations of the company to provide information to its shareholders; and financial reporting, including external auditor and internal audit requirements. Because we do not comply with all the provisions of the DCGC, shareholders may not have the same level of protection as a shareholder in a Dutch company that fully complies with the DCGC.

Risks for U.S. Holders

We may be classified as a passive foreign investment company for any taxable year, which may result in adverse U.S. federal income tax consequence to U.S. holders.

Based on our estimated gross income and average value of our gross assets, the expected price of our shares, and the nature of our business, we do not expect to be considered a "passive foreign investment company," or PFIC, for U.S. federal income tax for the 2014 tax year or in the foreseeable future. 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 for the production of 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 not be considered a PFIC for the current taxable year or any future taxable year. 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 to be treated as a PFIC for any taxable year during which a U.S. holder held our ordinary shares, however, certain adverse U.S. federal income tax consequences could apply to the U.S. holder. See "Additional Information—Taxation—Taxation in the United States—Passive foreign investment company considerations."

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

We are incorporated under the laws of the Netherlands. The majority of our managing directors, supervisory directors 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 managing directors or supervisory directors 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. In order 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 management board or supervisory board members, representatives or certain experts named herein 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.

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 supervisory board and management board under Dutch law are different than under the laws of some U.S. jurisdictions. In the performance of their duties, our supervisory board and management board 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.

In addition, the rights of holders of shares and many of the rights of shareholders as they relate to, for example, the exercise of shareholder rights, are governed by Dutch law and our articles of association and differ from the rights of shareholders under U.S. law. For example, Dutch law does not grant appraisal rights to a company's shareholders who wish to challenge the consideration to be paid upon a merger or consolidation of the company. See "Description of Share Capital—Comparison of Dutch corporate law and our Articles of Association and Delaware corporate law" in our F-3 registration statement.

Risks Related to this Offering

Management will have broad discretion as to the use of the net proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our ordinary shares. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates, and cause the price of our ordinary shares to decline.

If you purchase the ordinary shares sold in this offering, you will experience immediate and substantial dilution in your investment. You will experience further dilution if we issue additional equity securities in the future.

Since the price per ordinary share of our ordinary shares being offered is substantially higher than the net tangible book value per ordinary share of our ordinary shares, you will suffer substantial dilution with respect to the net tangible book value of the ordinary shares you purchase in this offering. Based on the public offering price of $33.61 per ordinary share, which is the last reported sale price for our common stock on The NASDAQ Global Select Market on April 6, 2015, and our net tangible book value as of December 31, 2014, if you purchase ordinary shares in this offering, you will suffer immediate and substantial dilution of $27.69 (or €22.81) per ordinary share with respect to the net tangible book value of the ordinary shares. See "Dilution" for a more detailed discussion of the dilution you will incur if you purchase ordinary shares in this offering.

In addition, we have a significant number of stock options and warrants outstanding. To the extent that outstanding stock options or warrants have been or may be exercised or other shares issued, investors purchasing our ordinary shares in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders or result in downward pressure on the price of our common stock.

Sales of a substantial number of our ordinary shares by our existing stockholders in the public market could cause our stock price to fall.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market, the trading price of our ordinary shares could decline. In addition a substantial number of ordinary shares are subject to outstanding options are or will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules. If these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares could decline.

We, the members of our supervisory board, the members of our management board and our senior management team have agreed that, subject to certain exceptions, during the period ending 90 days after the date of this prospectus supplement, they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any of our ordinary shares or securities convertible into or exchangeable or exercisable for any of our ordinary shares, enter into a transaction that would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our ordinary shares, whether any of these transactions are to be settled by delivery of our ordinary shares or other securities, in cash or otherwise, or publicly disclose the intention to make any offer, sale, pledge or disposition, or to enter into any transaction, swap, hedge or other arrangement, without, in each case, the prior written consent of Leerink Partners LLC and Cowen and Company, LLC, who may release any of the securities subject to these lock-up agreements at any time without notice. Exceptions to the lock-up restrictions are described in more detail in this prospectus supplement under the caption "Underwriting."

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering, based on an assumed public offering price of $33.61, which is the last reported sale price of our ordinary shares on the NASDAQ Global Select Market on April 6, 2015 after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $94.0 million (€77.5 million), or $108.2 million (€89.2 million) if the underwriters exercise their option to purchase additional ordinary shares from us in full.

We intend to use the net proceeds we receive from this offering as follows:

- to fund our share of the research and development of AMT-060 in hemophilia B;
- to support our further clinical development of Glybera, and our application for marketing approval of Glybera and preparation for potential commercial launch in the United States;
- exercise our options to acquire rights and pursue development of certain product candidates, the development of which is currently being conducted and funded by third parties;
- to fund the research and development of our early-stage product candidates for hemophilia A and various liver and CNS-related diseases;
- to fund the validation and operation of our manufacturing facility in Lexington, Massachusetts;
- to further enhance our gene therapy technology platform, including the support for our collaborations with 4D Molecular Therapeutics and Synpromics Limited;
- to expand our research capabilities and corporate infrastructure to support our collaboration with Bristol-Myers Squibb;
- for acquisitions or investments in other businesses, technologies or product candidates, though we have no binding agreements in place for any such acquisitions or investments as of the date of this prospectus supplement; and
- for working capital and for general corporate purposes, including service on our indebtedness including pursuant to our Amended and Restated Loan Agreement with Hercules Technology Growth Capital, Inc. (see Item 5: Operating and Financial Review and Prospects—Liquidity and Capital Resources—Hercules and Security Agreements" section in our Annual Report on Form 20-F for the year ended December 31, 2014, filed with the SEC on April 7, 2015).

This expected use of the net proceeds from this offering represents our intentions based upon our present plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our commercialization and development efforts, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs.

Pending the use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including term deposits, short-term, investment-grade, interest-bearing instruments and U.S. government securities.

PRICE RANGE OF ORDINARY SHARES

Our ordinary shares are listed on The NASDAQ Global Select Market under the symbol "QURE". On April 6, 2015, the closing price for our ordinary shares as reported on the NASDAQ Global Select Market was $33.61 per ordinary share. The following table shows the high and low sales prices per ordinary share as reported on the NASDAQ Global Select Market for the periods indicated.

	High	Low
Annual Highs and Lows		
2014 (from February 5)	$ 18.75	$ 8.29
Quarterly Highs and Lows		
First Quarter 2014	$ 18.75	$ 13.10
Second Quarter 2014	$ 16.50	$ 8.29
Third Quarter 2014	$ 14.50	$ 9.00
Fourth Quarter 2014	$ 17.33	$ 9.17
First Quarter 2015	$ 28.00	$ 14.67
Monthly Highs and Lows		
October 2014	$ 11.75	$ 9.17
November 2014	$ 15.70	$ 9.69
December 2014	$ 17.33	$ 12.28
January 2015	$ 23.80	$ 14.67
February 2015	$ 23.44	$ 18.59
March 2015	$ 28.00	$ 21.06
April 2015 (through April 6)	$ 35.50	$ 22.51

As of April 6, 2015, there was one shareholder of record in the United States, Cede & Co, as nominee for the Depository Trust Company which held 63.8% of our outstanding ordinary shares.

DIVIDEND POLICY

We have never declared or paid any dividends on our ordinary shares, and we currently do not plan to declare dividends on our ordinary shares in the foreseeable future. Under Dutch law, we may only pay dividends if our shareholders' equity exceeds the sum of the paid-up and called-up share capital plus the reserves required to be maintained by Dutch law or by our articles of association. In addition, our Amended and Restated Loan and Security Agreement with Hercules Technology Growth Capital, Inc. contains, and any other loan facilities that we may enter into may contain, restrictions on our ability, or that of our subsidiaries, to pay dividends. Subject to such restrictions, a proposal for the payment of cash dividends in the future, if any, will be at the discretion of our management board, subject to the approval of our supervisory board, and will depend upon such factors as earnings levels, capital requirements, contractual restrictions, our overall financial condition and any other factors deemed relevant by our management board.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2014:

- on an actual basis; and
- on an as adjusted basis to give effect to the issue and sale of 3,000,000 ordinary shares by us in this offering at an assumed public offering price of $33.61 per ordinary share, which is the last reported sale price of our ordinary shares on the NASDAQ Global Select Market on April 6, 2015, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of December 31, 2014	
(€ in thousands)	**Actual**	**As Adjusted**
Cash and cash equivalents	€ 53,219	€ 130,672
Total debt	17,270	17,270
Share capital:		
Ordinary shares	905	1,055
Share premium	206,111	284,031
Other reserves	17,149	17,149
Accumulated deficit	(181,081)	(181,699)
Total shareholders' equity	43,084	120,537
Total capitalization	€ 60,354	€ 137,807

The table above excludes:

- 2,596,532 ordinary shares issuable upon exercise of options outstanding under our equity incentive plans as of December 31, 2014, at a weighted average exercise price of €5.93 per share;
- up to 626,783 ordinary shares reserved for future issuance under our equity incentive plans as of December 31, 2014;
- 457,308 ordinary shares issuable as of December 31, 2014 upon exercise of options granted on January 17, 2014 in connection with our collaboration and license agreement with 4D Molecular Therapeutics, at an exercise price of €0.05 per share;
- 170,802 ordinary shares issuable upon the exercise of warrants outstanding as of December 31, 2014, at a weighted average exercise price of €10.31 per ordinary share; and
- 179,068 restricted share units outstanding as of December 31, 2014.

DILUTION

If you invest in our ordinary shares, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share after this offering.

Our net tangible book value as of December 31, 2014, was €25.4 million ($30.8 million), or €1.40 ($1.70) per ordinary share. Net tangible book value per ordinary share represents the amount of our total tangible assets less our total liabilities, divided by the number of ordinary shares outstanding.

After giving effect to the sale by us of 3,000,000 ordinary shares in this offering at an assumed public offering price of $33.61 per ordinary share (€27.68 per ordinary share), (the last reported sale price of our ordinary shares on the NASDAQ Global Select Market on April 6, 2015), and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2014, would have been €102.8 million ($124.9 million), or €4.88 per ordinary share ($5.92 per ordinary share). This amount represents an immediate increase in net tangible book value of €3.47 per ordinary share ($4.22 per ordinary share) to our existing shareholders and an immediate dilution in net tangible book value of €22.81 per ordinary share ($27.69 per ordinary share), or 82% per ordinary share, to investors purchasing ordinary shares in this offering at the public offering price. We determine dilution by subtracting the as adjusted net tangible book value per share after this offering from the amount of cash that a new investor paid for an ordinary share. The following table illustrates this dilution on a per share basis:

Assumed public offering price per ordinary share	$ 33.61	€27.68
Net tangible book value per ordinary share as of December 31, 2014	1.70	1.40
Increase per ordinary share attributable to investors in this offering	4.22	3.47
As adjusted net tangible book value per ordinary share as of December 31, 2014 after giving effect to this offering	5.92	4.88
Dilution per ordinary share to investors in this offering	27.69	22.81

If the underwriters exercise their option to purchase additional ordinary shares from us in full, the as adjusted net tangible book value per ordinary share would be $6.45 per ordinary share (€5.32 per ordinary share), and the dilution in as adjusted net tangible book value per ordinary share to investors in this offering would be $27.16 (€22.37).

The total number of ordinary shares reflected in the discussion and tables above is based on 18,092,194 ordinary shares outstanding as of December 31, 2014. This excludes:

- 2,584,532 ordinary shares issuable upon exercise of options outstanding under our equity incentive plans as of December 31, 2014, at a weighted average exercise price of €5.94 per share;
- up to 626,783 ordinary shares reserved for future issuance under our equity incentive plans as of December 31, 2014;
- 457,308 ordinary shares issuable as of December 31, 2014 upon exercise of options granted on January 17, 2014 in connection with our collaboration and license agreement with 4D Molecular Therapeutics, at an exercise price of €0.05 per share;
- 170,802 ordinary shares issuable upon the exercise of warrants outstanding as of December 31, 2014, at an exercise price of €10.31 per ordinary share; and
- 179,068 restricted share units outstanding as of December 31, 2014.

To the extent options are exercised and awards are granted under our equity incentive plans, there may be dilution to our shareholders. We may also choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

UNDERWRITING

Leerink Partners LLC, One Federal Street, 37th Floor, Boston, MA 02110, and Cowen and Company, LLC, 599 Lexington Avenue, 27th Floor, New York, NY 10022, are acting as representative of each of the underwriters named below and as joint book-running managers of this offering. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of ordinary shares set forth opposite its name below.

Underwriter	Number of Ordinary Shares
Leerink Partners LLC	
Cowen and Company, LLC	
Piper Jaffray & Co.	
Oppenheimer & Co. Inc.	
H.C. Wainwright & Co., LLC	
Total	3,000,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the ordinary shares sold under the underwriting agreement if any of these ordinary shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the ordinary shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the ordinary shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the ordinary shares to the public at the public offering price set forth on the cover of this prospectus supplement and to dealers at that price less a concession not in excess of $ per ordinary share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional ordinary shares.

	Per Ordinary Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $750,000. We also have agreed to

reimburse the underwriters for up to $16,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus supplement, to purchase up to 450,000 additional ordinary shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional ordinary shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, the members of our supervisory board, the members of our management board, our senior management team and certain shareholders have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-l(h) under the Securities Exchange Act of 1934, as amended, ordinary shares or securities exchangeable or exercisable for or convertible into share ordinary shares; or

- otherwise dispose of any ordinary shares, options or warrants to acquire ordinary shares, or securities exchangeable or exercisable for or convertible into ordinary shares currently or hereafter owned either of record or beneficially; or

- publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus without the prior written consent of Leerink Partners LLC and Cowen and Company, LLC.

This restriction terminates after the close of trading of our ordinary shares on and including the 90th day after the date of this prospectus supplement.

Leerink Partners LLC and Cowen and Company, LLC may, in their sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of the individuals who will execute a lock-up agreement, providing consent to the sale of ordinary shares prior to the expiration of the lock-up period.

NASDAQ Global Select Market Listing

Our ordinary shares are listed on The NASDAQ Global Select Market under the symbol "QURE."

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the ordinary shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our ordinary shares. However, the representatives may engage in transactions that stabilize the price of our ordinary shares, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our ordinary shares in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option described

above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our ordinary shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our ordinary shares or preventing or retarding a decline in the market price of our ordinary shares. As a result, the price of our ordinary shares may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the NASDAQ Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our ordinary shares. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates in the past have engaged, and may in the future engage, in investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have or may in the future receive customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers.

Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area that has implemented the Prospectus Directive (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any ordinary shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any ordinary shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the ordinary shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any ordinary shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

We, the representatives and each of our and the representatives' affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus supplement has been prepared on the basis that any offer of ordinary shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of ordinary shares. Accordingly any person making or intending to make an offer in that Relevant Member State of ordinary shares which are the subject of the offering contemplated in this prospectus supplement may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of ordinary shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any ordinary shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe the ordinary shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (as amended, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

TAXATION

Taxation in the Netherlands

This taxation summary solely addresses the principal Dutch tax consequences of the acquisition, ownership and disposal of ordinary shares. It does not purport to describe all the tax considerations that may be relevant to a particular holder of our ordinary shares, or a Shareholder. Shareholders are advised to consult their tax counsel with respect to the tax consequences of acquiring, holding and/or disposing of ordinary shares. Where in this summary English terms and expressions are used to refer to Dutch concepts, the meaning to be attributed to such terms and expressions shall be the meaning to be attributed to the equivalent Dutch concepts under Dutch tax law.

This summary does not address the tax consequences of:

- A Shareholder who is an individual, either resident or non-resident in the Netherlands, and who has a substantial interest (*aanmerkelijk belang*) in us within the meaning of the Dutch Income Tax Act 2001 (*Wet inkomstenbelasting 2001*). Generally, if a person holds an interest in us, such interest forms part of a substantial interest, or a deemed substantial interest, in us, if any or more of the following circumstances is present:

  - If a Shareholder, either alone or, in the case of an individual, together with his partner owns or is deemed to own, directly or indirectly, either a number of shares in us representing five percent or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of our shares), or rights to acquire, directly or indirectly, shares, whether or not already issued, representing five percent or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of our shares), or profit participating certificates (*winstbewijzen*), relating to five percent or more of our annual profit or to five percent of our liquidation proceeds.

  - If the shares, profit participating certificates or rights to acquire shares in us are held or deemed to be held following the application of a non-recognition provision.

  - If the partner of a Shareholder, or one of certain relatives of the Shareholder or of this partner has a substantial interest (as described under 1. and 2. above) in us.

- A Shareholder receiving income or realizing capital gains in their capacity as future, present or past employee (*werknemer*) or member of a management board (*bestuurder*), or supervisory director (*commissaris*).

- Pension funds, investment institutions (*fiscale beleggingsinstellingen*), exempt investment institutions (*vrijgestelde beleggingsinstellingen*) and other entities that are exempt from corporate income tax in the Netherlands, as well as entities that are exempt from corporate income tax in their country of residence, such country of residence being another state of the European Union, Norway, Liechtenstein, Iceland or any other state with which the Netherlands have agreed to exchange information in line with international standards.

- A Shareholder who is a qualifying non-resident taxpayer within the meaning of article 7.8, paragraph 6, of the Dutch Income Tax Act 2001.

For purposes of Dutch personal income tax and Dutch corporate income tax, ordinary shares legally owned by a third party, such as a trustee, foundation or similar entity or arrangement, may under certain circumstances have to be allocated to the (deemed) settler, grantor or similar organiser, or, upon the death of the Settlor, his/her beneficiaries in proportion to their entitlement to the estate of the Settlor of such trust or similar arrangement.

This summary is based on the tax laws and principles (unpublished case law not included) in the Netherlands as in effect on the date of this annual report, which are subject to changes that could

prospectively or retroactively affect the stated tax consequences. Where in this summary the terms "the Netherlands" and "Dutch" are used, these refer solely to the European part of the Kingdom of the Netherlands.

Dividend Withholding Tax

General

We are generally required to withhold Dutch dividend withholding tax at a rate of 15% from dividends distributed by us. The concept dividends "distributed by us" as used in this section includes, but is not limited to:

- distributions of profits in cash or in kind, deemed and constructive distributions, and repayments of paid-in capital which are not recognized for Dutch dividend withholding tax purposes;
- liquidation proceeds, or proceeds from the repurchase of ordinary shares by us in excess of the average paid-in capital recognized for Dutch dividend withholding tax purposes;
- the par value of ordinary shares issued to a Shareholder in us or an increase of the par value of ordinary shares, to the extent that it does not appear that a contribution, recognized for Dutch dividend withholding tax purposes, has been made or will be made; and
- partial repayment of share capital, if and to the extent that there are net profits (zuivere winst), unless (a) the general meeting of shareholders has resolved in advance to make such repayment and (b) the par value of the shares concerned has been reduced by an equal amount by way of an amendment to our articles of association.

In general, we will be required to remit all amounts withheld as Dutch dividend withholding tax to the Dutch tax authorities. However, under certain circumstances, we are allowed to reduce the amount to be remitted to the Dutch tax authorities by the lesser of:

- 3% of the portion of the distribution paid by us that is subject to Dutch dividend withholding tax; and
- 3% of the dividends and profit distributions, before deduction of foreign withholding taxes, received by us from qualifying foreign subsidiaries in the current calendar year (up to the date of the distribution by us) and the two preceding calendar years, as far as such dividends and profit distributions have not yet been taken into account for purposes of establishing the above mentioned reduction.

Although this reduction reduces the amount of Dutch dividend withholding tax that we are required to remit to the Dutch tax authorities, it does not reduce the amount of tax that we are required to withhold on dividends distributed.

Residents of the Netherlands

A Shareholder which is resident or deemed resident in the Netherlands is generally entitled to a full credit of any Dutch dividend withholding tax against the Dutch (corporate) income tax liability of such Shareholder, and is generally entitled to a refund in the form of a negative assessment of Dutch (corporate) income tax, insofar such Dutch dividend withholding tax, together with any other creditable domestic and/or foreign taxes, exceeds such Shareholder's aggregate Dutch income tax or Dutch corporate income tax liability.

If and to the extent that such a corporate Shareholder is eligible for the application of the participation exemption with respect to the ordinary shares, dividends distributed by us are in principle exempt from Dutch dividend withholding tax.

Pursuant to domestic anti-dividend stripping rules, no exemption from Dutch dividend withholding tax, credit against Dutch (corporate) income tax, refund or reduction of Dutch dividend withholding tax shall apply if the recipient of the dividend paid by us is not considered to be the beneficial owner (*uiteindelijk gerechtigde*) as meant in these rules, of such dividends.

Non-residents of the Netherlands (including but not limited to U.S. Shareholders)

A non-resident Shareholder, which is resident in the non-European part of the Kingdom of the Netherlands or in a country that has concluded a tax treaty with the Netherlands, may be eligible for a full or partial relief from Dutch dividend withholding tax, provided such relief is timely and duly claimed.

In addition, a non-resident Shareholder that is not an individual, is entitled to an exemption from Dutch dividend withholding tax, provided that each of the following tests are satisfied:

- the non-resident Shareholder is, according to the tax law of a Member State of the European Union or a state designated by a ministerial decree, that is a party to the Agreement regarding the European Economic Area, resident there and it is not transparent for tax purposes according to the tax law of such state;

- anyone or more of the following threshold conditions are satisfied:

    - at the time the dividend is distributed by us, the non-resident Shareholder holds shares representing at least five percent of our nominal paid-up capital; or

    - the non-resident Shareholder has held shares representing at least five percent of our nominal paid-up capital for a continuous period of more than one year at any time during four years preceding the time the dividend is distributed by us; or

    - the non-resident Shareholder is connected with us within the meaning of article 10a, paragraph 4 of the Dutch Corporate Income Tax Act 1969 (Wet op de vennootschapsbelasting 1969, or CITA); or

    - an entity connected with the non-resident Shareholder within the meaning of article 10a, paragraph 4 of CITA holds at the time of the dividends distributed by us, shares representing at least five per cent of our nominal paid-up capital; and

- the non-resident Shareholder is not considered to be resident outside the Member States of the European Union or the states designated by ministerial decree, that are party to the Agreement regarding the European Economic Area, under the terms of a tax treaty concluded with a third state.

A non-resident Shareholder which is resident in a Member State of the European Union with which the Netherlands has concluded a tax treaty that provides for a reduction of Dutch tax on dividends based on the ownership of the number of voting rights, the test under 2.a. above is also satisfied if the non-resident Shareholder owns at least five percent of the voting rights in us.

The exemption from Dutch dividend withholding tax is not available to a non-resident Shareholder if pursuant to a provision for the prevention of fraud or abuse included in a tax treaty between the Netherlands and the country of residence of the non-resident Shareholder, the non-resident Shareholder is not entitled to the reduction of Dutch tax on dividends provided for by such treaty.

Furthermore, pursuant to domestic anti-dividend stripping rules, no exemption from Dutch dividend withholding tax, refund or reduction of Dutch dividend withholding tax shall apply if the recipient of the dividend paid by us is not considered to be the beneficial owner (*uiteindelijk gerechtigde*) as meant in these rules, of such dividends. The Dutch tax authorities have taken the position that this beneficial ownership test can also be applied to deny relief from Dutch dividend

withholding tax under tax treaties and the Tax Arrangement for the Kingdom (*Belastingregeling voor het Koninkrijk*).

A non-resident Shareholder which is subject to Dutch income tax or Dutch corporate income tax in respect of any benefits derived or deemed to be derived from ordinary shares, including any capital gain realized on the disposal thereof, can generally credit Dutch dividend withholding tax against its Dutch income tax or its Dutch corporate income tax liability, as applicable, and is generally entitled to a refund pursuant to a negative tax assessment if and to the extent the Dutch dividend withholding tax, together with any other creditable domestic and/or foreign taxes, exceeds its aggregate Dutch income tax or its aggregate Dutch corporate income tax liability, respectively.

Taxes on Income and Capital Gains

Residents of the Netherlands

Individuals

A Shareholder, who is an individual resident or deemed to be resident in the Netherlands will be subject to regular Dutch personal income tax at progressive rates (up to a maximum rate of 52%) under the Dutch Income Tax Act 2001 on the income derived from the ordinary shares and gains realized on the disposal thereof if:

- such Shareholder derives any benefits from the ordinary shares, which are attributable to an enterprise of such Shareholder, whether as an entrepreneur or pursuant to a co-entitlement to the net worth of an enterprise, other than as a shareholder or an entrepreneur; or

- such income or gain is taxable in the hands of such Shareholder as benefits from miscellaneous activities (*resultaat uit overige werkzaamheden*), including but not limited to activities with respect to the ordinary shares that are beyond the scope of regular active portfolio management activities.

If neither of the two abovementioned conditions apply, such Shareholder must determine his or her taxable income with regard to the ordinary shares on the basis of a deemed return on income from savings and investments (*sparen en beleggen*), rather than on the basis of income actually received or gains actually realized. This deemed return on income from savings and investments has been fixed at a rate of 4% of the individual's yield basis at the beginning of the calendar year, insofar as the individual's yield basis exceeds a certain threshold. The individual's yield basis is determined as the fair market value of certain qualifying assets held by the individual less the fair market value of certain qualifying liabilities at the beginning of the calendar year.

Corporate entities

Generally, a Shareholder that is a corporation, another entity with a capital divided into shares, a cooperative (association), or another legal entity that has an enterprise to which the ordinary shares are attributable, that is resident or deemed to be resident in the Netherlands for Dutch corporate income tax purposes will be subject to regular Dutch corporate income tax, levied at a rate of 25% (20% over profits up to €200,000) over income derived from the ordinary shares and gains realized upon acquisition, redemption and disposal of ordinary shares.

If and to the extent that such Shareholder is eligible for the application of the participation exemption with respect to the ordinary shares, income derived from the ordinary shares and gains and losses (with the exception of liquidation losses under strict conditions) realized on the ordinary shares may be exempt from Dutch corporate income tax.

Non-residents of the Netherlands (including but not limited to U.S. Shareholders)

Individuals

A Shareholder, who is an individual not resident or deemed to be resident in the Netherlands will not be subject to any Dutch taxes on income or capital gains in respect of dividends distributed by us or in respect of any gain realized on the disposal of ordinary shares (other than dividend withholding tax as described above), except if:

- such holder has an enterprise or an interest in an enterprise that is, in whole or in part, carried on through a permanent establishment or a permanent representative in the Netherlands and to which enterprise or part of an enterprise, as the case may be, the ordinary shares are attributable; or

- such income or gain such income or gain is taxable in the hands of such Shareholder as benefits from miscellaneous activities including but not limited to activities with respect to the ordinary shares that are beyond the scope of regular active portfolio management.

If one of the two abovementioned conditions apply, the income or gains in respect of dividends distributed by us or in respect of any capital gain realized on the disposal of ordinary shares will in general be subject to Dutch personal income tax at the progressive rates up to 52%.

Corporate entities

A Shareholder, that is not an individual and not resident or deemed to be resident in the Netherlands for Dutch corporate income tax purposes, will not be subject to any Dutch taxes on income or capital gains in respect of dividends distributed by us, or in respect of any gain realized, on the disposal of ordinary shares (other than dividend withholding tax as described above), except if:

- such Shareholder has an enterprise or an interest in an enterprise that is, in whole or in part, carried on through a permanent establishment or a permanent representative in the Netherlands, to which the ordinary shares are attributable; or

- such Shareholder has a substantial interest or a deemed substantial interest in us (as described above), that (i) is held with the evasion of income tax or dividend withholding tax as (one of) the main purpose(s) and (ii) is not attributable to the assets of an enterprise of such Shareholder; or

- such Shareholder is an entity resident of Aruba, Curaçao or Saint Martin with a permanent establishment or permanent representative in Bonaire, Saint Eustatius or Saba to which such income or gain is attributable, and the permanent establishment or permanent representative would be deemed to be resident of the Netherlands for Dutch corporate income tax purposes (i) had the permanent establishment been a corporate entity (lichaam), or (ii) had the activities of the permanent representative been conducted by a corporate entity, respectively.

If one of the abovementioned conditions applies, income derived from the ordinary shares and gains realized on ordinary shares will, in general, be subject to regular Dutch corporate income tax levied at a rate of 25% (20% over profits up to €200,000), except that a holder referred to under (2) above will generally be subject to an effective corporate income tax rate of 15% if it holds the substantial interest in us only with the purpose of avoiding dividend withholding tax and not with (one of) the main purposes to avoid income tax.

Gift or Inheritance Taxes

No Dutch gift or Dutch inheritance tax is due in respect of any gift, in form or in substance, of the ordinary shares by, or inheritance of the shares on the death of, a Shareholder except if:

- at the time of the gift or death of the Shareholder, the Shareholder is resident, or deemed to be resident, in the Netherlands for purposes of Dutch gift tax or Dutch inheritance tax, as applicable; or

- in the case of a gift of ordinary shares by an individual who at the date of the gift was neither resident nor deemed to be resident in the Netherlands (i) such individual dies within 180 days after the date of the gift, while being resident or deemed to be resident in the Netherlands; or (ii) the gift of ordinary shares is made under a condition precedent (opschortende voorwaarde) and the Shareholder is resident, or is deemed to be resident in the Netherlands at the time the condition is fulfilled.

For purposes of the above, a gift of ordinary shares made under a condition precedent is deemed to be made at the time the condition precedent is satisfied.

For purposes of Dutch gift or Dutch inheritance taxes, an individual not holding the Dutch nationality will be deemed to be resident in the Netherlands, *inter alia*, if he or she has been resident in the Netherlands at any time during the ten years preceding the date of the gift or his or her death. Additionally, for purposes of Dutch gift tax, an individual not holding the Dutch nationality will be deemed to be resident in the Netherlands if he or she has been resident in the Netherlands at any time during the twelve months preceding the date of the gift. Applicable tax treaties may override deemed residency in the Netherlands.

Value Added Tax

No Dutch value added tax will arise in respect of payments in consideration for the issue, acquisition, ownership and disposal of ordinary shares, other than value added taxes on fees payable in respect of services not exempt from Dutch value added tax.

Other Taxes and Duties

No Dutch registration tax, capital tax, custom duty, transfer tax, stamp duty or any other similar tax or duty, other than court fees, will be payable in the Netherlands in respect of or in connection with the subscription, issue, placement, allotment, delivery or transfer of the ordinary shares.

Residence

A Shareholder will not become resident, or deemed resident in the Netherlands for tax purposes by reason only of holding the ordinary shares.

Taxation in the United States

The following summary of the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares is based upon current law and does not purport to be a comprehensive discussion of all the tax considerations that may be relevant to our ordinary shares. This summary is based on current provisions of the Code, existing, final, temporary and proposed U.S. Treasury Regulations, administrative rulings and judicial decisions, in each case as available on the date of this annual report. All of the foregoing are subject to change, which change could apply retroactively and could affect the tax consequences described below.

This section summarizes the material U.S. federal income tax consequences to U.S. holders, as defined below, of ordinary shares. This summary addresses only the U.S. federal income tax

considerations for U.S. holders that acquire the ordinary shares at their original issuance and hold the ordinary shares as capital assets. This summary does not address all U.S. federal income tax matters that may be relevant to a particular U.S. holder. **Each prospective investor should consult a professional tax advisor with respect to the tax consequences of the acquisition, ownership or disposition of the ordinary shares**. This summary does not address tax considerations applicable to a holder of ordinary shares that may be subject to special tax rules including, without limitation, the following:

- certain financial institutions;
- insurance companies;
- dealers or traders in securities, currencies, or notional principal contracts;
- tax-exempt entities;
- regulated investment companies;
- persons that hold the ordinary shares as part of a hedge, straddle, conversion, constructive sale or similar transaction involving more than one position;
- persons that hold the ordinary shares through partnerships or certain other pass-through entities;
- holders (whether individuals, corporations or partnerships) that are treated as expatriates for some or all U.S. federal income tax purposes;
- holders that own (or are deemed to own) 10% or more of our voting shares; and
- holders that have a "functional currency" other than the U.S. dollar.

Further, this summary does not address alternative minimum tax consequences or the indirect effects on the holders of equity interests in entities that own our ordinary shares. In addition, this discussion does not consider the U.S. tax consequences to holders of ordinary shares that are not "U.S. holders" (as defined below).

For the purposes of this summary, a "U.S. holder" is a beneficial owner of ordinary shares that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is either a citizen or resident of the United States;
- a corporation, or other entity that is treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or any state of the United States or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust or has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

If a partnership holds ordinary shares, the tax treatment of a partner will generally depend upon the status of the partner and upon the activities of the partnership.

We will not seek a ruling from the U.S. Internal Revenue Service, or IRS, with regard to the U.S. federal income tax treatment of an investment in our ordinary shares, and we cannot provide assurance that that the IRS will agree with the conclusions set forth below.

Distributions. Subject to the discussion under "*Passive Foreign Investment Company Considerations*" below, the gross amount of any distribution (including any amounts withheld in respect of Dutch withholding tax) actually or constructively received by a U.S. holder with respect to ordinary shares will be taxable to the U.S. holder as a dividend to the extent of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of earnings and profits will be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in the ordinary shares. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as capital gain from the sale or exchange of property. However, since we do not calculate our earnings and profits under U.S. federal income tax principles, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. The amount of any distribution of property other than cash will be the fair market value of that property on the date of distribution. The U.S. holder will not be eligible for any dividends-received deduction in respect of the dividend otherwise allowable to corporations.

Under the Code and subject to the discussion below regarding the "Medicare tax," qualified dividends received by non-corporate U.S. holders (*i.e.*, individuals and certain trusts and estates) are subject to a maximum income tax rate of 20%. This reduced income tax rate is applicable to dividends paid by "qualified foreign corporations" to such non-corporate U.S. holders that meet the applicable requirements, including a minimum holding period (generally, at least 61 days during the 121-day period beginning 60 days before the ex-dividend date). We expect to be considered a qualified foreign corporation under the Code. Accordingly, dividends paid by us to non-corporate U.S. holders with respect to shares that meet the minimum holding period and other requirements are expected to be treated as "qualified dividend income." However, dividends paid by us will not qualify for the 20% maximum U.S. federal income tax rate if we are treated, for the tax year in which the dividends are paid or the preceding tax year, as a "passive foreign investment company" for U.S. federal income tax purposes, as discussed below.

Dividends received by a U.S. holder with respect to ordinary shares generally will be treated as foreign source income for the purposes of calculating that holder's foreign tax credit limitation. Subject to applicable conditions and limitations, and subject to the discussion in the next paragraph, any Dutch income tax withheld on dividends may be deducted from taxable income or credited against a U.S. holder's U.S. federal income tax liability. The limitation on foreign taxes eligible for the U.S. foreign tax credit is calculated separately with respect to specific classes of income. For this purpose, dividends distributed by us generally will constitute "passive category income" (but, in the case of some U.S. holders, may constitute "general category income").

Upon making a distribution to shareholders, we may be permitted to retain a portion of the amounts withheld as Dutch dividend withholding tax. See "—Taxation in the Netherlands—Dividend Withholding Tax—General." The amount of Dutch withholding tax that we may retain reduces the amount of dividend withholding tax that we are required to pay to the Dutch tax authorities but does not reduce the amount of tax we are required to withhold from dividends paid to U.S. holders. In these circumstances, it is likely that the portion of dividend withholding tax that we are not required to pay to the Dutch tax authorities with respect to dividends distributed to U.S. holders would not qualify as a creditable tax for U.S. foreign tax credit purposes.

Sale or other disposition of ordinary shares. A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale or exchange of ordinary shares in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange and the U.S. holder's tax basis for those ordinary shares. Subject to the discussion under "*Passive Foreign Investment Company Considerations*" below, this gain or loss will generally be a capital gain or loss and will generally be treated as from sources within the United States. Such capital gain or loss will be treated as long-term capital gain or loss if the U.S. holder has held the ordinary shares for more than

one year at the time of the sale or exchange. Long-term capital gains of non-corporate holders may be eligible for a preferential tax rate; the deductibility of capital losses is subject to limitations.

Medicare Tax. A "United States person," within the meaning of the Code, that is an individual, an estate or a nonexempt trust is generally subject to a 3.8% surtax on the lesser of (i) the United States person's "net investment income" for the year and (ii) the excess of the United States person's "modified adjusted gross income" for that year over a threshold (which, in the case of an individual, will be between $125,000 and $250,000, depending on the individual's U.S. tax filing status). A U.S. holder's net investment income generally will include, among other things, dividends on, and gains from the sale or other taxable disposition of, our ordinary shares, unless (with certain exceptions) those dividends or gains are derived in the ordinary course of a trade or business. Net investment income may be reduced by deductions properly allocable thereto; however, the U.S. foreign tax credit may not be available to reduce the surtax.

Passive foreign investment company considerations. A corporation organized outside the United States generally will be classified as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in any taxable year in which either: (i) at least 75% of its gross income is passive income, or (ii) on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held for the production of passive income. In arriving at this calculation, a pro rata portion of the income and assets of each corporation in which we own, directly or indirectly, at least a 25% interest, as determined by the value of such corporation, must be taken into account. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions.

We believe that we were not a PFIC for the 2014 taxable year. Based on our estimated gross income, the average value of our gross assets, and the nature of the active businesses conducted by our "25% or greater" owned subsidiaries, we do not believe that we will be classified as a PFIC in the current taxable year and do not expect to become one in the foreseeable future. However, our status for 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 not be considered a PFIC for the current taxable year or any future taxable year. 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 technology companies have been especially volatile. In addition, the composition of our income and assets will be affected by how, and how quickly, we spend our cash.

If we were a PFIC for any taxable year during which a U.S. holder held ordinary shares, under the "default PFIC regime" (i.e., in the absence of one of the elections described below) gain recognized by the U.S. holder on a sale or other disposition (including a pledge) of the ordinary shares would be allocated ratably over the U.S. holder's holding period for the ordinary shares. The amounts allocated to the taxable year of the sale or other disposition and to any year before we became a PFIC would be taxed as ordinary income. The amount allocated to each other taxable year would be subject to tax at the highest rate in effect for individuals or corporations, as appropriate, for that taxable year, and an interest charge would be imposed on the resulting tax liability for that taxable year. Similar rules would apply to the extent any distribution in respect of ordinary shares exceeds 125% of the average of the annual distributions on ordinary shares received by a U.S. holder during the preceding three years or the holder's holding period, whichever is shorter.

In the event we were treated as a PFIC, the tax consequences under the default PFIC regime described above could be avoided by either a "mark- to-market" or "qualified electing fund" election. As long as our ordinary shares are regularly traded on the NASDAQ Global Select Market or another "qualified exchange," a U.S. holder making a mark-to-market election generally would not be subject to the PFIC rules discussed above, except with respect to any portion of the holder's holding period

that precedes the effective date of the election. Instead, the electing holder would include in ordinary income, for each taxable year in which we were a PFIC, an amount equal to any excess of (a) the fair market value of the ordinary shares as of the close of such taxable year over (b) the electing holder's adjusted tax basis in such ordinary shares. In addition, an electing holder would be allowed a deduction in an amount equal to the lesser of (a) the excess, if any, of (i) the electing holder's adjusted tax basis in the ordinary shares over (ii) the fair market value of such ordinary shares as of the close of such taxable year or (b) the excess, if any, of (i) the amount included in ordinary income because of the election for prior taxable years over (ii) the amount allowed as a deduction because of the election for prior taxable years. The election would cause adjustments in the electing holder's tax basis in the ordinary shares to reflect the amount included in gross income or allowed as a deduction because of the election. In addition, upon a sale or other taxable disposition of ordinary shares, an electing holder would recognize ordinary income or loss (not to exceed the excess, if any, of (a) the amount included in ordinary income because of the election for prior taxable years over (b) the amount allowed as a deduction because of the election for prior taxable years).

Alternatively, a U.S. holder making a valid and timely "QEF election" generally would not be subject to the default PFIC regime discussed above. Instead, for each PFIC year to which such an election applied, the electing holder would be subject to U.S. federal income tax on the electing holder's pro rata share of our net capital gain and ordinary earnings, regardless of whether such amounts were actually distributed to the electing holder. However, because we do not intend to prepare or provide the information that would permit the making of a valid QEF election, that election will not be available to U.S. holders.

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 or not the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year.

Backup Withholding and Information Reporting. U.S. holders generally will be subject to information reporting requirements with respect to dividends on ordinary shares and on the proceeds from the sale, exchange or disposition of ordinary shares that are paid within the United States or through U.S.-related financial intermediaries, unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding (at a 28% rate) on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

EXPENSES RELATED TO THE OFFERING

We estimate the fees and expenses to be incurred by us in connection with the sale of the ordinary shares in this offering, other than underwriting discounts and commissions payable by us, to be as follows:

SEC registration fees	$ 13,500
FINRA filing fee	17,500
Transfer agent's fees	5,000
Legal fees and expenses	350,000
Accounting fees and expenses	200,000
Printing expenses	100,000
Miscellaneous expenses	64,000
Total	$ 750,000

LEGAL MATTERS

Legal matters with respect to U.S. federal and New York law in connection with this offering will be passed upon for us by Morgan, Lewis & Bockius UK LLP, London, England. Certain legal matters with respect to Dutch law in connection with the validity of the shares being offered by this prospectus and other legal matters will be passed upon for us by Rutgers Posch Visée Endedijk N.V., Amsterdam, the Netherlands. The underwriters are represented by Covington & Burling LLP, New York, New York.

EXPERTS

The financial statements incorporated in this Prospectus Supplement by reference to the Annual Report on Form 20-F for the year ended December 31, 2014 have been so incorporated in reliance on the report of PricewaterhouseCoopers Accountants N.V., an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

ENFORCEABILITY OF CIVIL LIABILITIES

uniQure N.V. is incorporated under the laws of the Netherlands. Substantially all of our business is conducted, and substantially all of our assets are currently located, in the Netherlands. Most of the members of our management and supervisory boards and the experts named in this prospectus are residents of, and most of their assets are located in, jurisdictions outside the United States. As a result, it may be difficult for you to serve process on us or these persons within the United States or to enforce against us or these persons in courts in the United States, judgments of these courts predicated upon the civil liability provisions of U.S. securities laws. In addition, it is not clear whether a Dutch court would impose civil liability on us, members of our management or supervisory boards or any of the experts named in this prospectus 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.

As there is no treaty on the reciprocal recognition and enforcement of judgments in civil and commercial matters between the United States and the Netherlands, courts in the Netherlands will not automatically recognize and enforce a final judgment rendered by a U.S. court. In order to obtain a judgment enforceable in the Netherlands, claimants must litigate the relevant claim again before a Dutch court of competent jurisdiction. Under current practice, however, a Dutch court will generally uphold and consider as conclusive evidence a final and conclusive judgment for the payment of money rendered by a U.S. court and not rendered by default, provided that the Dutch court finds that:

- the jurisdiction of the United States court has been based on grounds that are internationally acceptable;

- the final judgment results from proceedings compatible with Dutch concepts of due process;
- the final judgment does not contravene public policy of the Netherlands; and
- the final judgment has not been rendered in proceedings of a penal, revenue or other public law nature.

If a Dutch court upholds and regards as conclusive evidence the final judgment, that court generally will grant the same judgment without litigating again on the merits.

In the event a third party is liable to a Dutch company, only the company itself can bring a civil action against that party. The individual shareholders do not have the right to bring an action on behalf of the company. Only in the event that the cause for the liability of a third party to the company also constitutes a tortious act directly against a shareholder does that shareholder have an individual right of action against such third party in its own name. The Dutch Civil Code *(Burgerlijk Wetboek)* does provide for the possibility to initiate such actions collectively. A foundation or an association whose objective is to protect the rights of a group of persons having similar interests can institute a collective action. The collective action itself cannot result in an order for payment of monetary damages but may only result in a declaratory judgment (*verklaring voor recht*). In order to obtain compensation for damages, the foundation or association and the defendant may reach—often on the basis of such declaratory judgment—a settlement. A Dutch court may declare the settlement agreement binding upon all the injured parties with an opt-out choice for an individual injured party. An individual injured party may also itself institute a civil claim for damages.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form F-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. You may read and copy the registration statement and its exhibits at the SEC's Public Reference Room at 100 F Street N.E., Room 1580, Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains an internet website at www.sec.gov, from which you can electronically access the registration statement and its exhibits.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act, applicable to foreign private issuers. Because we are a foreign private issuer, the SEC's rules do not require us to deliver proxy statements pursuant to Section 14 of the Exchange Act or to file quarterly reports on Form 10-Q, among other things. In addition, our "insiders" are not subject to the SEC's rules that prohibit short-swing trading. Our annual consolidated financial statements are prepared in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board and certified by an independent public accounting firm.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with the SEC, by referring you to other documents filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus will be deemed to incorporate by reference our Annual Report on Form 20-F for the year ended December 31, 2014, filed with the SEC on April 7, 2014, as well as our Report on Form 6-K filed with the SEC on April 6, 2015, announcing our collaboration and license agreement with Bristol-Myers Squibb Company.

Any information that we file later with the SEC and that is deemed incorporated by reference will automatically update and supersede the information in this prospectus supplement and the accompanying prospectus. In all such cases, you should rely on the later information over different information included in this prospectus supplement, the accompanying prospectus or in any incorporated document. You should not assume that information in any document incorporated by reference into this prospectus supplement or the accompanying prospectus is current as of any date other than the date of that document.

You may request a copy of these filings, at no cost, by writing, telephoning or emailing us at the following address:

uniQure N.V.
Meibergdreef 61
1105 BA Amsterdam, the Netherlands
Attention: Company Secretary
Tel.: 011-31-20-240-6000
IR@uniqure.com

PROSPECTUS

$250,000,000

DEBT SECURITIES
WARRANTS
RIGHTS
PURCHASE CONTRACTS
UNITS
ORDINARY SHARES

We may offer debt securities, warrants, rights, purchase contracts, units, or ordinary shares from time to time. We may also offer securities of the types listed above that are convertible or exchangeable into one or more of the other securities so listed. When we decide to sell a particular class or series of securities, we will provide specific terms of the offered securities in a prospectus supplement. The securities offered by us pursuant to this prospectus will have an aggregate public offering price of up to $250,000,000.

The securities covered by this prospectus may be offered and sold from time to time in one or more offerings, which may be through one or more underwriters, dealers and agents, or directly to purchasers. The names of any underwriters, dealers or agents, if any, will be included in a supplement to this prospectus.

This prospectus describes some of the general terms that may apply to these securities and the general manner in which they may be offered. The specific terms of any securities to be offered, and the specific manner in which they may be offered, will be described in one or more supplements to this prospectus.

Our ordinary shares are listed on the NASDAQ Global Select Market under the symbol "QURE."

uniQure N.V. is a public company with limited liability *(naamloze vennootschap)* incorporated under the laws of the Netherlands. Our principal executive offices are located at Meibergdreef 61, Amsterdam 1105 BA, the Netherlands. Our telephone number at such address is 011 31 20 566 7394.

Investing in our securities involves risks. See the section entitled "*Risk Factors*" on page iii of this prospectus.

Neither the Securities and Exchange Commission nor any state or other securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Prospectus dated March 13, 2015.

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You should rely only on the information provided in this prospectus and the accompanying prospectus supplement, as well as the information incorporated by reference. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should not assume that the information in this prospectus, any prospectus supplement or any documents incorporated by reference is accurate as of any date other than the date of the applicable document.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the documents incorporated herein and therein by reference contain forward-looking statements based on beliefs of our management. Any statements contained in this prospectus, any prospectus supplement or the documents incorporated herein and therein that are not historical facts are forward-looking statements as defined in Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934 (the "Exchange Act"). We have based these forward-looking statements on our current expectations and projections about future events, including:

- the timing of commencement of and receipt of data from our planned clinical trials;
- the timing of the ongoing and planned clinical trials conducted by our collaborators and other third parties;
- our ongoing and planned discovery and development of product candidates;
- our expectations regarding the timing or likelihood of regulatory filings and approvals for our product candidates;
- our ability to expand our sales, marketing and medical affairs infrastructure;
- our ability to successfully commercialize Glybera and our product candidates;
- the potential advantages of Glybera and our product candidates;
- our estimates regarding the market opportunities for our product candidates;
- the rate and degree of market acceptance and clinical benefit of Glybera and our product candidates;
- our expectations regarding milestone, royalty and expense reimbursement payments under our licensing arrangements;
- our estimates of the net amount will we retain from sales of Glybera;
- the operating costs of our manufacturing facility in Lexington, Massachusetts;
- our ability to establish and maintain collaborations;
- our ability to develop, acquire or in-license additional product candidates and other key intellectual property;
- our future intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and
- other factors discussed in the section entitled "Risk Factors" in our Annual Report on Form 20-F.

The words "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "predict," "potential," "should" and "will" and similar expressions as they relate to us are intended to identify such forward-looking statements. These forward-looking statements are not statements of historical fact and represent only our management's belief as of the date of such statement, and involve risks and uncertainties that could cause actual results to differ materially and inversely from expectations expressed in or indicated by the forward-looking statements. Assumptions, expectations, projections, intentions and beliefs about future events may, and often do, vary from actual results and these differences can be material. There are a variety of factors, many of which are beyond our control, which affect our operations, performance, business strategy and results and could cause actual reported

results and performance to differ materially from the performance and expectations expressed in these forward-looking statements. We caution readers of this prospectus and any prospectus supplement not to place undue reliance on these forward-looking statements, which speak only as of their dates. We undertake no obligation to publicly update or revise any forward-looking statements.

RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the risks and discussion of risks set forth under the heading "Item 3. Key Information—D. Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2013, filed with the SEC on April 25, 2014, and the other documents we have incorporated by reference in this prospectus, including the section entitled "Item 3. Key Information—D. Risk Factors" in future Annual Reports on Form 20-F that summarize the risks that may materially affect our business, before making an investment in our securities. Please see the sections of this prospectus entitled "Where You Can Find Additional Information" and "Incorporation of Certain Information By Reference."

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are a Netherlands corporation and our principal executive offices are located outside of the United States in Amsterdam, the Netherlands. The majority of our directors and officers and some of the experts named in this prospectus reside outside the United States. In addition, a substantial portion of our assets and the assets of our directors, officers and experts are located outside of the United States. As a result, you may have difficulty serving legal process within the United States upon us or any of these persons. You may also have difficulty enforcing, both in and outside of the United States, judgments you may obtain in U.S. courts against us or these persons in any action, including actions based upon the civil liability provisions of U.S. Federal or state securities laws.

Furthermore, there is substantial doubt that the courts of the Netherlands would enter judgments in original actions brought in those courts predicated on U.S. federal or state securities laws.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC utilizing a "shelf" registration process. Under this shelf process, we may sell from time to time any combination of the securities described in this prospectus having an aggregate public offering price of $250,000,000 in one or more offerings. This prospectus provides you with a general description of the securities we may offer. When we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described under the heading "Where You Can Find Additional Information" and "Incorporation Of Certain Information By Reference."

PROSPECTUS SUMMARY

This summary provides a brief overview of the key aspects of uniQure N.V. and certain material terms of the securities that may be offered that are known as of the date of this prospectus. Before you decide to invest in our ordinary shares, you should carefully consider the risks and discussion of risks set forth under the heading "Item 3. Key Information—D. Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2013, filed with the SEC on April 25, 2014 and the subsequent Annual Reports on Form 20-F that we filed with the SEC. When we use the words "the Company," "we," "us," "ours" and "our," we are referring t uniQure N.V. For a more complete understanding of the terms of a particular issuance of offered securities, and before making your investment decision, you should carefully read:

- *this prospectus, which explains the general terms of the securities that we may offer;*
- *the accompanying prospectus supplement for such issuance, which explains the specific terms of the securities being offered and which may update or change information in this prospectus; and*
- *the documents referred to in "Where You Can Find Additional Information" for information about us, including our financial statements.*

Our Company

We are a leader in the field of gene therapy and have a robust technology platform that we use as the basis for our proprietary and collaborative product lines across multiple therapeutic areas. Our core gene therapies include AMT-060 for the treatment of hemophilia B, which we expect to enter into a Phase I/II clinical trial in the first half of 2015; InoCor for the treatment of congestive heart failure, which is at the preclinical/proof of concept phase; and Glybera, the first and currently the only gene therapy product to receive regulatory approval in the European Union.

Our aim is to make gene therapy a mainstay of modern medicine by:

- using our strong technology platform to develop our own programs in three therapeutic areas, liver-based diseases, cardio/metabolic diseases, and central nervous system diseases, in which we have a competitive advantage, with the potential to significantly de-risk development programs, and reduce development cost and time to market;
- sponsoring and acquiring additional early-stage programs in these areas from other biopharmaceutical companies and academic investigators;
- enhancing and accelerating these programs through our modularized research and development platform and our experience of the EU and FDA regulatory environments for gene therapies;
- applying our industrialized manufacturing process to produce the highest-quality material for our own and our collaborators' programs, and
- collaborating with pharmaceutical companies with the necessary expertise to enhance our late-stage therapy development and maximize the value of our therapies at the commercialization stage.

We believe that our technology platform and strategic collaborations place us at the forefront of gene therapy within our chosen therapeutic areas. Our transgene delivery system is based on common, adeno-associated viruses, or AAV, which we believe are safe and effective delivery methods for efficient expression of transgenes. We have the exclusive or non-exclusive rights to natural AAV serotypes for lipoprotein lipase deficiency, or LPLD, liver and CNS applications and the capability to identify and develop synthetic AAV vectors that are designed to optimize the expression of a particular transgene in specific tissue types. We produce ou AAV-based vectors in our own facilities with a proprietary, commercial-scale, consistent, and robust manufacturing process using insect cells and baculoviruses, a common family of viruses found in invertebrates. We believe our Lexington, Massachusetts-based

facility, which is currently being qualified, is one of the world's largest, most versatile, gene therapy manufacturing facilities. We believe this robust technology platform, combined with our know-how derived from achieving the first regulatory approval of a gene therapy in the European Union, provides us a significant advantage in bringing our gene therapy products to the market ahead of our competitors.

We seek to develop gene therapies targeting a range of liver-based, cardio/metabolic and CNS indications, from ultra-orphan diseases, such as LPLD (for which Glybera is designated), to orphan diseases such as hemophilia B, to common diseases that affect far larger populations, such as congestive heart failure. The core of uniQure is a versatile and universal technology backbone, applicable to multiple therapeutic areas with the potential to significantly de-risk development programs, and reduce development cost and time to market. As part of our strategy, we are accessing important medical expertise for our therapeutic focuses through strong ties with academic thought leaders and clinical institutions. For cardio/metabolic diseases we are building a center of expertise in our German subsidiary, uniQure GmbH, in close cooperation with leading academic clinicians and surgeons at the university hospital and heart center in Heidelberg, Germany. Our CNS activities are based o strong collaborations with the University of California at San Francisco, the National Institutes of Health, and the Institut Pasteur, Paris, France. Our hemophilia B product originates from St. Jude Children's research Hospital in Memphis, Tennessee. We also seek to collaborate with or acquire emerging companies within our chosen therapeutic areas that are conducting or sponsoring early-stage clinical trials. Our collaborations allow us to cost-effectively obtain access to pre-clinical and early-stage programs without expending significant resources of our own. We generally have the rights to the data generated in these collaborator-sponsored programs but do not control their design or timing. Our collaboration programs include gene therapy candidates for Parkinson's disease, Sanfilippo B syndrome, Acute Intermittent Porphyria, and amyotrophic lateral sclerosis.

Risks Associated with our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision, including the following:

- We have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future. As of September 30, 2014, we had an accumulated deficit of €169.9 million. We will likely need additional funding, and such funding may cause substantial dilution to our shareholders.

- Our gene therapies are novel technologies and face uncertainty in the regulatory review and approval process. Although we have received marketing approval under exceptional circumstances for Glybera in the European Union, we cannot predict when or if we will obtain marketing approval in any other jurisdiction or for any other product candidate. Any approval we may receive may be for a narrower indication than we expect or may be subject to costly post-approval requirements, which could restrict or eliminate the potential commercial success of the product candidate.

- Glybera and any of our product candidates for which we obtain marketing approval in the future, as well as our manufacturing processes, post-approva studies and other activities, will be subject to continued requirements of and review by the FDA, EMA and other regulatory authorities. Any failure by us to meet these requirements could require us to expend significant resources or conduct further studies, and ultimately could potentially result in the limitation or revocation of the relevant marketing approval.

- Gene therapies are complex and difficult to manufacture, and we could experience manufacturing problems that result in delays in our development or commercialization

schedules, prevent us from meeting our commercial obligations to our collaborators, or otherwise adversely affect our business.

- Our product candidates are in early clinical or preclinical development and there is significant risk of failure or delay in these programs. We rely on ou collaborators for important aspects of our development program and in many cases we have limited or no control over the design and conduct of the trials our collaborators conduct, or the efforts and resources our collaborators expend.

- The future growth of our business depends in significant part on our ability to enter into additional collaborations or to in-license or acquire rights to new product candidates and technologies. If we are unable to attract collaborators or successfully identify or compete for the rights to new technologies, our prospects for growth could be limited.

- We may be unable to obtain, maintain and protect necessary intellectual property rights, which could harm our ability to compete and impair our business. We rely upon licenses of proprietary technology from third parties and these licenses may not provide adequate rights, we may lose or be unable to protect these rights, or we may be unable to acquire additional intellectual property required for our development programs.

- We face substantial competition, and others may discover, develop or commercialize products before or more successfully than we do.

Corporate Information

We were incorporated on January 9, 2012 as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) under the laws of the Netherlands. Our business was founded in 1998 and was initially operated through our predecessor company, Amsterdam Molecular Therapeutics (AMT) Holding N.V, or AMT. In 2011, 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 in the first half of 2012. In February 2014, we completed an initial public offering of shares of our ordinary shares in the United States and our ordinary shares began trading on the Nasdaq Stock Market. In connection with our initial public offering, we converted to a public company with limited liability (naamloze vennootschap) under the laws of the Netherlands. In connection with this conversion, our legal name changed from uniQure B.V. to uniQure N.V.

Our principal executive offices are located at Meibergdreef 61, Amsterdam 1105 BA, the Netherlands. Our telephone number at such address is 011 31 20 566 7394.

The Securities We May Offer

We may use this prospectus to offer any of the following types of securities having an aggregate public offering price of $250,000,000:

- debt securities;
- warrants;
- rights;
- purchase contracts;
- units; and
- ordinary shares;

We may issue securities of the types listed above which are convertible or exchangeable for other securities so listed.

When we decide to sell a particular class or series of securities, we will provide specific terms of the offered securities in a prospectus supplement.

A prospectus supplement will describe the specific types, amounts, prices, and detailed terms of any of these offered securities and may describe certain risks associated with an investment in the securities. Terms used in the prospectus supplement will have the meanings described in this prospectus, unless otherwise specified.

Ratio of Earnings to Fixed Charges

The following table shows our ratios of earnings to fixed charges for the periods indicated, computed using amounts derived from our consolidated financial statements prepared in accordance with International Financial Reporting Standards.

	(Unaudited)			
	Nine Months Ended September 30, 2014	Year Ended December 31,		
		2013	2012	2011
Ratio of Earnings to Fixed Charges	*	*	*	*
Amount of the coverage deficiency (€ in '000s)	€(25,879)	€(26,820)	€(14,716)	€(17,300)

* Our earnings were insufficient to cover fixed charges in each period presented. We would have needed to generate additional earnings in the amounts indicated above in each period to achieve a coverage ratio of 1:1.

For the purpose of computing the consolidated ratio of earnings to fixed charges, earnings consist of pre-tax loss plus fixed charges. Fixed charges consist of interest expensed, the interest portion of rental expense and amortization of debt expenses relating to indebtedness.

Listing

Our ordinary shares are listed on the NASDAQ Global Select Market under the symbol "QURE." If any other securities are to be listed or quoted on a securities exchange or quotation system, the applicable prospectus supplement will so state.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

As required by the Securities Act, we have filed a registration statement relating to the securities offered by this prospectus with the SEC. This prospectus is a part of that registration statement, which includes additional information.

We file annual and other reports and other information with the SEC. Such filings are available to the public from the SEC's website at http://www.sec.gov. You may also read and copy any documents we file at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at that address. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with the SEC, by referring you to other documents filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus. Any information that we file later with the SEC and that is deemed incorporated by reference will automatically update and supersede the information in this prospectus. In all such cases, you should rely on the later information over different information included in this prospectus or in any incorporated document. You should not assume that information in any document incorporated by reference into this prospectus or any accompanying prospectus supplement is current as of any date other than the date of that document. This prospectus will be deemed to incorporate by reference the following documents:

- Our Annual Report on Form 20-F for the year ended December 31, 2013, filed with the SEC on April 25, 2014;
- Our Reports on Form 6-K, filed with the SEC on May 20, 2014, June 16, 2014, July 2, 2014, August 12, 2014, December 1, 2014, January 9, 2015 and March 3, 2015; and.
- The description of our ordinary shares contained in our registration statement on Form 8-A (File No. 001-36294), filed with the SEC on January 31, 2014.

* Pursuant to Rule 406T of Regulation S-T, the interactive data files contained in such document are deemed not filed or part of this prospectus, or the registration statement of which this prospectus forms a part, for purposes of sections 11 or 12 of the Securities Act, are deemed not filed for purposes of Section 18 of the Exchange Act, and otherwise are not subject to liability under those sections.

We will also incorporate by reference any future filings made with the SEC under the Exchange Act after (i) the date of the initial registration statement and prior to the effectiveness of the registration statement and (ii) the date of this prospectus and before the completion of the offering of the securities under the registration statement. In addition, we will incorporate by reference certain future materials furnished to the SEC on Form 6-K after the date of the initial registration statement, but only to the extent specifically indicated in those submissions or in a future prospectus supplement. Each subsequently filed Annual Report should be deemed to supersede entirely each earlier filed Annual Report and Reports on Form 6-K containing our quarterly earnings releases and, unless explicitly stated otherwise, such earlier reports should not be deemed to be part of this prospectus or any accompanying prospectus supplement and you should not rely upon statements made in those earlier periodic reports.

You may request a copy of these filings, at no cost, by writing, telephoning or emailing us at the following address:

uniQure N.V.
Meibergdreef 61
Amsterdam 1105 BA, the Netherlands
Attention: Company Secretary
Tel.: 011-31-20-566-7394
IR@uniqure.com

USE OF PROCEEDS

Unless otherwise set forth in a prospectus supplement, we intend to use the net proceeds received from the sale of the securities we offer by this prospectus as follows:

- to fund our share of the costs of our planned Phase I/II clinical trial of AMT-060 in hemophilia B;
- to support our further clinical development of Glybera, and our application for marketing approval of Glybera and preparation for potential commercial launch in the United States;
- to pursue the pre-clinical and clinical development of product candidates for cardiovascular diseases targeting S100A1, a novel target we obtained as part of our acquisition of InoCard;
- to fund the operation of our manufacturing facility in Lexington, Massachusetts;
- to advance the development of our other product candidates and research activities, including our collaboration with 4D Molecular Therapeutics; and
- for working capital and for general corporate purposes, including the costs of operating our facilities in Amsterdam and in Lexington, Massachusetts, service on our indebtedness and possibly acquisitions or investments in other businesses, technologies or product candidates.

We may raise additional funds from time to time through equity or debt financings not involving the issuance of securities described in this prospectus, including borrowings under credit facilities, to finance our business and operations and our new vessel acquisitions.

CAPITALIZATION

Information on our consolidated capitalization will be contained in a prospectus supplement.

DESCRIPTION OF SECURITIES WE MAY OFFER

DEBT SECURITIES

In this section, references to "holders" mean those who own debt securities registered in their own names on the books that uniQure N.V. or the indenture trustee maintains for this purpose, and not those who own beneficial interests in debt securities registered in street name or in debt securities issued in book-entry form through one or more depositaries. Owners of beneficial interests in the debt securities should read the section below entitled "Book-Entry Procedures and Settlement."

General

The debt securities offered by this prospectus will be either senior or subordinated debt. Senior debt securities or subordinated debt securities may be convertible or exchangeable into our ordinary shares or other securities as described under "—Convertible or Exchangeable Securities" below. We will issue senior debt under a senior debt indenture, we will issue subordinated debt under a subordinated debt indenture and we will issue convertible debt securities under a convertible debt indenture. We sometimes refer to the senior debt indenture, the subordinated debt indenture and the convertible debt indenture individually as an indenture and collectively as the indentures. The indentures will be between us and a trustee. The terms of the indenture governing the convertible debt securities will be substantially similar to the terms of the indenture governing the senior debt securities described below, except that the indenture governing the convertible debt securities will include provisions with respect to the conversion of such convertible debt securities, omit certain provisions described under "—Defeasance" below, prohibit any modification to the terms of convertibility without the consent of the holders and permit any holder to institute action to enforce such terms of convertibility. The indentures are exhibits to the registration statement of which this prospectus forms a part. You can obtain copies of the indentures by following the directions outlined in "Where You Can Find Additional Information" or by contacting the indenture trustee.

The following briefly summarizes the material provisions of the indentures and the debt securities, other than pricing and related terms which will be disclosed for a particular series of debt securities in a prospectus supplement. You should read the more detailed provisions of the applicable indenture, including the defined terms, for provisions that may be important to you. You should also read the particular terms of a series of debt securities, which will be described in more detail in a prospectus supplement. Wherever particular sections or defined terms of the applicable indenture are referred to, such sections or defined terms are incorporated into this prospectus by reference, and the statement in this prospectus is qualified by that reference.

The indentures provide that our debt securities may be issued in one or more series, with different terms, in each case as we authorize from time to time. We also have the right to reopen a previous issue of a series of debt securities by issuing additional debt securities of such series.

Information in the Prospectus Supplement

The prospectus supplement for any offered series of debt securities will describe the following terms, as applicable:

- the title or designation of the offered debt securities;
- whether the debt is senior or subordinated;
- whether there is any collateral securing the debt securities;
- whether the debt securities are convertible or exchangeable into other securities;
- the aggregate principal amount offered and the authorized denominations;

- the initial public offering price;
- the maturity date or dates;
- any sinking fund or other provision for payment of the debt securities prior to their stated maturity;
- whether the debt securities are fixed rate debt securities or floating rate debt securities or original issue discount debt securities;
- if the debt securities are fixed rate debt securities, the yearly rate at which the debt securities will bear interest, if any;
- if the debt securities are floating rate debt securities, the method of calculating the interest rate;
- if the debt securities are original issue discount debt securities, their yield to maturity;
- the date or dates from which any interest will accrue, or how such date or dates will be determined, and the interest payment dates and any related record dates;
- if other than in U.S. Dollars, the currency or currency unit in which payment will be made;
- any provisions for the payment of additional amounts for taxes;
- the denominations in which the currency or currency unit of the securities will be issuable if other than denominations of $1,000 and integral multiples thereof;
- the terms and conditions on which the debt securities may be redeemed at the option of the Company;
- any obligation of the Company to redeem, purchase or repay the debt securities at the option of a holder upon the happening of any event and the terms and conditions of redemption, purchase or repayment;
- the names and duties of any co-indenture trustees, depositaries, authenticating agents, calculation agents, paying agents, transfer agents or registrars for the debt securities;
- any material provisions of the applicable indenture described in this prospectus that do not apply to the debt securities;
- the ranking of the specific series of debt securities relative to other outstanding indebtedness;
- if the debt securities are subordinated, the aggregate amount of outstanding indebtedness, as of a recent date, that is senior to the subordinated securities, and any limitation on the issuance of additional senior indebtedness;
- the place where we will pay principal and interest;
- additional provisions, if any, relating to the defeasance of the debt securities;
- any United States federal income tax consequences, if material;
- the dates on which premium, if any, will be paid;
- our right, if any, to defer payment of interest and the maximum length of this deferral period;
- any listing of the debt securities on a securities exchange; and
- any other specific terms of the debt securities.

We will issue the debt securities only in registered form. As currently anticipated, debt securities of a series will trade in book-entry form, and global notes will be issued in physical (paper) form, as described below under "Book-Entry Procedures and Settlement."

Senior Debt

We will issue senior debt securities under the senior debt indenture. These senior debt securities will rank on an equal basis with all our other unsecured debt except subordinated debt.

Subordinated Debt

We will issue subordinated debt securities under the subordinated debt indenture. Subordinated debt will rank subordinate and junior in right of payment, to the extent set forth in the subordinated debt indenture, to all our senior debt (both secured and unsecured).

In general, the holders of all senior debt are first entitled to receive payment of the full amount unpaid on senior debt before the holders of any of the subordinated debt securities are entitled to receive a payment on account of the principal or interest on the indebtedness evidenced by the subordinated debt securities in certain events.

If we default in the payment of any principal of, or premium, if any, or interest on any senior debt when it becomes due and payable after any applicable grace period, then, unless and until the default is cured or waived or ceases to exist, we cannot make a payment on account of or redeem or otherwise acquire the subordinated debt securities.

If there is any insolvency, bankruptcy, liquidation or other similar proceeding relating to us or our property, then all senior debt must be paid in full before any payment may be made to any holders of subordinated debt securities.

Furthermore, if we default in the payment of the principal of and accrued interest on any subordinated debt securities that is declared due and payable upon an event of default under the subordinated debt indenture, holders of all our senior debt will first be entitled to receive payment in full in cash before holders of such subordinated debt can receive any payments.

Senior debt means:

- the principal, premium, if any, interest and any other amounts owing in respect of indebtedness of the Company and/or of our subsidiaries that may guarantee our debt for money borrowed and indebtedness evidenced by securities, notes, debentures, bonds or other similar instruments issued by us, including the senior debt securities and letters of credit;
- all capitalized lease obligations;
- all hedging obligations;
- all obligations representing the deferred purchase price of property; and
- all deferrals, renewals, extensions and refundings of obligations of the type referred to above;

but senior debt does not include:

- subordinated debt securities; and
- any indebtedness that by its terms is subordinated to, or ranks on an equal basis with, our subordinated debt securities.

Convertible Debt

We will issue convertible debt securities under the convertible debt indenture. Convertible debt securities will be convertible into common stock on the terms set forth in the convertible debt indenture. The convertible debt indenture will provide that the conversion price is subject to customary anti-dilution adjustments in connection with stock dividends, stock splits, stock combinations, reclassifications and other similar events.

Covenants

Amalgamation and Sale of Assets. We may not, in a single transaction or a series of related transactions:

- consolidate, amalgamate or merge with or into any other person; or
- directly or indirectly, transfer, sell, lease or otherwise dispose of all or substantially all of our assets,

unless, in either such case:

- in a transaction in which we do not survive or in which we sell, lease or otherwise dispose of all or substantially all of our assets, the successor entity to us expressly assumes, by a supplemental indenture executed and delivered to the indenture trustee in a form reasonably satisfactory to the indenture trustee, all of our obligations under the indenture;
- immediately before and after giving effect to the transaction, no default on the debt securities exists; and
- an officer's certificate and an opinion of counsel setting forth certain statements are delivered to the indenture trustee.

Other Covenants. In addition, any offered series of debt securities may have additional covenants which will be described in the prospectus supplement, limiting or restricting, among other things:

- our ability to incur indebtedness;
- our ability to pay dividends, to repurchase or redeem our capital stock;
- our ability to create dividend and other payment restrictions affecting our subsidiaries;
- mergers and consolidations by us;
- sales of assets by us;
- our ability to enter into transactions with affiliates;
- our ability to incur liens; and
- our ability to enter into sale and leaseback transactions.

Modification of the Indentures

Under the indentures, we and the indenture trustee may amend the indentures, without the consent of any holder of the debt securities to:

- cure ambiguities, defects or inconsistencies;
- comply with the covenants described under "—Amalgamation and Sale of Assets";
- add to our covenants for the benefit of the holders of all or any series of debt securities (and if such covenants are to be for the benefit of less than all series of debt securities, stating that such covenants are expressly being included for the benefit of such series) or to surrender any rights or power conferred upon us;
- add any additional events of default for the benefit of the holders of all or a series of debt securities;
- establish the form or terms of debt securities of any series;
- provide for uncertificated debt securities in addition to or in place of certificated debt securities;

- add guarantors of the debt securities;
- secure the debt securities of one or more series;
- evidence the succession of another person to the Company and the assumption of the covenants in the indentures and in the debt securities by such successor; or any co-issuer of the debt securities;
- add or change any provision of the indentures to permit the issuance of the debt securities in bearer form, registrable or not registrable as to principal, with or without interest coupons;
- appoint a successor indenture trustee under either indenture;
- add to, change or eliminate any provision of the indentures so long as such addition, change or elimination does not affect the rights of the holders; or
- conform any provision of the indentures to the description of securities contained in this prospectus or any similar provision in any prospectus supplement relating to an offer of a series of debt securities under the indentures.

We and the indenture trustee may, with the consent of the holders of at least a majority in aggregate principal amount of the debt securities of a series, modify the applicable indenture or the rights of the holders of the securities of such series. However, no such modification may, without the consent of each holder of an affected debt security:

- extend the fixed maturity of any such debt securities;
- reduce the rate or change the time of payment of interest on such debt securities;
- reduce the principal amount of such securities or the premium, if any, on such debt securities;
- change or waive the redemption provisions of such debt securities;
- change any obligation of ours to maintain an office or agency;
- reduce the amount of the principal payable on acceleration of any debt securities issued originally at a discount;
- adversely affect in any material respect the ranking on such debt securities;
- adversely affect in any material respect the right, if any, to convert such debt securities;
- adversely affect any right of repayment or repurchase at the option of the holder;
- reduce or postpone any sinking fund or similar provision;
- change the currency or currency unit in which any such debt securities are payable or the right of selection thereof;
- impair the right to sue for the enforcement of any payment on such debt securities;
- reduce the percentage of debt securities of a series whose holders need to consent to the modification or a waiver; or
- with respect to subordinated debt securities, modify or change any provisions of the indenture or the related definitions affecting the subordination or ranking of any debt securities, in a manner which adversely affects the holders.

Defaults

Each indenture provides that events of default regarding any series of debt securities will be:

- our failure to pay required interest on any debt security of such series for 30 days;
- our failure to pay principal or premium, if any, on any debt security of such series when due;
- our failure to make any deposit of any sinking fund payment when due on debt securities of such series;
- our failure to perform for 30 days after notice any other covenant in the relevant indenture other than a covenant included in the relevant indenture solely for the benefit of a series of debt securities other than such series;
- a breach by us of the covenant with respect to amalgamation and sale of assets;
- our failure to pay beyond any applicable grace period, or the acceleration of, indebtedness in excess of $35,000,000; and
- certain events of bankruptcy or insolvency, whether voluntary or not.

If an event of default regarding debt securities of any series issued under the indentures should occur and be continuing, either the indenture trustee or the holders of 25% in the principal amount of outstanding debt securities of such series may declare each debt security of that series due and payable. If an event of default regarding debt securities results from certain events of bankruptcy, insolvency or reorganization with respect to us, such amount with respect to the debt securities will be due and payable immediately without any declaration or other act on the part of the holders of outstanding debt securities or the indenture trustee. We are required to file annually with the indenture trustee a statement of an officer as to the fulfillment by us of our obligations under the indenture during the preceding year.

No event of default regarding one series of debt securities issued under an indenture is necessarily an event of default regarding any other series of debt securities.

Holders of a majority in principal amount of the outstanding debt securities of any series will be entitled to control certain actions of the indenture trustee under an indenture and to waive past defaults regarding such series. The indenture trustee generally cannot be required by any of the holders of debt securities to take any action, unless one or more of such holders shall have provided to the indenture trustee satisfactory security or indemnity.

If an event of default occurs and is continuing regarding a series of debt securities, the indenture trustee may use any sums that it holds under the relevant indenture for its own reasonable compensation and expenses incurred prior to paying the holders of debt securities of such series.

Before any holder of any series of debt securities may institute action for any remedy, the holders of not less than 25% in principal amount of the debt securities of that series outstanding must request the indenture trustee to take action. Holders must also offer and give satisfactory security and indemnity against liabilities incurred by the indenture trustee for taking such action, and the indenture trustee must have failed to institute any proceeding within 60 days after receiving such request and offer of indemnity. These limitations do not apply, however, to a suit by a holder of any series of debt securities to enforce payment of principal, interest or premium.

Defeasance

After we have deposited with the indenture trustee cash or government securities, in trust for the benefit of the holders, sufficient to pay the principal of, premium, if any, and interest on the debt securities of such series when due, and satisfied certain other conditions, including receipt of an

opinion of counsel that holders will not recognize taxable gain or loss for U.S. Federal income tax purposes, we may elect to have our obligations discharged with respect to the outstanding debt securities of any series ("defeasance and discharge"). Defeasance and discharge means that we will be deemed to have paid and discharged the entire indebtedness represented by the outstanding debt securities of such series under the applicable indenture, except for:

- the rights of holders of the debt securities to receive principal, interest and any premium when due;
- our obligations with respect to the debt securities concerning issuing temporary debt securities, registration of transfer of debt securities, mutilated, destroyed, lost or stolen debt securities and the maintenance of an office or agency for payment for security payments held in trust;
- the rights, powers, trusts, duties and immunities of the indenture trustee; and
- the defeasance provisions of the indenture.

Alternatively, we may elect to have our obligations released with respect to certain covenants in the applicable indenture ("covenant defeasance"). Any omission to comply with these obligations will not constitute a default or an event of default with respect to the debt securities of any series. In the event covenant defeasance occurs, certain events, not including non-payment, bankruptcy and insolvency events, described under "Events of Default" will no longer constitute an event of default for that series.

Governing Law

Unless otherwise stated in the prospectus supplement, the debt securities and the indentures will be governed by New York law.

Payment and Paying Agents

Distributions on the debt securities other than those represented by global notes will be made in the designated currency against surrender of the debt securities at the corporate trust office of the indenture trustee. Payment will be made to the registered holder at the close of business on the record date for such payment. Interest payments will be made at the principal corporate trust office of the indenture trustee, or by a check mailed to the holder at his or her registered address. Payments in any other manner will be specified in the prospectus supplement applicable to the particular series of debt securities.

Transfer and Exchange

Debt securities may be presented for exchange, and debt securities other than a global security may be presented for registration of transfer, at the corporate trust office of the indenture trustee. Holders will not have to pay any service charge for any registration of transfer or exchange of debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with such registration of transfer or exchange of debt securities.

WARRANTS

We may issue warrants to purchase our debt or equity securities or securities of third parties or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing. Warrants may be issued independently or together with any other securities and may be attached to, or separate from, such securities. A series of warrants may be issued under a separate warrant indenture between us and a warrant agent. The terms of any warrants to be issued and a

description of the material provisions of any applicable warrant indenture will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement will describe the following terms of any warrants in respect of which this prospectus is being delivered:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the currency or currencies, in which the price of such warrants will be payable;
- the securities or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing, purchasable upon exercise of such warrants;
- the price at which and the currency or currencies, in which the securities or other rights purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants shall commence and the date on which such right shall expire;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;
- information with respect to book-entry procedures, if any;
- if applicable, a discussion of any material United States Federal income tax considerations; and
- any other terms of such warrants, including terms, procedures and limitations relating to the exchange and exercise of such warrants.

RIGHTS

We may issue rights to purchase our securities. These rights may be issued independently or together with any other security offered by this prospectus and may or may not be transferable by the person receiving the rights in the rights offering. In connection with any rights offering, we may enter into a standby underwriting agreement with one or more underwriters pursuant to which the underwriter will purchase any securities that remain unsubscribed for upon completion of the rights offering.

The applicable prospectus supplement relating to any rights will describe the terms of the offered rights, including, where applicable, the following:

- the exercise price for the rights;
- the number of rights issued to each securityholder;
- the extent to which the rights are transferable;
- any other terms of the rights, including terms, procedures and limitations relating to the exchange and exercise of the rights;

- the date on which the right to exercise the rights will commence and the date on which the right will expire;
- the amount of rights outstanding;
- the extent to which the rights include an over-subscription privilege with respect to unsubscribed securities; and
- the material terms of any standby underwriting arrangement entered into by us in connection with the rights offering.

PURCHASE CONTRACTS

We may issue purchase contracts, including contracts obligating holders to purchase from us, and us to sell to the holders, a specified number of shares of our ordinary shares at a future date or dates. The price per ordinary share and the number of ordinary shares may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula set forth in the purchase contracts. The purchase contracts may require us to make periodic payments to holders or vice versa, and these payments may be unsecured or prefunded on some basis. The purchase contracts may require holders to secure their obligations under those contracts in a specified manner. The applicable prospectus supplement will describe the terms of the purchase contracts, including if applicable, any collateral arrangements.

UNITS

We may issue units consisting of one or more debt securities, purchase contracts, warrants, rights, ordinary shares or any combination of such securities. The applicable prospectus supplement will describe:

- the terms of the units and of the securities comprising the units, including whether and under what circumstances the securities comprising the units may be traded separately;
- a description of the terms of any unit agreement governing the units; and
- a description of the provisions for the payment, settlement, transfer or exchange or the units.

CONVERTIBLE OR EXCHANGEABLE SECURITIES

We may issue securities of the types described in this prospectus that are convertible or exchangeable into other securities described herein. The terms of such convertible or exchangeable securities will be set forth in a prospectus supplement.

DESCRIPTION OF SHARE CAPITAL

General

We were incorporated under the name of uniQure B.V. on January 9, 2012 as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) under Dutch law. At an extraordinary general meeting of shareholders held on January 27, 2014, our shareholders resolved to amend our articles of association and to convert into a public company with limited liability by means of the Deed of Amendment and Conversion. Effective February 10, 2014, we converted to a public company with limited liability (*naamloze vennootschap*) under the laws of the Netherlands. In connection with this conversion, our legal name changed from uniQure B.V. to uniQure N.V.

Our company is registered with the Dutch Trade Register of the Chamber of Commerce (*handelsregister van de Kamer van Koophandel en Fabrieken*) in Amsterdam, the Netherlands under number 54385229. Our corporate seat is in Amsterdam, the Netherlands, and our registered office is at Meibergdreef 61, 1105 BA Amsterdam, the Netherlands.

In concert with our conversion from a private company with limited liability into a public company with limited liability, we reclassified our class A, B and C ordinary shares as ordinary shares.

On January 31, 2014, we effected a 5-for-1 consolidation of our shares, which had the effect of a reverse share split. All share, per-share and related information presented in this prospectus has been retroactively adjusted, where applicable, to reflect the impact of this reverse share split.

As of the date hereof, our authorized share capital is €3,000,000, divided into 60,000,000 ordinary shares, each with a nominal value of €0.05. Under Dutch law, our authorized share capital is the maximum capital that we may issue without amending our articles of association.

Our ordinary shares are listed on the Nasdaq Global Select Market under the symbol "QURE".

Initial settlement of the ordinary shares offered in this offering is expected to take place on or about the completion date of this offering through The Depository Trust Company, or DTC, in accordance with its customary settlement procedures for equity securities. Each person owning ordinary shares held through DTC must rely on the procedures thereof and on institutions that have accounts therewith to exercise any rights of a holder of the ordinary shares.

We will list our ordinary shares in registered form and such shares will not be certificated. We have appointed Computershare Trust Company, N.A. as our agent in New York to maintain our shareholders register and to act as transfer agent, registrar and paying agent for the ordinary shares. Our ordinary shares will be traded on the NASDAQ Global Select Market in book-entry form.

Articles of Association and Dutch Law

Set forth below is a summary of relevant information concerning the material provisions of our articles of association and applicable Dutch law. This summary does not constitute legal advice regarding those matters and should not be regarded as such.

Company's Shareholder Register

Subject to Dutch law and the articles of association, we must keep our shareholders' register accurate and up-to-date. Our management board keeps our shareholders' register and records names and addresses of all holders of shares, showing the date on which the shares were acquired, the date of the acknowledgement by or notification of us as well as the amount paid on each share. The shareholders' register also includes the names and addresses of those with a right of use and enjoyment (*vruchtgebruik*) in shares belonging to another or a pledge over shares. The ordinary shares offered in

this offering will be held through DTC, therefore DTC or its nominee will be recorded in the shareholders register as the holder of the ordinary shares.

Corporate objectives

Under our articles of association, our corporate objectives are:

- to research, develop, produce and commercialize products, services and technology in the biopharmaceutical sphere;
- to incorporate, participate in, conduct the management of and take any other financial interest in other companies and enterprises;
- to render administrative, technical, financial, economic or managerial services to other companies, persons or enterprises;
- to acquire, dispose of manage and exploit real and personal property, including patents, marks, licenses, permits and other intellectual property rights;
- 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.

Limitation on liability and indemnification matters

Under Dutch law, managing directors, supervisory directors and certain other representatives may be held liable for damages in the event of improper or negligent performance of their duties. They may be held jointly and severally liable for damages to the company and to third parties for infringement of the articles of association or of certain provisions of the Dutch Civil Code. In certain circumstances, they may also incur additional specific civil and criminal liabilities. We have a policy insuring managing directors, supervisory directors and certain other representatives against damages resulting from their conduct when acting in their capacities as such directors or representatives. In addition, our articles of association provide for indemnification of our managing directors and supervisory directors, including reimbursement for reasonable legal fees and damages or fines incurred based on acts or failures to act in the performance of their duties. Such indemnification will not be available in instances of willful (*opzettelijk*), intentionally reckless (*bewust roekeloos*) or seriously culpable (*ernstig verwijtbaar*) conduct unless Dutch law provides otherwise.

Shareholders' meetings and consents

General meeting

General meetings of shareholders are held in Amsterdam, or in the municipality of Haarlemmermeer (Schiphol Airport), the Netherlands. The annual general meeting of shareholders must be held within six months of the end of each financial year. Additional extraordinary general meetings of shareholders may also be held whenever considered appropriate by the management board or the supervisory board.

Pursuant to Dutch law, one or more shareholders, who alone or jointly represent at least one-tenth of the issued capital, may, on their application, be authorized by the Dutch court to convene a general meeting of shareholders. The Dutch court will disallow the application if it does not appear that the applicants have previously requested that the management board and the supervisory board convene a general meeting of shareholders and neither the management nor the supervisory board has taken the

necessary steps so that the general meeting of shareholders could be held within six weeks after the request.

General meetings of shareholders are convened by a notice which includes an agenda stating the items to be discussed. For the annual general meeting of shareholders the agenda will include, among other things, the adoption of our annual accounts, the appropriation of our profits and proposals relating to the composition of the management board and/or the supervisory board, including filling any vacancies in the management board and/or the supervisory board. In addition, the agenda for the general meeting of shareholders includes such items as have been (1) included therein by the management board or the supervisory board and (2) requested by one or more shareholders and/or others entitled to attend general meetings of shareholders representing at least 3% of the issued share capital of a company or such lower percentage as the articles of association may provide. Our articles of association do not state such lower percentage. Such requests must be made in writing and received by the management board at least sixty days before the day of the meeting. Our management board may decide not to place items so requested on the agenda, if it believes that doing so would be detrimental to our vital interests. No resolutions will be adopted on items other than those which have been included in the agenda.

Pursuant to our articles of association, the general meeting of shareholders is chaired by the chairman of the supervisory board. However, the chairman may charge another person to chair the general meeting in his place even if he is present at the meeting. If the chairman of our supervisory board is absent and has not charged another person to chair the meeting in his place, the supervisory directors present at the meeting shall appoint one of them to be chairman. If no supervisory directors are present at the general meeting of shareholders, the general meeting of shareholders will be chaired by the chairman of our management board or, if the chairman of our management board is absent, by one of the other managing directors designated for that purpose by the management board. Managing directors and supervisory directors may attend a general meeting of shareholders. In these meetings, they have an advisory vote. The chairman of the meeting may decide at his discretion to admit other persons to the meeting.

All shareholders and others entitled to attend general meetings of shareholders are authorized to attend the general meeting of shareholders, to address the meeting and, in so far as they have such right, to vote.

Quorum and voting requirements

Each ordinary share confers the right on the holder thereof to cast one vote at the general meeting of shareholders. Shareholders may vote by proxy. The voting rights attached to any shares held by us are suspended as long as they are held in treasury. If a right of use and enjoyment (*vruchtgebruik*) or a right of pledge over ordinary shares was granted prior to the time such ordinary share was acquired by us, the holders of such right of use and enjoyment in ordinary shares belonging to another and the holders of a right of pledge in respect of ordinary shares held by us are not excluded from any right such holders may have to vote on such ordinary shares. We may not cast votes in respect of a share in respect of which there is a right of use and enjoyment or a right of pledge. Shares which are not entitled to voting rights pursuant to the preceding sentences will not be taken into account for the purpose of determining the number of shareholders that vote and that are present or represented, or the amount of the share capital that is present or that is represented, at a general meeting of shareholders.

In accordance with Dutch law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. To this extent, our practice varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an

issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting shares.

Decisions are made at the general meeting of shareholders by an absolute majority of votes cast, except where Dutch law or our articles of association provide for a qualified majority or unanimity.

Managing directors and supervisory directors

Election of managing directors and supervisory directors

Under our articles of association, the managing directors and supervisory directors are appointed by the general meeting of shareholders, upon nomination by our supervisory board. However, the shareholders at the general meeting of shareholders 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 of the issued share capital of our company. If the general meeting of shareholders overrules the binding nomination, the supervisory board shall make a new nomination.

Duties and liabilities of managing directors and supervisory directors

Under Dutch law, the management board is responsible for our day-to-day management, strategy, policy and operations. The supervisory board is responsible for supervising the conduct of, and providing advice to the management board and for, supervising our business generally. Furthermore, each managing director and supervisory director has a duty to act in the corporate interest of our company. Under Dutch law, the corporate interest extends to the interests of all corporate stakeholders, such as shareholders, creditors, employees, customers and suppliers. The duty to act in the corporate interest of our company also applies in the event of a proposed sale or split-up of our company, whereby the circumstances generally dictate how such duty is to be applied. Any resolution of the management board regarding a significant change in our identity or character requires shareholder approval. For additional information, please see "Shareholder vote on certain reorganizations."

Dividends and other distributions

Amount available for distribution

We may only make distributions to our shareholders if our shareholders' equity exceeds the sum of the paid-up and called-up share capital plus the reserves as required to be maintained by Dutch law or by our articles of association. Any amount remaining out of the profit is carried to reserve as the management board determines, subject to the approval of the supervisory board. After reservation by the management board of any profit, the remaining profit will be at the disposal of shareholders. The management board is permitted, subject to certain requirements and subject to approval of the supervisory board, to declare interim dividends without the approval of the general meeting of shareholders. Our corporate policy is that we only make a distribution of dividends to our shareholders after the adoption of our annual accounts demonstrating that such distribution is legally permitted.

Dividends and other distributions shall be made payable not later than the date determined by the management board. Claims to dividends and other distributions not made within five years from the date that such dividends or distributions became payable will lapse and any such amounts will be considered to have been forfeited to us (*verjaring*).

We do not anticipate paying any cash dividends for the foreseeable future.

Exchange controls

Under Dutch law, there are no exchange controls applicable to the transfer of dividends or other distributions with respect to, or of the proceeds from the sale of, shares in a Dutch company, to persons outside the Netherlands.

Squeeze-out proceedings

Pursuant to Section 92a, Book 2, Dutch Civil Code, a shareholder who for its own account contributes at least 95% of our issued share capital may initiate proceedings against all our minority shareholders jointly for the transfer of their shares to it. The proceedings are held before the Enterprise Chamber of the Court of Appeal in Amsterdam (*Ondernemingskamer*) and can be instituted by means of a writ of summons served upon each of the minority shareholders in accordance with the provisions of the Dutch Code of Civil Procedure (*Wetboek van Burgerlijke Rechtsvordering*). The Enterprise Chamber may grant the claim for squeeze out in relation to all minority shareholders and will determine the price to be paid for the shares, if necessary after appointment of one or three experts who will offer an opinion to the Enterprise Chamber on the value to be paid for the shares of the minority shareholders. Once the order to transfer becomes final before the Enterprise Chamber, the majority shareholder that institutes the squeeze-out proceedings shall give written notice to all minority shareholders whose addresses are known by the majority shareholder of the date and place of payment and the price. Unless the majority shareholder knows the addresses of all minority shareholders, the majority shareholder is required to publish the same in a daily newspaper with a national circulation.

Obligation to disclose holdings and transactions

Pursuant to the Dutch Financial Markets Supervision Act (*Wet op het financieel toezicht*, or FMSA), any managing director or supervisory director and any other person who has managerial or co-managerial responsibilities in respect of us and who has the authority to make decisions affecting our future developments and business prospects and who may have regularly access to inside information relating, directly or indirectly, to us, must give written notice to the Dutch Authority for the Financial Markets, or AFM, by means of a standard form of any transactions conducted for his own account relating to our shares or in financial instruments the value of which is also based on the value of our shares.

Furthermore, in accordance with the FMSA and the regulations promulgated thereunder, certain persons who are closely associated with members of our management board, our supervisory board or any of the other persons as described above, are required to notify the AFM of any transactions conducted for their own account relating to our shares or in financial instruments the value of which is also based on the value of our shares. The FMSA and the regulations promulgated thereunder cover the following categories of persons: (1) the spouse, registered partner, life companion or other persons considered by national law as equivalent, (2) dependent children, (3) other relatives who have shared the same household for at least one year at the relevant transaction date, and (4) any legal person, trust or partnership whose, among other things, managerial responsibilities are discharged by a person referred to under (1), (2) or (3) above or by the relevant managing director, supervisory director or other person with any authority in respect of us as described above.

The AFM must be notified no later than the fifth business day following the relevant transaction date. Notification may be postponed until the date the value of the transactions performed for that person's own account, together with transactions carried out by the persons closely associated with that person, amounts to €5,000 or more in the calendar year in question.

Non-compliance with the notification obligations under the FMSA could lead to criminal fines, administrative fines, imprisonment or other sanctions.

The AFM does not issue separate public announcements of notifications received by it. It does, however, keep a public register of all notifications under the FMSA on its website, http://www.afm.nl. Third parties can request to be notified automatically by e-mail of changes to the public register in relation to a particular company's shares or a particular notifying party.

The FMSA contains rules intended to prevent market abuse, such as insider trading, tipping and market manipulation.

In accordance with the rules intended to prevent market abuse, we have adopted an internal code on inside information in respect of the holding of and carrying out of transactions in our shares or financial instruments the value of which is determined by the value of our shares by managing directors, supervisory directors and employees. Furthermore, we have drawn up a list of those persons working for us who could have access to inside information on a regular or incidental basis and have informed such persons of the rules on insider trading and market manipulation, including the sanctions which can be imposed in the event of a violation of those rules.

Comparison of Dutch corporate law and our Articles of Association and Delaware corporate law

The following comparison between Dutch corporate law, which applies to us, and Delaware corporate law, the law under which many publicly listed companies in the United States are incorporated, discusses additional matters not otherwise described in this prospectus. This summary is subject to Dutch law, including Book 2 of the Dutch Civil Code and Delaware corporation law, including the Delaware General Corporation Law.

Corporate governance

Duties of managing directors and supervisory directors

The Netherlands. We have a two tier board structure consisting of our management board (*raad van bestuur*) and a separate supervisory board (*raad van commissarissen*).

Under Dutch law, the management board is responsible for the day-to-day management and the strategy, policy and operations of a company. The supervisory board is responsible for supervising the conduct of, and providing advice to, the management board and for supervising the company's general affairs and business. Each managing director and supervisory director has a duty to act in the corporate interest of the company. Under Dutch law, the corporate interest extends to the interests of all corporate stakeholders, such as shareholders, creditors, employees, customers and suppliers. The duty to act in the corporate interest of the company also applies in the event of a proposed sale or split-up of a company, whereby the circumstances generally dictate how such duty is to be applied. Any resolution of the management board regarding a significant change in the identity or character of a company requires shareholders' approval.

Delaware. The board of directors bears the ultimate responsibility for managing the business and affairs of a corporation. In discharging this function, directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its stockholders. Delaware courts have decided that the directors of a Delaware corporation are required to exercise informed business judgment in the performance of their duties. Informed business judgment means that the directors have informed themselves of all material information reasonably available to them. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the stockholders.

Supervisory director terms

The Netherlands. Under Dutch law, supervisory directors of a listed company are generally appointed for an individual term of a maximum of four years. A limit of twelve years generally applies. Our supervisory directors are appointed by the general meeting of shareholders for a term of up to three years. A supervisory director may be reappointed for a term of up to three years at a time. A supervisory director may serve on the supervisory board for a period not longer than twelve years, which period may or may not be interrupted, unless resolved otherwise by the general meeting of shareholders.

The general meeting of shareholders are entitled at all times to suspend or dismiss a supervisory director. The general meeting of shareholders may only adopt a resolution to suspend or dismiss such supervisory director by at least a two-thirds majority of the votes cast, if such majority represents more than half of the issued share capital of the company, unless the proposal was made by the supervisory board, in which case a simple majority of the votes cast is sufficient.

Delaware. The Delaware General Corporation Law generally provides for a one-year term for directors, but permits directorships to be divided into up to three classes with up to three-year terms, with the years for each class expiring in different years, if permitted by a company's certificate of incorporation, an initial bylaw or a bylaw adopted by the stockholders. A director elected to serve a term on such a classified board may not be removed by stockholders without cause. There is no limit in the number of terms a director may serve.

Managing director and supervisory director vacancies

The Netherlands. Under Dutch law, managing directors and supervisory directors are appointed by the general meeting of shareholders. Under our articles of association, managing directors and supervisory directors are appointed by the general meeting of shareholders upon the binding nomination by our supervisory board. However, the general meeting of shareholders may at all times overrule such binding nomination by a resolution adopted by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital of our company. If the general meeting of shareholders overrules the binding nomination, the supervisory board must make a new nomination.

Delaware. The Delaware General Corporation Law provides that vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) unless (1) otherwise provided in the certificate of incorporation or bylaws of the corporation or (2) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case any other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

Conflict-of-interest transactions

The Netherlands. Pursuant to Dutch law and our articles of association, managing directors and supervisory directors may not take part in any discussion or decision-making that involves a subject or transaction in relation to which it has a conflict of interest with us. Our articles of association provide that if as a result thereof no resolution of the management board can be adopted, the resolution will be adopted by the supervisory board. If as a result of a conflict of interest of supervisory directors no resolution of the supervisory board can be adopted, the resolution can nonetheless be adopted by the supervisory board as if there was no conflict of interest. In that case, each supervisory board member is entitled to participate in the discussion and decision making process and to cast a vote.

Delaware. The Delaware General Corporation Law generally permits transactions involving a Delaware corporation and an interested director of that corporation if:

- the material facts as to the director's relationship or interest are disclosed and a majority of disinterested directors consent;
- the material facts are disclosed as to the director's relationship or interest and a majority of shares entitled to vote thereon consent; or
- the transaction is fair to the corporation at the time it is authorized by the board of directors, a committee of the board of directors or the stockholders.

Proxy voting by managing directors and supervisory directors

The Netherlands. An absent managing director may issue a proxy for a specific management board meeting in writing but only to another management board member. An absent supervisory director may issue a proxy for a specific supervisory board meeting in writing but only to another supervisory board member.

Delaware. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

Shareholder rights

Voting rights

The Netherlands. In accordance with Dutch law and our articles of association, each issued ordinary share confers the right to cast one vote at the general meeting of shareholders. Each holder of ordinary shares may cast as many votes as it holds shares. Shares that are held by us or our direct or indirect subsidiaries do not confer the right to vote. Dutch law does not permit cumulative voting for the election of managing directors and supervisory directors.

For each general meeting of shareholders, a record date will be applied with respect to ordinary shares in order to establish which shareholders are entitled to attend and vote at a specific general meeting of shareholders. Such record date is set by the management board. The record date and the manner in which shareholders can register and exercise their rights will be set out in the convocation notice of the meeting.

Delaware. Under the Delaware General Corporation Law, each stockholder is entitled to one vote per share of stock, unless the certificate of incorporation provides otherwise. In addition, the certificate of incorporation may provide for cumulative voting at all elections of directors of the corporation, or at elections held under specified circumstances. Either the certificate of incorporation or the bylaws may specify the number of shares and/or the amount of other securities that must be represented at a meeting in order to constitute a quorum, but in no event will a quorum consist of less than one third of the shares entitled to vote at a meeting.

Stockholders as of the record date for the meeting are entitled to vote at the meeting, and the board of directors may fix a record date that is no more than 60 nor less than ten days before the date of the meeting, and if no record date is set then the record date is the close of business on the day next preceding the day on which notice is given, or if notice is waived then the record date is the close of business on the day next preceding the day on which the meeting is held. The determination of the stockholders of record entitled to notice or to vote at a meeting of stockholders shall apply to any adjournment of the meeting, but the board of directors may fix a new record date for the adjourned meeting.

Shareholder proposals

The Netherlands. Pursuant to our articles of association, extraordinary general meetings of shareholders will be held whenever our supervisory board and/or our management board deem such to be necessary. Pursuant to Dutch law, one or more shareholders representing at least one-tenth of the issued share capital of the company may request the Dutch courts to order that a general meeting of shareholders be held and may, on their application, be authorized by the court to convene a general meeting of shareholders. The court shall disallow the application if it does not appear that the applicants have previously requested the management board and the supervisory board to convene a general meeting of shareholders and neither the management nor the supervisory board has taken the necessary steps so that the general meeting of shareholders could be held within six weeks after the request.

The agenda for a general meeting of shareholders must include such items requested by one or more shareholders and/or others entitled to attend general meetings of shareholders representing at least 3% of the issued share capital of a company or such lower percentage as the articles of association may provide. Our articles of association do not state such lower percentage.

Delaware. Delaware law does not specifically grant stockholders the right to bring business before an annual or special meeting. However, if a Delaware corporation is subject to the SEC's proxy rules, a stockholder who owns at least $2,000 in market value, or 1% of the corporation's securities entitled to vote, may propose a matter for a vote at an annual or special meeting in accordance with those rules.

Action by written consent

The Netherlands. Under Dutch law, shareholders' resolutions may be adopted in writing without holding a meeting of shareholders, provided that (i) all shareholders agree on this practice for decision making and, (ii) the resolution is adopted unanimously by all shareholders that are entitled to vote. For a listed company, this method of adopting resolutions is not feasible.

Delaware. Although permitted by Delaware law, publicly listed companies do not typically permit stockholders of a corporation to take action by written consent.

Appraisal rights

The Netherlands. The concept of appraisal rights does not exist under Dutch law.

However, pursuant to Dutch law a shareholder who for his own account contributes at least 95% of our issued share capital may initiate proceedings against our minority shareholders jointly for the transfer of their shares to the claimant. The proceedings are held before the Enterprise Chamber (*Ondernemingskamer*). The Enterprise Chamber may grant the claim for squeeze-out in relation to all minority shareholders and will determine the price to be paid for the shares, if necessary after appointment of one or three experts who will offer an opinion to the Enterprise Chamber on the value to be paid for the shares of the minority shareholders. For additional information, please see "Squeeze-out proceedings."

Furthermore, in accordance with directive 2005/56/EC of the European Parliament and the Council of October 26, 2005 on cross-border mergers of limited liability companies, Dutch law provides that, to the extent the acquiring company in a cross-border merger is organized under the laws of another EU member state, a shareholder of a Dutch disappearing company who has voted against the cross-border merger may file a claim with the Dutch company for compensation. The compensation is to be determined by one or more independent experts.

Delaware. The Delaware General Corporation Law provides for stockholder appraisal rights, or the right to demand payment in cash of the judicially determined fair value of the stockholder's shares, in connection with certain mergers and consolidations.

Shareholder suits

The Netherlands. In the event a third party is liable to a Dutch company, only a company itself can bring a civil action against that third party. An individual shareholder does not have the right to bring an action on behalf of a company. This individual shareholder may, in its own name, have an individual right to take action against such third party in the event that the cause for the liability of that third party also constitutes a tortious act directly against that individual shareholder. The Dutch Civil Code provides for the possibility to initiate such action collectively. A collective action can be instituted by a foundation or an association whose objective is to protect the rights of a group of persons having similar interests. The collective action itself cannot result in an order for payment of monetary damages but may only result in a declaratory judgment (*verklaring voor recht*). In order to obtain compensation for damages, the foundation or association and the defendant may reach —often on the basis of such declaratory judgment—a settlement. A Dutch court may declare the settlement agreement binding upon all the injured parties with an opt-out choice for an individual injured party. An individual injured party may also itself—outside the collective action—institute a civil claim for damages.

Delaware. Under the Delaware General Corporation Law, a stockholder may bring a derivative action on behalf of the corporation to enforce the rights of the corporation. An individual also may commence a class action suit on behalf of himself and other similarly situated stockholders where the requirements for maintaining a class action under Delaware law have been met. A person may institute and maintain such a suit only if that person was a stockholder at the time of the transaction which is the subject of the suit. In addition, under Delaware case law, the plaintiff normally must be a stockholder at the time of the transaction that is the subject of the suit and throughout the duration of the derivative suit. Delaware law also requires that the derivative plaintiff make a demand on the directors of the corporation to assert the corporate claim before the suit may be prosecuted by the derivative plaintiff in court, unless such a demand would be futile.

Repurchase of shares

The Netherlands. Under Dutch law, a company such as ours may not subscribe for newly issued shares in its own capital. Such company may, however, subject to certain restrictions under Dutch law and its articles of association, acquire shares in its own capital. We may acquire fully paid shares in our own capital at any time for no valuable consideration. Furthermore, subject to certain provisions of Dutch law and our articles of association, we may repurchase fully paid-up shares in our own share capital if (1) such repurchase would not cause our shareholders' equity to fall below an amount equal to the sum of the paid-up and called-up part of the issued share capital and the reserves we are required to maintain pursuant to applicable law and (2) we would not as a result of such repurchase hold more than 50% of our own issued share capital.

Other than shares acquired for no valuable consideration, ordinary shares may only be acquired following a resolution of our management board, acting pursuant to an authorization for the repurchase of shares granted by the general meeting of shareholders. An authorization by the general meeting of shareholders for the repurchase of shares can be granted for a maximum period of 18 months. Such authorization must specify the number and class of shares that may be acquired, the manner in which these shares may be acquired and the price range within which the shares may be acquired. Our management board has been authorized, acting with the approval of our supervisory board, for a period of 18 months to cause the repurchase of ordinary shares by us of up to 10% of our issued share capital, for a price per share not exceeding 110% of the average closing price of the

ordinary shares on The NASDAQ Global Select Market for the 30 trading days prior to the day of purchase.

No authorization of the general meeting of shareholders is required if ordinary shares are acquired by us with the intention of transferring such ordinary shares to our employees under an applicable employee stock purchase plan.

Delaware. Under the Delaware General Corporation Law, a corporation may purchase or redeem its own shares unless the capital of the corporation is impaired or the purchase or redemption would cause an impairment of the capital of the corporation. A Delaware corporation may, however, purchase or redeem out of capital any of its preferred shares or, if no preferred shares are outstanding, any of its own shares if such shares will be retired upon acquisition and the capital of the corporation will be reduced in accordance with specified limitations.

Anti-takeover provisions

The Netherlands. Under Dutch law, various protective measures are possible and permissible within the boundaries set by Dutch statutory law and Dutch case law. We have adopted several provisions that may have the effect of making a takeover of our company more difficult or less attractive, including:

- the staggered three-year terms of our supervisory directors, as a result of which only approximately one-third of our supervisory directors will be subject to election in any one year;
- a provision that our managing directors and supervisory directors may only be removed at the general meeting of shareholders by a two-thirds majority of votes cast representing more than half of our outstanding share capital if such removal is not proposed by our supervisory board; and
- requirements 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 management board that has been approved by our supervisory board.

Delaware. In addition to other aspects of Delaware law governing fiduciary duties of directors during a potential takeover, the Delaware General Corporation Law also contains a business combination statute that protects Delaware companies from hostile takeovers and from actions following the takeover by prohibiting some transactions once an acquirer has gained a significant holding in the corporation.

- Section 203 of the Delaware General Corporation Law prohibits "business combinations," including mergers, sales and leases of assets, issuances of securities and similar transactions by a corporation or a subsidiary with an interested stockholder that beneficially owns 15% or more of a corporation's voting stock, within three years after the person becomes an interested stockholder, unless: the transaction that will cause the person to become an interested stockholder is approved by the board of directors of the target prior to the transactions;
- after the completion of the transaction in which the person becomes an interested stockholder, the interested stockholder holds at least 85% of the voting stock of the corporation not including shares owned by persons who are directors and representatives of interested stockholders and shares owned by specified employee benefit plans; or
- after the person becomes an interested stockholder, the business combination is approved by the board of directors of the corporation and holders of at least 66.67% of the outstanding voting stock, excluding shares held by the interested stockholder.

A Delaware corporation may elect not to be governed by Section 203 by a provision contained in the original certificate of incorporation of the corporation or an amendment to the original certificate of incorporation or to the bylaws of the company, which amendment must be approved by a majority of the shares entitled to vote and may not be further amended by the board of directors of the corporation. Such an amendment is not effective until twelve months following its adoption.

Inspection of books and records

The Netherlands. Our management board and our supervisory board provide the shareholders, at the general meeting of shareholders, with all information that the shareholders require for the exercise of their powers, unless doing so would be contrary to an overriding interest of ours. Our management board or our supervisory board must give reason for electing not to provide such information on the basis of overriding interest.

Delaware. Under the Delaware General Corporation Law, any stockholder may inspect certain of the corporation's books and records, for any proper purpose, during the corporation's usual hours of business.

Removal of managing directors and supervisory directors

The Netherlands. Under our articles of association, the general meeting of shareholders, are at all times entitled to suspend or dismiss a managing director or supervisory director. The general meeting of shareholders may only adopt a resolution to suspend or dismiss such a member by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital of our company, unless the proposal was made by the supervisory board in which case a simple majority of the votes cast is sufficient.

Delaware. Under the Delaware General Corporation Law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (1) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board is classified, stockholders may effect such removal only for cause, or (2) in the case of a corporation having cumulative voting, if less than the entire board is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

Preemptive rights

The Netherlands. Under Dutch law, in the event of an issuance of ordinary shares, each shareholder will have a pro rata preemptive right in proportion to the aggregate nominal value of the ordinary shares held by such holder (with the exception of ordinary shares to be issued to employees or ordinary shares issued against a contribution other than in cash). Under our articles of association, the preemptive rights in respect of newly issued ordinary shares may be restricted or excluded by a resolution of the general meeting of shareholders upon proposal of our management board. The general meeting of shareholders may designate a corporate body, for example our management board, to restrict or exclude the preemptive rights in respect of newly issued ordinary shares, subject to the approval of our supervisory board. Such designation can be granted for a period not exceeding five years. A resolution of the general meeting of shareholders to restrict or exclude the preemptive rights or to designate the management board as the authorized body to do so requires a two-thirds majority of the votes cast, if less than one half of our issued share capital is represented at the meeting.

At our extraordinary general meeting held on June 11, 2014, the general meeting of shareholders resolved to authorize our management board acting with the approval of our supervisory board for a

period of 18 months from the closing date of this offering to limit or exclude preemptive rights accruing to shareholders in connection with the issue of ordinary shares or rights to subscribe for ordinary shares.

Delaware. Under the Delaware General Corporation Law, stockholders have no preemptive rights to subscribe for additional issues of stock or to any security convertible into such stock unless, and to the extent that, such rights are expressly provided for in the certificate of incorporation.

Dividends

The Netherlands. Dutch law provides that dividends may be distributed after adoption of the annual accounts by the general meeting of shareholders from which it appears that such dividend distribution is allowed. Moreover, dividends may be distributed only to the extent the shareholders' equity exceeds the amount of the paid-up and called-up part of the issued share capital of the company and the reserves that must be maintained under the law or the articles of association. Interim dividends may be declared as provided in the articles of association and may be distributed to the extent that the shareholders' equity exceeds the amount of the issued and paid-up and called-up part of the issued share capital in our company and the required legal reserves as described above as apparent from our financial statements. Under Dutch law, the articles of association may prescribe that the management board decides what portion of the profits is to be held as reserve.

Under our articles of association, any amount of profit may carried to a reserve as our management board determines, subject to the approval of our supervisory board. After reservation by our management board of any profit, the remaining profit will be at the disposal of the shareholders. Our corporate policy is to only make a distribution of dividends to our shareholders after the adoption of our annual accounts demonstrating that such distribution is legally permitted. However, our management board is permitted, subject to certain requirements and subject to approval of the supervisory board, to declare interim dividends without the approval of the general meeting of shareholders.

Dividends and other distributions will be made payable not later than the date determined by the management board. Claims to dividends and other distribution not made within five years from the date that such dividends or distributions became payable will lapse and any such amounts will be considered to have been forfeited to us (*verjaring*).

Delaware. Under the Delaware General Corporation Law, a Delaware corporation may pay dividends out of its surplus (the excess of net assets over capital), or in case there is no surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year (provided that the amount of the capital of the corporation is not less than the aggregate amount of the capital represented by the issued and outstanding stock of all classes having a preference upon the distribution of assets). In determining the amount of surplus of a Delaware corporation, the assets of the corporation, including stock of subsidiaries owned by the corporation, must be valued at their fair market value as determined by the board of directors, without regard to their historical book value. Dividends may be paid in the form of shares, property or cash.

Shareholder vote on certain reorganizations

The Netherlands. Under Dutch law, the general meeting of shareholders must approve resolutions of the management board relating to a significant change in the identity or the character of the company or the business of the company, which includes:

- a transfer of the business or virtually the entire business to a third party;
- the entry into or termination of a long-term cooperation of the company or a subsidiary with another legal entity or company or as a fully liable partner in a limited partnership or general

partnership, if such cooperation or termination is of a far-reaching significance for the company; and

- the acquisition or divestment by the company or a subsidiary of a participating interest in the capital of a company having a value of at least one third of the amount of its assets according to its balance sheet and explanatory notes or, if the company prepares a consolidated balance sheet, according to its consolidated balance sheet and explanatory notes, in the last adopted annual accounts of the company.

Under Dutch law, a shareholder who owns shares representing at least 95% of the nominal value of a company's issued share capital may institute proceedings against the company's other shareholders jointly for the transfer of their shares to that shareholder. For additional information, please see "Squeeze-out proceedings."

Delaware. Under the Delaware General Corporation Law, the vote of a majority of the outstanding shares of capital stock entitled to vote thereon generally is necessary to approve a merger or consolidation or the sale of all or substantially all of the assets of a corporation. The Delaware General Corporation Law permits a corporation to include in its certificate of incorporation a provision requiring for any corporate action the vote of a larger portion of the stock or of any class or series of stock than would otherwise be required.

Under the Delaware General Corporation Law, no vote of the stockholders of a surviving corporation to a merger is needed, however, unless required by the certificate of incorporation, if (1) the agreement of merger does not amend in any respect the certificate of incorporation of the surviving corporation, (2) the shares of stock of the surviving corporation are not changed in the merger and (3) the number of shares of common stock of the surviving corporation into which any other shares, securities or obligations to be issued in the merger may be converted does not exceed 20% of the surviving corporation's common stock outstanding immediately prior to the effective date of the merger. In addition, stockholders may not be entitled to vote in certain mergers with other corporations that own 90% or more of the outstanding shares of each class of stock of such corporation, but the stockholders will be entitled to appraisal rights.

Remuneration of managing directors and supervisory directors

The Netherlands. Under Dutch law and our articles of association, we must adopt a remuneration policy for managing directors. Such remuneration policy shall be adopted by the general meeting of shareholders upon the proposal of our supervisory board. The supervisory board determines the remuneration of the managing directors in accordance with the remuneration policy. A proposal by the supervisory board with respect to remuneration schemes in the form of shares or rights to shares is submitted for approval by the supervisory board to the general meeting of shareholders. Such proposal must set out at least the maximum number of shares or rights to shares to be granted to the management board and the criteria for granting such shares.

The general meeting of shareholders may determine the remuneration of supervisory directors. The supervisory directors will be reimbursed for their expenses.

Delaware. Under the Delaware General Corporation Law, the stockholders do not generally have the right to approve the compensation policy for directors or the senior management of the corporation, although certain aspects of executive compensation may be subject to binding or advisory stockholder votes due to the provisions of U.S. federal securities and tax law, as well as stock exchange requirements.

Transfer Agent and Registrar

Computershare Trust Company, N.A. serves as transfer agent and registrar for our ordinary shares.

FORM, EXCHANGE AND TRANSFER

We will issue securities only in registered form; no securities will be issued in bearer form. We will issue each security other than ordinary shares in book-entry form only, unless otherwise specified in the applicable prospectus supplement. We will issue ordinary shares in both certificated and book-entry form, unless otherwise specified in the applicable prospectus supplement. Securities in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the securities represented by the global security. Those who own beneficial interests in a global security will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. Only the depositary will be entitled to transfer or exchange a security in global form, since it will be the sole holder of the security. These book-entry securities are described below under "Book-Entry Procedures and Settlement."

If any securities are issued in non-global form or cease to be book-entry securities (in the circumstances described in the next section), the following will apply to them:

- The securities will be issued in fully registered form in denominations stated in the prospectus supplement. You may exchange securities for securities of the same series in smaller denominations or combined into fewer securities of the same series of larger denominations, as long as the total amount is not changed.

- You may exchange, transfer, present for payment or exercise securities at the office of the relevant indenture trustee or agent indicated in the prospectus supplement. You may also replace lost, stolen, destroyed or mutilated securities at that office. We may appoint another entity to perform these functions or we may perform them ourselves.

- You will not be required to pay a service charge to transfer or exchange your securities, but you may be required to pay any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with your proof of legal ownership. The transfer agent may also require an indemnity before replacing any securities.

- If we have the right to redeem, accelerate or settle any securities before their maturity or expiration, and we exercise that right as to less than all those securities, we may block the transfer or exchange of those securities during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any security selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any security being partially settled.

- If fewer than all of the securities represented by a certificate that are payable or exercisable in part are presented for payment or exercise, a new certificate will be issued for the remaining amount of securities.

BOOK-ENTRY PROCEDURES AND SETTLEMENT

Most offered securities will be book-entry (global) securities. Upon issuance, all book-entry securities will be represented by one or more fully registered global securities, without coupons. Each global security will be deposited with, or on behalf of, The Depository Trust & Clearing Corporation, or DTC, a securities depositary, and will be registered in the name of Cede & Co. or another nominee of DTC. DTC, Cede & Co., or such nominee, will thus be the only registered holder of these securities. Except as set forth below, the registered global securities may be transferred, in whole but not in part, only to Cede & Co., another nominee of DTC or to a successor of DTC or its nominee.

Purchasers of securities may only hold interests in the global securities through DTC if they are participants in the DTC system. Individual certificates in respect of the securities will not be issued in exchange for the registered global securities, except in very limited circumstances. Purchasers may also hold interests through a securities intermediary—banks, brokerage houses and other institutions that maintain securities accounts for customers—that has an account with DTC or its nominee. DTC will maintain accounts showing the security holdings of its participants, and these participants will in turn maintain accounts showing the security holdings of their customers. Some of these customers may themselves be securities intermediaries holding securities for their customers. Thus, each beneficial owner of a book-entry security will hold that security indirectly through a hierarchy of intermediaries, with DTC at the top and the beneficial owner's own securities intermediary at the bottom.

The securities of each beneficial owner of a book-entry security will be evidenced solely by entries on the books of the beneficial owner's securities intermediary. The actual purchaser of the securities will generally not be entitled to have the securities represented by the global securities registered in its name and will not be considered the owner under the declaration. In most cases, a beneficial owner will also not be able to obtain a paper certificate evidencing the holder's ownership of securities. The book-entry system for holding securities eliminates the need for physical movement of certificates and is the system through which most publicly traded common stock is held in the United States. However, the laws of some jurisdictions require some purchasers of securities to take physical delivery of their securities in definitive form. These laws may impair the ability to transfer book-entry securities.

Title to book-entry interests in the securities will pass by book-entry registration of the transfer within the records of DTC in accordance with its procedures.

If DTC notifies us that it is unwilling or unable to continue as a clearing system in connection with the registered global securities or ceases to be a clearing agency registered under the Exchange Act, and a successor clearing system is not appointed by us within 90 days after receiving that notice from DTC or upon becoming aware that DTC is no longer so registered, we will issue or cause to be issued individual certificates in registered form on registration of transfer of, or in exchange for, book-entry interests in the securities represented by registered global securities upon delivery of those registered global securities for cancellation. We may also permit beneficial owners of book-entry securities represented by a global security to exchange their beneficial interests for definitive (paper) securities if, in our sole discretion, we decide to allow some or all book-entry securities to be exchangeable for definitive securities in registered form.

Unless we indicate otherwise, any global security that is exchangeable will be exchangeable in whole for definitive securities in registered form, with the same terms and of an equal aggregate principal amount. Definitive securities will be registered in the name or names of the person or persons specified by DTC in a written instruction to the registrar of the securities. DTC may base its written instruction upon directions that it receives from its participants.

In this prospectus, for book-entry securities, references to actions taken by security holders will mean actions taken by DTC upon instructions from its participants, and references to payments and notices of redemption to security holders will mean payments and notices of redemption to DTC as the registered holder of the securities for distribution to participants in accordance with DTC's procedures.

Initial settlement for the securities offered on a global basis through DTC will be made in immediately available funds. Secondary market trading between DTC's participants will occur in the ordinary way in accordance with DTC's rules and will be settled in immediately available funds using DTC's Same-Day Funds Settlement System.

Although DTC has agreed to the foregoing procedures in order to facilitate transfers of interests in the securities among participants thereof, it is under no obligation to perform or continue to perform the foregoing procedures and these procedures may be changed or discontinued at any time.

DTC is a limited purpose trust company organized under the laws of the State of New York, a member of the Federal Reserve System, a clearing corporation within the meaning of the New York Uniform Commercial Code and a clearing agency registered under section 17A of the Securities Exchange Act of 1934. The rules applicable to DTC and its participants are on file with the SEC.

We will not have any responsibility or liability for any aspect of the records relating to, or payments made on account of, beneficial ownership interest in the book-entry securities or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

PLAN OF DISTRIBUTION

We may offer the offered securities in one or more of the following ways from time to time:

- to or through underwriters or dealers;
- by ourselves directly;
- through agents; or
- through a combination of any of these methods of sale.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum commission or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate principal amount of securities offered pursuant to this prospectus. We anticipate, however, that the maximum commission or discount to be received in any particular offering of securities will be significantly less than this amount.

The prospectus supplement relating to a particular offering of securities will set forth the terms of such offering, including:

- the type of securities to be offered;
- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- the purchase price of the offered securities and the proceeds to us from such sale;
- any underwriting discounts and commissions or agency fees and other items constituting underwriters' or agents' compensation, which in the aggregate will not exceed 8% of the gross proceeds of the offering;
- the initial public offering price;
- any discounts or concessions to be allowed or reallowed or paid to dealers; and
- any securities exchanges on which such offered securities may be listed.

Any initial public offering prices, discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

The distribution of the offered securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices.

If underwriters are used in an offering of offered securities, such offered securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The securities may be either offered to the public through underwriting syndicates represented by one or more managing underwriters or by one or more underwriters without a syndicate. Unless otherwise set forth in the prospectus supplement, the underwriters will not be obligated to purchase offered securities unless specified conditions are satisfied, and if the underwriters do purchase any offered securities, they will purchase all offered securities.

In connection with underwritten offerings of the offered securities and in accordance with applicable law and industry practice, underwriters may over-allot or effect transactions that stabilize, maintain or otherwise affect the market price of the offered securities at levels above those that might otherwise prevail in the open market, including by entering stabilizing bids, effecting syndicate covering transactions or imposing penalty bids, each of which is described below.

- A stabilizing bid means the placing of any bid, or the effecting of any purchase, for the purpose of pegging, fixing or maintaining the price of a security.

- A syndicate covering transaction means the placing of any bid on behalf of the underwriting syndicate or the effecting of any purchase to reduce a short position created in connection with the offering.

- A penalty bid means an arrangement that permits the managing underwriter to reclaim a selling concession from a syndicate member in connection with the offering when offered securities originally sold by the syndicate member are purchased in syndicate covering transactions.

These transactions may be effected on an exchange or automated quotation system, if the securities are listed on that exchange or admitted for trading on that automated quotation system, or in the over-the-counter market or otherwise.

If a dealer is utilized in the sales of offered securities, we will sell such offered securities to the dealer as principal. The dealer may then resell such offered securities to the public at varying prices to be determined by such dealer at the time of resale. Any such dealer may be deemed to be an underwriter, as such term is defined in the Securities Act, of the offered securities so offered and sold. The name of the dealer and the terms of the transaction will be set forth in the related prospectus supplement.

We may enter into derivative transactions with third parties or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, such third parties (or their affiliates) may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, such persons may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of securities, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of securities. Such persons will be underwriters and, if not identified in this prospectus, will be identified in the applicable prospectus supplement (or a post-effective amendment).

Sales to or through one or more underwriters or agents in at-the-market offerings will be made pursuant to the terms of a distribution agreement with the underwriters or agents. Such underwriters or agents may act on an agency basis or on a principal basis. During the term of any such agreement, shares may be sold on a daily basis on any stock exchange, market or trading facility on which the ordinary shares are traded, in privately negotiated transactions or otherwise as agreed with the underwriters or agents. The distribution agreement will provide that any ordinary share sold will be sold at negotiated prices or at prices related to the then prevailing market prices for our ordinary shares. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined at this time and will be described in a prospectus supplement. Pursuant to the terms of the distribution agreement, we may also agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase, blocks of our ordinary shares or other securities. The terms of each such distribution agreement will be described in a prospectus supplement.

We may sell our ordinary shares pursuant to dividend reinvestment, share purchase plans and similar plans in which our stockholders as well as other investors may participate. Purchasers of shares under such plans may, upon resales, be deemed to be underwriters. These shares may be resold in market transactions (including coverage of short positions), in privately negotiated transactions or otherwise. Ordinary shares sold under any such plans may be issued at a discount to the market price of the ordinary shares. The difference between the price owners who may be deemed to be underwriters pay us for our ordinary shares acquired under any such plan, after deduction of the applicable discount from the market price, and the price at which such shares are resold, may be

deemed to constitute underwriting commissions or fees received by these owners in connection with such transactions.

We may also issue our ordinary shares to officers, directors, employees, consultants, agents or other persons pursuant to awards made under our equity incentive plans. Such ordinary shares may be resold by our officers and directors under this prospectus as indicated in a prospectus supplement.

We may loan ordinary shares to underwriters, agents and others, pursuant to share lending agreements, which may be offered for sale in transactions, including block sales, on any securities exchange, market or trading facility.

We may loan or pledge securities to a financial institution or other third party that in turn may sell the securities using this prospectus. Such financial institution or third party may transfer its short position to investors in our securities or in connection with a simultaneous offering of other securities offered by this prospectus.

Offered securities may be sold directly by us to one or more institutional purchasers, or through agents designated by us from time to time, at a fixed price or prices, which may be changed, or at varying prices determined at the time of sale. Any such agent may be deemed to be an underwriter as that term is defined in the Securities Act. Any agent involved in the offer or sale of the offered securities in respect of which this prospectus is delivered will be named, and any commissions payable by us to such agent will be set forth, in the prospectus supplement relating to that offering. Unless otherwise indicated in such prospectus supplement, any such agent will be acting on a best efforts basis for the period of its appointment.

If so indicated in the applicable prospectus supplement, we will authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase offered securities from us at the public offering price set forth in such prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject only to those conditions set forth in the prospectus supplement and the prospectus supplement will set forth the commission payable for solicitation of such contracts.

In addition, ordinary shares may be issued in exchange for debt securities.

Each series of offered securities, other than the ordinary shares which is listed on the Nasdaq Global Select Market, will be a new issue of securities and will have no established trading market. Any underwriters to whom offered securities are sold for public offering and sale may make a market in such offered securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. The offered securities may or may not be listed on a national securities exchange. No assurance can be given that there will be a market for the offered securities.

One or more firms, referred to as "remarketing firms," may also offer or sell the securities, if the prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as agents for us. These remarketing firms will offer or sell the securities in accordance with a redemption or repayment pursuant to the terms of the securities. The prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

Underwriters, dealers, agents and remarketing firms may be entitled, under agreements with us, to indemnification by us against certain civil liabilities, including liabilities under the Securities Act

relating to material misstatements and omissions, or to contribution with respect to payments which the underwriters, dealers or agents may be required to make in respect thereof. Underwriters, dealers, agents and remarketing firms may be customers of, engage in transactions with, or perform services for, us and our affiliates in the ordinary course of business.

LEGAL MATTERS

Legal matters with respect to U.S. federal and New York law in connection with this offering will be passed upon for us by Morgan, Lewis & Bockius LLP, London, England. Certain legal matters with respect to Dutch law in connection with the validity of the shares being offered by this prospectus and other legal matters will be passed upon for us by Rutgers Posch Visée Endedijk N.V., Amsterdam, the Netherlands.

EXPERTS

The consolidated financial statements as of December 31, 2013 and 2012 and for each of the three years in the period ended December 31, 2013, included in this prospectus have been so included in reliance on the report of PricewaterhouseCoopers Accountants N.V., an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting. The current address of PricewaterhouseCoopers Accountants N.V. is Newtonlaan 205, 3584 BH Utrecht, the Netherlands.

EXPENSES

The following table sets forth the expenses (other than underwriting discounts and commissions or agency fees and other items constituting underwriters' or agents' compensation, if any) expected to be incurred by us in connection with a possible offering of $250 million of the securities registered under this registration statement. All amounts other than the SEC registration fee and FINRA filing fee are estimates.

SEC Registration Fee	$ 29,050
Printing and Engraving Expenses	*
Legal Fees and Expenses	*
Accountants' Fees and Expenses	*
Nasdaq Fees	*
FINRA Filing Fee	
Trustee's fees and expenses	*
Miscellaneous Costs	*
Total	$ *

* To be provided by a prospectus supplement or as an exhibit to a Report on Form 6-K that is incorporated by reference into this prospectus.

DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, the registrant has been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is therefore unenforceable.

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3,000,000 Shares

Ordinary Shares

PROSPECTUS SUPPLEMENT

April , 2015

Joint Book-Running Managers

Leerink Partners **Cowen and Company** **Piper Jaffray & Co.**

Co-Managers

Oppenheimer & Co. **H.C. Wainwright & Co.**