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As confidentially submitted to the Securities and Exchange Commission on July 10, 2014

Registration no.

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

Form F-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

PROQR THERAPEUTICS B.V.*

(Exact Name of Registrant as Specified in Its Charter)

N/A
(Translation of Registrant's Name into English)

The Netherlands	2834	Not applicable
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

Daniel de Boer, Chief Executive Officer
ProQR Therapeutics B.V.
Darwinweg 24
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+31 (0)85 4 89 49 32
(Address, Including ZIP Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

(Name, Address, Including ZIP Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies to:

Mitchell S. Bloom, Esq.	**René Beukema, Chief Corporate**	**Brian A. Johnson, Esq.**
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Goodwin Procter LLP	**ProQR Therapeutics B.V.**	**Wilmer Cutler Pickering Hale and Dorr LLP**
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Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE(1)(2)	AMOUNT OF REGISTRATION FEE
Ordinary shares, par value € per share	$	$

(1) Estimated solely for the purpose of determining the amount of registration fee in accordance with Rule 457(o) under the Securities Act of 1933.
(2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

* We intend to convert the legal form of our company under Dutch law prior to the completion of this offering from a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) to a public company with limited liability (*naamloze vennootschap*) and to change our name from ProQR Therapeutics B.V. to ProQR Therapeutics N.V.

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The information contained in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JULY 10, 2014

PRELIMINARY PROSPECTUS

Shares

ORDINARY SHARES

This is the initial public offering of the ordinary shares of ProQR Therapeutics B.V. We are offering ordinary shares.

Currently, no public market exists for our ordinary shares. We expect the initial public offering price to be between $ and $ per ordinary share.

ProQR Therapeutics B.V. is a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) incorporated under the laws of the Netherlands. Prior to the completion of this offering, we intend to convert into a public company with limited liability (*naamloze vennootschap*), and our name will be ProQR Therapeutics N.V.

We intend to apply for the listing of our ordinary shares on the NASDAQ Global Market under the symbol " ". We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

	PER ORDINARY SHARE	TOTAL
Public offering price	$	$
Underwriting discounts and commissions(1)		
Proceeds to us, before expenses		

(1) The underwriters will also be reimbursed for certain expenses incurred in this offering. See "Underwriting" for details.

We have granted the underwriters an option for a period of 30 days to purchase an additional ordinary shares. If the underwriters exercise their option in full, the total underwriting discounts and commissions payable by us will be $, and the total proceeds to us, before expenses, will be $.

Investing in our ordinary shares involves a high degree of risk. See "Risk Factors" beginning on page 8 of this prospectus.

Neither the Securities and Exchange Commission nor any state 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.

Delivery of the ordinary shares is expected to be made on or about , 2014.

Leerink Partners **Deutsche Bank Securities**

JMP Securities
H.C. Wainwright & Co., LLC

Prospectus dated , 2014.

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Neither we nor the underwriters have authorized anyone to provide you with any information other than that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus may only be used where it is legal to offer and sell our ordinary shares. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our ordinary shares. Our business, financial condition, results of operations and prospects may have changed since that date. Neither we nor the underwriters are making an offer of these securities in any jurisdiction where the offer is not permitted.

Through and including , 2014 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction, other than the United States, where action for that purpose is required. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of our ordinary shares and the distribution of this prospectus outside the United States.

MARKET AND INDUSTRY DATA

This prospectus includes estimates of market size and industry data and forecasts that we have obtained from the medical literature and industry publications, surveys and forecasts, as well as from internal company sources. Industry publications, surveys and forecasts generally state that the information contained therein has

been obtained from sources believed to be reliable. However, we and the underwriters have not independently verified any of the data from third-party sources, nor have we or the underwriters ascertained the underlying economic or other assumptions relied upon therein. In addition, this prospectus includes market size and industry data that we have prepared primarily based on our knowledge of the industry in which we operate. Unless otherwise noted, internal analysis and estimates may not have been verified by independent sources. All information regarding our market and industry is based on the latest data currently available to us, which in some cases may be several years old. Our estimates, in particular as they relate to market size and our general expectations, involve risks and uncertainties and are subject to change based on various factors, including those discussed in the sections entitled "Special Note Regarding Forward-Looking Statements" and "Risk Factors".

EXCHANGE RATES

All references in this prospectus to "U.S. dollars" or "$" are to the legal currency of the United States, and all references to "€" or "euro" are to the currency of the European Economic and Monetary Union.

Our business to date has been conducted primarily in the European Union, and we prepare our financial statements in euros. This prospectus contains translations of euro amounts into U.S. dollars at specific rates. Unless otherwise noted, all translations from euros to U.S. dollars and from U.S. dollars to euros in this prospectus were made at a rate of $1.36 per euro, the noon buying rate quoted as of July 9, 2014 by the Federal Reserve Bank of New York. We make no representation that any euro or U.S. dollar amounts could have been, or could be, converted into U.S. dollars or euro, as the case may be, at any particular rate, at the rates stated below, or at all.

The table below shows the period end, average, high and low exchange rates of U.S. dollars per euro for the periods shown. Average rates are computed by using the noon buying rate of the Federal Reserve Bank of New York for the euro on each business day during the relevant year indicated or each business day during the relevant month indicated. The rates set forth below are provided solely for your convenience and may differ from the actual rates used in the preparation of the combined financial statements included in this prospectus and other financial data appearing in this prospectus.

	Period End	Average	Low	High
		(U.S. dollar per euro)		
Year Ended December 31:				
2009	1.43	1.39	1.25	1.51
2010	1.33	1.33	1.20	1.45
2011	1.30	1.39	1.29	1.49
2012	1.32	1.29	1.21	1.35
2013	1.38	1.33	1.28	1.38
Month Ended:				
January 2014	1.35	1.36	1.35	1.37
February 2014	1.38	1.37	1.35	1.38
March 2014	1.38	1.38	1.37	1.39
April 2014	1.39	1.38	1.37	1.39
May 2014	1.36	1.37	1.36	1.39
June 2014	1.37	1.36	1.35	1.37

The noon buying rate of the Federal Reserve Bank of New York for the euro on July 9, 2014 was €1.00 = $1.36.

TRADEMARKS

"ProQR" is our trademark. Other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent permissible under applicable law, their rights thereto.

CERTAIN DEFINITIONS

Unless the context specifically indicates otherwise, references in this prospectus to "ProQR Therapeutics B.V.", "ProQR Therapeutics N.V.", "ProQR Therapeutics", "ProQR", "we", "our", "ours", "us", "our company" or similar terms refer to (1) ProQR Therapeutics B.V. prior to our conversion into a public company with limited liability (*naamloze vennootschap*), and (2) ProQR Therapeutics N.V. after giving effect to the conversion into a public company with limited liability (*naamloze vennootschap*), which is expected to occur prior to the completion of this offering.

PROSPECTUS SUMMARY

This summary does not contain all of the information you should consider before buying our ordinary shares. You should read the entire prospectus carefully, especially the "Risk Factors" section beginning on page 8, "Management's Discussion and Analysis of Financial Condition and Results of Operations" beginning on page 50 and our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our ordinary shares.

Overview

We are an innovative biopharmaceutical company engaged in the discovery and development of RNA-based therapeutics for the treatment of severe genetic disorders, with an initial focus on Cystic Fibrosis, or CF. Utilizing our unique, proprietary RNA repair technologies, we believe we will be able to treat genetic disorders in which a single protein is defective due to certain types of genetic mutation. We design our therapeutic candidates to specifically target and repair the defective messenger RNA, or mRNA, that is a product of a mutated gene in order to restore the expression and function of normal, or wild-type, protein. Our technologies employ single-stranded RNA-based oligonucleotides, which act as guide sequences to repair the targeted abnormal mRNA. The repaired mRNA then acts as a template to generate wild-type protein to address the underlying cause of the genetic disorder. We believe that this is a unique approach that offers advantages compared with small molecule, gene therapy and other therapeutic strategies.

Our current efforts are dedicated to the development of a disease-modifying therapy for the treatment of CF, the most common fatal inherited disease in the western world, which affects an estimated 70,000 to 100,000 patients worldwide. We are also developing a treatment for Leber's Congenital Amaurosis, or LCA, the leading genetic cause of blindness in childhood. Further, based on our own research and initial selection criteria, we believe that our RNA repair technologies can potentially be used to treat a broad range of other severe genetic diseases that are currently untreatable or have limited effective treatment options, and to date, we have identified approximately 50 potential target indications.

Development of Our Lead Product Candidate, QR-010, in Cystic Fibrosis

CF is a genetic disease that currently has no cure. The median age of death for CF patients is 29, and more than 90% of CF patients die from respiratory failure. To date, all but one of the therapies approved to treat CF patients are designed to treat the symptoms of the disease rather than address the underlying cause. CF results from mutations in the gene that encodes a protein called cystic fibrosis transmembrane conductance regulator, or CFTR. Although there are more than 1,900 different genetic mutations that cause CF, the DF508 mutation that we are targeting is the most prevalent and is present in approximately 70% of all CF patients.

Our lead product candidate, QR-010, which we believe is a first-in-class RNA-based oligonucleotide, is designed to address the underlying cause of the disease by repairing the mRNA defect encoded by the DF508 mutation in the CFTR gene of CF patients. QR-010 has been granted orphan drug designation in the United States and the European Union.

The DF508 mutation is a deletion of three coding base pairs, or nucleotides, in the CFTR gene, which results in the production of a misfolded CFTR protein that does not function normally. QR-010 is designed to bind to the defective CFTR mRNA sequences on both sides of the DF508 region of the mRNA and guide the insertion of the three missing nucleotides, thus repairing the mRNA and subsequently producing wild-type CFTR protein. This protein is expressed on the cell surface and restores normal CFTR functionality, including chloride transport, chloride-bicarbonate exchange and regulation of the epithelial sodium channel.

QR-010 is designed to be delivered through a small, handheld aerosol delivery device, or nebulizer, in the form of a mist inhaled into the lungs. We believe this method will allow maximum exposure of QR-010 to the primary target organ, the lung, as well as significant exposure to other affected organs through systemic absorption into the blood.

To date, we have conducted extensive *in vitro* and *in vivo* pre-clinical studies of QR-010. In these pre-clinical studies, we demonstrated repair of CFTR mRNA and activity of wild-type protein through improved chloride ion efflux in DF508 mutant human cell lines. We also evaluated *in vivo* activity of QR-010 in DF508 mice and detected increased amounts of repaired mRNA and functional CFTR protein in multiple organs. Most notably, QR-010 treatment of DF508 mutant mice restored CFTR function as measured by two independent *in vivo* tests, which are similar to human diagnostic tests, namely Nasal Potential Difference, or NPD, and a salivary secretion assay, a mouse equivalent of the sweat chloride test. We believe these results in pre-clinical models of CF provide support for the clinical development and therapeutic potential of QR-010.

In the fourth quarter of 2014, we plan to file an Investigational New Drug application, or IND, with the U.S. Food and Drug Administration, or FDA, and a Clinical Trial Application, or CTA, with the European Medicines Agency, or EMA, for QR-010. We have had a pre-IND meeting with the FDA and scientific advice and protocol assistance meetings with the EMA, and we intend to initiate our first clinical trial directly in CF patients. This clinical trial will be a Phase 1b, randomized, double-blind, placebo-controlled, 28-day dose-escalation study to evaluate the safety, tolerability and pharmacokinetics of QR-010 in CF patients who have two copies of the DF508 mutation. We will also assess exploratory outcome measures that could be indicative of the potential efficacy of QR-010. In parallel with our Phase 1b trial, we will also conduct a proof-of-concept, or POC, study designed to demonstrate restoration of CFTR function in the nasal lining of CF patients with the DF508 mutation. We expect to report top-line data from our Phase 1b trial and our POC study in the fourth quarter of 2015.

Development of Our First Non-CF Program, QR-110, in Leber's Congential Amaurosis

Our second program is focused on LCA, which affects 116,000 people worldwide. The most common cause of LCA is a mutation in the centrosome- and cilium-associated gene centrosomal protein 290 or CEP290. This mutation is present in at least 11,000 of all LCA patients worldwide and accounts for the most severe LCA disease phenotype. We are developing QR-110 to treat this form of congenital blindness. In pre-clinical studies to date, QR-110 has demonstrated repair of CEP290 mRNA in cultured lymphoblastoid cells of LCA patients with two copies of the CEP290 mutation. We also observed significantly increased CEP290 protein levels and a complete rescue of ciliation and cilium length to normal levels. The next steps in the program include compound optimization, chemistry, manufacturing and control, and pre-clinical safety studies. If we choose to advance QR-110 into clinical development, we anticipate that we would initiate our first clinical trial in 2016.

Our Business Strategy

We are dedicated to improving the lives of patients through the development of RNA-based therapies for severe genetic diseases and have an initial focus on patients with CF.

Key elements of our strategy include:

- ***Rapidly advance QR-010 for the treatment of CF.*** Our lead product candidate, QR-010, has generated compelling data in pre-clinical studies, which we believe support its potential as a disease modifying therapy for CF patients. We intend to advance QR-010 into clinical trials in CF patients with the DF508 mutation, which affects approximately 70% of all CF patients. In the fourth quarter of 2014, we plan to file our IND with the FDA, file our CTA with the EMA and initiate our first clinical trial directly in CF patients. We are also studying applications of our RNA repair technologies for mutations other than DF508 that could potentially be used to treat an additional 10% of CF patients, including those with the G551D mutation.

- ***Utilize our proprietary RNA repair technologies and know-how to develop additional product candidates targeting genetic diseases with high unmet medical need.*** We aim to develop a product pipeline targeting severe genetic diseases with no or limited effective treatments caused by mutations that we believe can be treated with our RNA repair technologies. Based on our own research and initial selection criteria, we have to date identified approximately 50 potential target indications. As our first non-CF therapeutic program, we are developing QR-110 to treat the most common mutation causing Leber's Congenital Amaurosis, the leading genetic cause of blindness in childhood.
- ***Independently commercialize QR-010 and any other CF product we successfully develop.*** We intend to commercialize QR-010 independently, if approved, and retain all commercial rights in major markets. There are extensive CF patient registries, and CF patients are treated in centralized, specialized care centers. Because of this well-organized CF community, we believe we will be able to market QR-010 effectively, if approved, with an initially small, targeted sales force of approximately 35 representatives in the United States and Europe.
- ***Consider collaborative partnerships to develop and commercialize our RNA repair technologies or programs in specific indications outside of CF.*** We will consider collaborative partnerships with pharmaceutical companies and others to leverage our core technologies in therapeutic areas outside of CF depending on the attractiveness of the opportunities. These partnerships may provide us with further validation of our RNA repair technologies, funding to advance our product candidates and access to development, manufacturing and commercial expertise and capabilities.

Our Corporate Information

We are a private company with limited liability *(besloten vennootschap met beperkte aansprakelijkheid)* incorporated under the laws of the Netherlands, and prior to the completion of this offering we intend to convert to a public company with limited liability (*naamloze vennootschap*). Our executive offices are located at Darwinweg 24, 2333CR Leiden, the Netherlands, and our telephone number is +31 (0)85 4 89 49 32. Our website address is www.proqr-tx.com. The information contained on, or accessible through, our website is not a part of this prospectus.

Risk Associated with Our Business

Our business is subject to numerous risks and uncertainties, including those highlighted in the section entitled "Risk Factors" immediately following this prospectus summary. These risks include, but are not limited to, the following:

- We are a pre-clinical stage biopharmaceutical company with a history of losses. We expect to continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability, which could result in a decline in the market value of our ordinary shares.
- We depend almost entirely on the success of one product candidate, QR-010, which is still in pre-clinical development. We cannot be certain that we will be able to successfully complete the clinical development of, obtain regulatory approval for, or successfully commercialize QR-010.
- We will require additional capital to fund our operations and if we fail to obtain necessary financing, we will not be able to complete the development and commercialization of QR-010.
- We have a limited operating history, which may make it difficult to evaluate the success of our business to date and to assess our future viability.
- The regulatory approval processes of the FDA, the EMA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for QR-010, our business will be substantially harmed.

- Failures or delays in the commencement or completion of our pre-clinical studies or planned clinical trials of QR-010 could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.
- Positive results from pre-clinical testing of QR-010 are not necessarily predictive of the results of our planned clinical trials. If we cannot achieve positive results in our clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize QR-010.
- Our RNA repair technologies are unproven and may not result in marketable products.
- Our development and commercialization strategy for QR-010 relies in part upon certain patent rights that we license from Massachusetts General Hospital, and termination of that license could have a materially adverse effect on our business, financial condition, results of operations and prospects.
- We face competition from entities that have developed or may develop product candidates for our target indications, including companies developing novel treatments for CF patients. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize our product candidates may be adversely affected.
- We license patent rights from third-party owners or licensees and if we fail to comply with our obligations in our intellectual property licenses, we could lose rights that are fundamental to our business. If such owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be adversely affected.
- We may not be able to protect our intellectual property rights throughout the world.
- Any inability to attract and retain qualified key management, such as Daniel de Boer, our chief executive officer, and Noreen Henig, our chief development officer, and technical personnel would impair our ability to implement our business plan.
- Members of our management board and supervisory board and our principal shareholders and their affiliates will continue to exercise significant control over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Implications of Being an Emerging Growth Company

We qualify as an “emerging growth company” as defined in the Jumpstart our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. As an emerging growth company, we are electing to take advantage of the following exemptions:

- not providing an auditor attestation report on our system of internal control over financial reporting; and
- not complying 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 (auditor discussion and analysis).

The JOBS Act permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We are irrevocably electing not to avail ourselves of this extended transition period for complying with new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not “emerging growth companies.”

We may take advantage of these exemptions for up to five years or such earlier time as we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1.0 billion in annual revenues, have more than $700 million in market value of our ordinary shares held by non-affiliates or issue more than $1.0 billion of non-convertible debt over a three-year period.

THE OFFERING

Ordinary shares offered by us	ordinary shares
Ordinary shares to be outstanding immediately after this offering	ordinary shares
Offering price	The initial public offering price per ordinary share is expected to be between $ and $.
Option to purchase additional shares	We have granted to the underwriters an option, which is exercisable within 30 days from the date of this prospectus, to purchase an aggregate of up to an additional ordinary shares. See "Underwriting" for more information.
Use of proceeds	We intend to use the net proceeds from this offering to fund development of QR-010 through Phase 2a clinical trials, to fund development costs associated with non-clinical studies and related activities for QR-110 and for discovery and other pipeline projects, as well as working capital and other general corporate purposes. See "Use of Proceeds" for additional information.
Risk factors	See "Risk Factors" and other information included in this prospectus for a discussion of risks you should carefully consider before investing in our ordinary shares.
Listing	We intend to apply for the listing of our ordinary shares on the NASDAQ Global Market under the symbol " ."

The total number of ordinary shares that will be outstanding immediately after this offering is based on 144,524 ordinary shares outstanding as of June 30, 2014 and excludes 11,617 ordinary shares held by Stichting ProQR Therapeutics Participation, or the Foundation, for which no depository receipts have been issued and includes 601 ordinary shares for which depository receipts have been issued by the Foundation.

Unless otherwise indicated, all information in this prospectus assumes:

- that the underwriters do not exercise their option to purchase an aggregate of up to an additional ordinary shares from us;
- our conversion into a public company with limited liability (*naamloze vennootschap*) under the laws of the Netherlands and amendment of our articles of association, which will occur prior to the completion of this offering;
- the conversion of all of our outstanding preferred shares into 81,187 ordinary shares upon the closing of this offering; and
- the -for- split of our ordinary shares (including the converted preferred shares), which will occur upon or prior to completion of this offering.

SUMMARY FINANCIAL DATA

The following summary financial data as of December 31, 2013 and for the period from February 21, 2012 (inception) through December 31, 2012 and the year ended December 31, 2013 have been derived from our audited financial statements included elsewhere in this prospectus. The summary financial data below should be read together with those financial statements as well as the "Selected Financial Data" and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Period From February 21, 2012 (Inception) Through December 31, 2012	Year Ended December 31, 2013
	€ in thousands (except share and per share data)	
Statement of comprehensive loss data:		
Other income	€ 23	€ 116
Research and development costs	(285)	(2,550)
General and administrative costs	(157)	(764)
Share-based compensation	—	(41)
Operating loss	**(419)**	**(3,239)**
Financial income and expense	1	(14)
Net loss and comprehensive loss	(418)	(3,253)
Net loss per share		
Basic and diluted	(17.04)	(60.01)
Weighted average shares outstanding	24,556	54,199

	As of December 31, 2013		
	Actual	Pro Forma	Pro Forma As Adjusted
	(€ in thousands)		
Statement of financial position data			
Cash and cash equivalents	€ 4,129		
Total assets	4,504		
Total debt	4,593		
Total shareholders' equity (deficit)	(89)		

RISK FACTORS

Investing in our ordinary shares involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our ordinary shares. If any of the following risks actually occurs, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our ordinary shares could decline and you could lose part or all of your investment.

Risks Related to Our Capital Needs and Financial Position

We are a pre-clinical stage biopharmaceutical company with a history of losses. We expect to continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability, which could result in a decline in the market value of our ordinary shares.

We are a pre-clinical stage biopharmaceutical company with a limited operating history, engaged in the discovery and development of RNA-based therapeutics for the treatment of severe genetic disorders. Since our inception in February 2012, we have devoted substantially all of our resources to the development of our lead product candidate, QR-010. We have had significant operating losses since our inception. As of December 31, 2013, we had an accumulated deficit of €3,671,000. For the twelve months ended December 31, 2013, our net loss was €3,253,000 and for the period from February 21, 2012 (inception) through December 31, 2012, our net loss was approximately €418,000. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our technologies and product candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of product candidates based on novel technologies.

To date, the only revenue we have generated has been from the receipt of research grants. Our ability to generate revenue and become profitable depends upon our ability to obtain marketing approval and successfully commercialize QR-010 or other product candidates that we may develop, in-license or acquire in the future.

Even if we are able to successfully achieve regulatory approval for these product candidates, we do not know when any of these products will generate revenue for us, if at all. We have not generated, and do not expect to generate, any product revenue for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, pre-clinical studies and clinical trials and the regulatory approval process for product candidates. The amount of future losses is uncertain. Our ability to achieve profitability, if ever, will depend on, among other things, us or any future collaborators successfully developing product candidates, obtaining regulatory approvals to market and commercialize product candidates, manufacturing any approved products on commercially reasonable terms, establishing a sales and marketing organization or suitable third party alternatives for any approved product and raising sufficient funds to finance business activities. If we or any future collaborators are unable to develop and commercialize one or more of our product candidates or if sales revenue from any product candidate that receives approval is insufficient, we will not achieve profitability, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our ability to generate revenue from QR-010 or other product candidates also depends on a number of additional factors, including our ability to:

- successfully complete development activities, including the remaining pre-clinical studies and planned clinical trials for QR-010, which we expect to initiate in the fourth quarter of 2014;
- complete and submit New Drug Applications, or NDAs, to the U.S. Food and Drug Administration, or FDA, and Marketing Authorisation Applications, or MAAs, to the European Medicines Agency, or EMA, and obtain regulatory approval for indications for which there is a commercial market;

- complete and submit applications to, and obtain regulatory approval from, other foreign regulatory authorities;
- set a commercially viable price for any products for which we may receive approval;
- obtain commercial quantities of our products at acceptable cost levels;
- develop a commercial organization capable of sales, marketing and distribution for the products we intend to sell ourselves in the markets in which we have retained commercialization rights;
- find suitable partners to help us market, sell and distribute our approved products in other markets;
- achieve acceptance among patients, clinicians and advocacy groups for any products we develop; and
- obtain coverage and adequate reimbursement from third-party, including government, payors.

In addition, because of the numerous risks and uncertainties associated with product development, including the risk that our product candidates may not advance through development or be shown to be safe and effective for their intended uses, the FDA, the EMA or other regulatory agencies may require additional clinical trials or pre-clinical studies or impose post-approval requirements.

We are unable to predict the timing or amount of increased expenses, or when or if we will be able to achieve or maintain profitability. Even if we are able to complete the processes described above, we anticipate incurring significant costs associated with commercializing our product candidates.

Even if we are able to generate revenues from the sale of QR-010 or any other product candidate, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

We will require additional capital to fund our operations and if we fail to obtain necessary financing, we will not be able to complete the development and commercialization of QR-010.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to conduct further research and development and pre-clinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to launch and commercialize any product candidates for which we receive regulatory approval, including potentially building our own commercial organization to address the United States, the European Union and certain other markets. Based on our current operating plan, we believe that the net proceeds from this offering, together with existing cash, cash equivalents and short-term investments, will be sufficient to fund our anticipated level of operations for at least the next months. However, our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of pre-clinical studies and clinical trials for our product candidates;
- the clinical development plans we establish for these product candidates;
- the number and characteristics of product candidates that we develop or may in-license;
- the terms of any collaboration agreements we may choose to conclude;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the EMA and other comparable foreign regulatory authorities;

- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities; and
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our products or product candidates or one or more of our other research and development initiatives. We also could be required to seek collaborators for one or more of our current or future product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of private and public equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, existing ownership interests will be diluted and the terms of such financings may include liquidation or other preferences that adversely affect the rights of existing shareholders. Debt financings may be coupled with an equity component, such as warrants to purchase shares, which could also result in dilution of our existing shareholders' ownership. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business and may result in liens being placed on our assets and intellectual property. If we were to default on such indebtedness, we could lose such assets and intellectual property. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, or grant licenses on terms that are not favorable to us.

We have a limited operating history, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We were formed in February 2012 and began operations in May 2012. Our operations to date have been limited to organizing and staffing our company, acquiring and developing product and technology rights, and conducting development activities for our product candidates, primarily QR-010. We have not yet begun clinical development or obtained regulatory approval for any of our product candidates. Consequently, any predictions about our future success, performance or viability may not be as accurate as they could be if we had a longer operating history, more experience with clinical development or approved products on the market.

Risks Related to the Development and Regulatory Approval of our Product Candidates

We depend almost entirely on the success of one product candidate, QR-010, which is still in pre-clinical development. We cannot be certain that we will be able to successfully complete the clinical development of, obtain regulatory approval for, or successfully commercialize QR-010.

We currently have no products on the market, and our most advanced product candidate, QR-010, is still in pre-clinical development. Our business depends almost entirely on the successful clinical development, regulatory approval and commercialization of QR-010, and it will require additional pre-clinical testing and substantial additional clinical development and regulatory approval efforts before we are permitted to commence its commercialization, if ever. None of our product candidates have advanced into a clinical program, and it will be several years before we can commence and complete a pivotal study for QR-010, if ever. The clinical trials and manufacturing and marketing of QR-010 and any other product candidates will be subject to extensive and rigorous review and regulation by numerous government authorities in the United States, the European Union and other jurisdictions where we intend to test and, if approved, market our product candidates. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through pre-clinical testing and clinical trials that the product candidate is safe and effective for use in each target indication, and potentially in specific patient populations, including the pediatric population. This process can take many years and may include post-marketing studies and surveillance, which would require the expenditure of substantial resources beyond the proceeds we raise in this offering. Of the large number of drugs in development for approval in the United States and the European Union, only a small percentage successfully complete the FDA or EMA regulatory approval processes, as applicable, and are commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our research, development and clinical programs, we cannot assure you that QR-010 or any other of our product candidates will be successfully developed or commercialized.

The regulatory approval processes of the FDA, the EMA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for QR-010, our business will be substantially harmed.

We are not permitted to market QR-010 in the United States or the European Union until we receive approval of an NDA from the FDA or an MMA from the EMA, respectively, or in any other foreign countries until we receive the requisite approval from such countries. Prior to submitting an NDA to the FDA or an MMA to the EMA for approval of QR-010 to treat CF patients with the DF508 mutation, we will need to complete our ongoing pre-clinical and toxicology studies, as well as a proof-of-concept study and Phase 1, Phase 2 and Phase 3 clinical trials. We are still conducting pre-clinical studies and have not yet commenced our clinical program or exposed any humans to QR-010. Successfully initiating and completing our clinical program and obtaining approval of an NDA or a MAA is a complex, lengthy, expensive and uncertain process, and the FDA, the EMA or other comparable foreign regulatory authorities may delay, limit or deny approval of QR-010 for many reasons, including, among others:

- we may not be able to demonstrate that QR-010 is safe and effective in treating CF patients with the DF508 mutation to the satisfaction of the FDA or the EMA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or the EMA for marketing approval;
- the FDA or the EMA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA or the EMA may require that we conduct additional clinical trials;
- the FDA or the EMA or other applicable foreign regulatory agencies may not approve the formulation, labeling or specifications of QR-010;
- the clinical research organizations, or CROs, that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;

- the FDA or the EMA may find the data from pre-clinical studies and clinical trials insufficient to demonstrate that QR-010's clinical and other benefits outweigh its safety risks;
- the FDA or the EMA may disagree with our interpretation of data from our pre-clinical studies and clinical trials;
- the FDA or the EMA may not accept data generated at our clinical trial sites;
- if our NDAs or MMAs, if and when submitted, are reviewed by the FDA or the EMA, as applicable, the regulatory agency may have difficulties scheduling the necessary review meetings in a timely manner, may recommend against approval of our application or may recommend that the FDA or the EMA, as applicable, require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy as a condition of approval or post-approval, and the EMA may grant only conditional approval or impose specific obligations as a condition for marketing authorization, or may require us to conduct post-authorization safety studies;
- the FDA, the EMA or other applicable foreign regulatory agencies may not approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the FDA or the EMA may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market QR-010. Moreover, because our business is almost entirely dependent upon this one product candidate, any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

Failures or delays in the commencement or completion of our pre-clinical studies or planned clinical trials of QR-010 could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

We have not commenced any clinical trials for QR-010. Successful completion of such clinical trials is a prerequisite to submitting an NDA to the FDA or a MMA to the EMA and, consequently, the ultimate approval and commercial marketing of QR-010. Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. A product candidate can unexpectedly fail at any stage of clinical development. The historical failure rate for product candidates is high due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. We do not know whether our clinical trials will begin or be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including, among others:

- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inadequate quantity or quality of a product candidate or other materials necessary to conduct clinical trials;
- difficulties obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, the proximity of patients to clinical sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- severe or unexpected drug-related side effects experienced by patients in our clinical trials or by individuals using drugs similar to our product candidates;

- reports from pre-clinical or clinical testing of other RNA therapies that raise safety or efficacy concerns; or
- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to lack of efficacy, side effects, personal issues or loss of interest.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the EMA or the IRBs at the sites where the IRBs are overseeing a clinical trial, a data safety monitoring board, or DSMB, overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA, the EMA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;
- unforeseen safety issues, including any that could be identified in our ongoing toxicology studies, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical supply materials; and
- lack of adequate funding to continue the clinical trial.

Positive results from pre-clinical testing of QR-010 are not necessarily predictive of the results of our planned clinical trials of QR-010. If we cannot achieve positive results in our clinical trials for QR-010, we may be unable to successfully develop, obtain regulatory approval for and commercialize QR-010.

Positive results from our pre-clinical testing of QR-010 *in vitro* and *in vivo* may not necessarily be predictive of the results from our planned clinical trials in humans. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in pre-clinical development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including adverse events. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval. If we fail to produce positive results in our clinical trials of QR-010, the development timeline and regulatory approval and commercialization prospects for our leading product candidate, and, correspondingly, our business and financial prospects would be materially adversely affected.

Our RNA repair technologies are unproven and may not result in marketable products.

We plan to develop a pipeline of product candidates using our proprietary RNA repair technologies for severe genetic disorders, focusing initially on a treatment for CF patients with the DF508 mutation, which affects approximately 70% of all CF patients. We believe that targeting the mRNA to restore the production of normal protein is a unique approach that offers advantages versus small molecule, gene therapy and other therapeutic approaches. However, the scientific research that forms the basis of our efforts to develop product candidates is both preliminary and limited.

We believe that we are the only company currently pursuing RNA repair technologies for the treatment of severe genetic disorders. We may discover that the molecules we develop to repair RNA do not possess certain properties required for a drug to be effective, such as the ability to remain stable in the human body for the period of time required for the drug to reach the target tissue or the ability to cross the cell wall and enter into cells within the target tissue for effective delivery. We may spend substantial funds attempting to introduce these

properties and may never succeed in doing so. In addition, product candidates based on RNA repair may demonstrate different chemical and pharmacological properties in humans than they do in laboratory studies or animals. Even if our product candidates, such as QR-010, have successful results in animal studies, they may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems or other CF treatments in unforeseen, ineffective or harmful ways. Our RNA repair technologies may provoke an unwanted immune response, or immunogenicity, against wild-type CFTR protein in patients successfully treated with QR-010. Such unwanted immunogenicity may neutralize the therapeutic effects of our product candidates and could result in harmful outcomes for patients. As a result, we may never succeed in developing a marketable product, we may not become profitable and the value of our ordinary shares would decline.

Furthermore, the FDA and the EMA have relatively limited experience with therapeutics based on RNA repair. To our knowledge, no regulatory authority has granted approval to any person or entity, including us, to market and commercialize therapeutics using RNA repair technology, which may increase the complexity, uncertainty and length of the regulatory approval process for our product candidates. Neither we nor any future collaborator may receive approval to market and commercialize any product candidate. Even if we or a collaborator were to obtain regulatory approval, the approval may be for disease indications or patient populations that are not as broad as we intended or may require labeling that includes significant use or distribution restrictions or safety warnings. We or a collaborator may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If our RNA repair technology proves to be ineffective, unsafe or commercially unviable, our entire platform and pipeline would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

Failure to obtain regulatory approval in jurisdictions outside the United States and the European Union would prevent our product candidates from being marketed in those jurisdictions.

In order to market and sell our products in jurisdictions other than the United States and the European Union, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The regulatory approval process outside the United States and the European Union generally includes all of the risks associated with obtaining FDA and EMA approval, but can involve additional testing. We may need to partner with third parties in order to obtain approvals outside the United States and the European Union. In addition, in many countries worldwide, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States and the European Union on a timely basis, if at all. Even if we were to receive approval in the United States or the European Union, approval by the FDA or the EMA does not ensure approval by regulatory authorities in other countries or jurisdictions. Similarly, approval by one regulatory authority outside the United States and the European Union would not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA or the EMA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of QR-010 or any of our other product candidates by regulatory authorities in other foreign jurisdictions, the commercial prospects of those product candidates may be significantly diminished and our business prospects could decline.

If we are not able to maintain orphan product exclusivity for QR-010 or obtain such status for future product candidates for which we seek this status, or 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 United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is

generally defined as a patient population of fewer than 200,000 individuals in the United States who have been diagnosed as having the disease or condition at the time of the submission of the request for orphan drug designation or not more than five in 10,000 people in the European Union. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity, which precludes the EMA or the FDA, as applicable, from approving another marketing application for the same or, in the EU, a similar drug for the same indication for that time period, unless the later product is clinically superior. The applicable period is seven years in the United States and ten years in the European Union following marketing approval. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation, for example if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if the incidence and prevalence of patients who are eligible to receive the drug in these markets materially increase. Although we have obtained orphan designation for QR-010 in the European Union and the United States, even after an orphan drug is approved, the same or, in the EU, a similar drug can subsequently be approved for the same condition if the competent regulatory agency 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.

If we lose orphan drug exclusivity or if our competitors obtain orphan drug exclusivity for other rare diseases or conditions we are targeting before we do, we may be precluded from obtaining marketing authorization or we may lose out on the potential benefits of market exclusivity.

A breakthrough therapy designation by the FDA for QR-010 may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that QR-010 will receive marketing approval.

We intend to seek a breakthrough therapy designation for QR-010, and we may do so for other product candidates as well. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe QR-010 or another of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. The availability of breakthrough therapy designation was established with the passage of the Food and Drug Administration Safety and Innovation Act of 2012, and while the FDA has released guidance as to the criteria it uses in designating drugs as breakthrough therapies, we cannot be sure that our product candidates will meet the FDA's qualifying criteria for such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

A fast track designation by the FDA may not actually lead to a faster development, regulatory review or approval process.

We intend to seek fast track designation for QR-010, and we may do so for other product candidates as well. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation, and even if we believe QR-010 or another of our product candidates is eligible for this designation, we cannot be sure that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Risks Related to Our Dependence on Third Parties

Our development and commercialization strategy for QR-010 relies in part upon certain patent rights that we license from Massachusetts General Hospital, and termination of that license could have a materially adverse effect on our business, financial condition, results of operations and prospects.

Some of our RNA repair technologies rely in part upon certain patent rights that we license from Massachusetts General Hospital, or MGH. Pursuant to our license agreement with MGH, we are obligated to use commercially reasonable efforts to develop and make available to the public one or more products or processes in the United States under the licensed MGH patent rights, as well as to achieve certain specified development, regulatory and commercial milestones. If we do not meet the specified milestones, MGH may be able to terminate the license agreement. MGH may also terminate the license agreement if we are in breach of certain financial obligations or we are otherwise in default of certain obligations under the license agreement. If MGH terminated our license agreement, it could have a materially adverse effect on our business, financial condition, results of operations and prospects.

If third parties on which we depend to conduct our pre-clinical studies or any future clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development program could be delayed with materially adverse effects on our business, financial condition, results of operations and prospects.

We rely on CROs, clinical data management organizations and consultants to design, conduct, supervise and monitor pre-clinical studies of our product candidates and will do the same for our planned clinical trials for QR-010 and any other clinical trials. We and our CROs are required to comply with various regulations, including Good Clinical Practices, or GCP, which are enforced by the FDA, and guidelines of the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities to ensure that the health, safety and rights of patients are protected in clinical development and clinical trials, and that trial data integrity is assured. Regulatory authorities ensure compliance with these requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or other comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with such requirements. In addition, our clinical trials must be conducted with products produced under current Good Manufacturing Practice, or cGMP, requirements. Failure to comply with these regulations may require us to repeat pre-clinical and clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and pre-clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure

to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. Additionally, any significant delays could cause us to miss diligence milestones under our license agreement with MGH and could cause MGH to terminate the agreement, which would further harm our business, financial condition, results of operations and prospects.

Because we have relied on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of pre-clinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our pre-clinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA and the EMA require clinical trials to be conducted in accordance with GCP, including for conducting, recording and reporting the results of pre-clinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

We rely on third-party manufacturers and suppliers and we intend to rely on third parties to produce pre-clinical, clinical and commercial supplies of QR-010 and any future product candidates.

We rely on third parties to supply the materials and components for, and manufacture, our research and development, pre-clinical and clinical trial supplies. We also intend to rely on third-party manufacturers to manufacture the aerosol delivery device that we intend to use to deliver QR-010 to CF patients. We do not own manufacturing facilities or supply sources for such components and materials. There can be no assurance that our supply of research and development, pre-clinical and clinical development drugs and other materials will not be limited, interrupted, restricted in certain geographic regions or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our drug product formulation manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA, EMA and other foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards such as cGMP. In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or

proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

- an inability to initiate or continue pre-clinical studies or clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of a collaborator;
- subjecting our product candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

If a collaborative partner terminates or fails to perform its obligations under an agreement with us, the commercialization of QR-010, if approved, could be delayed or terminated.

We are not currently party to any collaborative arrangements for the commercialization of QR-010, if approved, or similar arrangements, although we may pursue such arrangements before any commercialization of QR-010, if approved. If we entered into future collaborative arrangements for the commercialization of QR-010 or similar arrangements and any of our collaborative partners does not devote sufficient time and resources to a collaboration arrangement with us, we may not realize the potential commercial benefits of the arrangement, and our results of operations may be materially adversely affected. In addition, if any such future collaboration partner were to breach or terminate its arrangements with us, the commercialization of QR-010 could be delayed, curtailed or terminated.

Much of the potential revenue from future collaborations may consist of contingent payments, such as payments for achieving regulatory milestones or royalties payable on sales of drugs. The milestone and royalty revenue that we may receive under these collaborations will depend upon our collaborators' ability to successfully develop, introduce, market and sell new products. In addition, collaborators may decide to enter into arrangements with third parties to commercialize products developed under collaborations using our technologies, which could reduce the milestone and royalty revenue that we may receive, if any. Future collaboration partners may fail to develop or effectively commercialize products using our products or technologies because they:

- decide not to devote the necessary resources due to internal constraints, such as limited personnel with the requisite expertise, limited cash resources or specialized equipment limitations, or the belief that other drug development programs may have a higher likelihood of obtaining marketing approval or may potentially generate a greater return on investment;

- decide to pursue other technologies or develop other product candidates, either on their own or in collaboration with others, including our competitors, to treat the same diseases targeted by our own collaborative programs;
- do not have sufficient resources necessary to carry the product candidate through clinical development, marketing approval and commercialization; or
- cannot obtain the necessary marketing approvals.

Competition may negatively impact a partner's focus on and commitment to QR-010 and, as a result, could delay or otherwise negatively affect the commercialization of QR-010. If any future collaboration partners fail to develop or effectively commercialize QR-010 for any of these reasons, our sales of QR-010, if approved, may be limited, which would have a material adverse effect on our operating results and financial condition.

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 play a primary role in the recommendation and prescription of any product candidates 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 our products for which we obtain marketing approval. As a biopharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate include the following:

- the U.S. federal healthcare Anti-Kickback Statute constrains our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement or record to avoid, decrease or conceal an obligation to pay money to the federal government;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the U.S. federal physician payment transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Law, require applicable manufacturers of covered drugs, devices, biologics and medical supplies to report annually to HHS information related to payments and other transfers of

value to physicians, certain other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and certain other healthcare providers and their immediate family members and applicable group purchasing organizations; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and certain other healthcare providers or marketing expenditures. Additionally, state and foreign laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA or EMA regulations or similar regulations of other foreign regulatory authorities, to provide accurate information to the FDA, the EMA or other foreign regulatory authorities, to comply with certain manufacturing standards, to comply with U.S. federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We will adopt, implement and enforce a Code of Business Conduct and Ethics, which will be effective as of the consummation of this offering, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity, such as employee training on enforcement of the Code of Business Conduct and Ethics, may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Our Intellectual Property

We license patent rights from third-party owners or licensees and if we fail to comply with our obligations in our intellectual property licenses, we could lose rights that are fundamental to our business. If such owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be adversely affected.

We rely, and will continue to rely, on intellectual property rights licensed from third parties to protect our technology. We are a party to licenses that give us rights to third-party intellectual property that are necessary or useful for our business. In particular, we have a license from MGH to certain patent rights that relate to certain RNA repair technologies. Pursuant to this agreement, we have an exclusive, sublicensable and royalty-bearing license from MGH for the exploitation of the in-licensed intellectual property rights in all therapeutic indications in the field of cystic fibrosis. See "Business—Intellectual Property—License Agreement with MGH." We also intend to license additional third-party intellectual property in the future.

Our licensing arrangement with MGH imposes diligence, development, regulatory and commercialization milestones, and royalty, insurance and other obligations on us. If we fail to comply with these obligations, MGH 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 this agreement or reduction or elimination of our rights under this agreement may result in our having to negotiate new or amended agreements with less favorable terms, or cause us to lose our rights under this agreement, including our rights to important intellectual property and technologies that form the basis of our RNA repair technology, which may then be in-licensed by one or more of our competitors.

Our success will further depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. MGH, as well as our other licensors, may not successfully prosecute the patent applications licensed to us. Even if patents issue or are granted, MGH or our other licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing products. Without protection for, or exclusive right to, the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the United States Patent and Trademark Office, or U.S. PTO, and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to timely file national and regional stage patent applications based on our international patent application, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We or our licensors or any future collaborators or strategic partners may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk.

We or our licensors or any future collaborators or strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license or collaboration agreements to indemnify and hold harmless our licensors or collaborators for damages arising from intellectual property infringement by us. If we or our licensors, or any future collaborators or strategic partners are found to infringe a third party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, or any future collaborators or strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or any future collaborator may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. Pursuant to our license with MGH, MGH has the initial right to prosecute infringers when, in its sole judgment, such action may be reasonably necessary, proper and justified. In the event that MGH notifies us that it does not intend to prosecute an infringement, we may, after providing notice to MGH, initiate an infringement action against the infringer. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

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.

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates, and to use our proprietary technologies without infringing the proprietary rights of third parties. We cannot guarantee that QR-010 or any of our product candidates, their manufacture, use, sale, offer for sale, or importation into the United States will not be held to infringe a third party patent. As a result, we may become

party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including litigation in a Federal District court, or an interference or a post grant proceeding before the U.S. PTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. We are aware of an issued U.S. patent with claims directed to purified DNA and RNA molecules encoding a CFTR protein or a mutant CFTR protein containing a DF508 mutation. Although we believe that the claims of this patent are not valid or infringed, particularly in light of a recent U.S. Supreme Court decision regarding the patentability of naturally-occurring nucleic acids, the patent owner may nonetheless initiate litigation. Any such litigation would cause us to incur substantial expenses, which would be costly and divert our management's attention, and there is no assurance that a court would find in our favor on questions of infringement or validity.

Furthermore, in the event a third party were to assert an infringement claim against us and we were ultimately found to infringe the third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and commercializing our products and technology. However, we may not be able to obtain an appropriate license on commercially reasonable terms or at all. Even if we are able to obtain a license, it may 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. In addition, in any such proceeding or litigation, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business.

If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our technology and products could be significantly diminished.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, contract manufacturers, vendors and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets.

Any party with whom we or they have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts 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 disclose such trade secrets, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third-party, our competitive position would be harmed.

We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.

Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or

disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could compromise our ability to commercialize, or prevent us from commercializing, our product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may be able to export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Risks Related to the Commercialization of Our Product Candidates

If QR-010 or another of our product candidates is approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to successfully commercialize any such future products.

Although we currently intend to develop and commercialize QR-010 on our own, we have no sales, marketing or distribution capabilities or experience. If QR-010 or another of our product candidates is approved, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our products directly, as we currently plan, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our products or decide to co-promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved product. If we are not successful in commercializing any product approved in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects could be materially adversely affected.

Even if we receive marketing approval for QR-010, it may not achieve broad market acceptance, which would limit the revenue that we generate from its sales.

The commercial success of QR-010, if approved by the FDA, the EMA or other regulatory authorities, will depend upon the awareness and acceptance of QR-010 among the medical community, including physicians, patients, patient advocacy groups and healthcare payors. Market acceptance of QR-010, if approved, will depend on a number of factors, including, among others:

- QR-010's demonstrated ability to treat CF patients with the DF508 mutation and, if required by any applicable regulatory authority in connection with the approval for this or any other indication, to provide patients with incremental therapeutic benefits, as compared with other available treatments;
- the relative convenience and ease of administration of QR-010, including as compared with other treatments for CF patients;
- the prevalence and severity of any adverse side effects;
- limitations or warnings contained in the labeling approved for QR-010 by the FDA or the EMA;
- availability of alternative treatments, including therapies that improve the function of the defective CFTR protein already approved or expected to be commercially launched in the near future;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of QR-010 through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

We face competition from entities that have developed or may develop product candidates for our target indications, including companies developing novel treatments for CF patients. If these companies develop technologies or product candidates more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to develop and successfully commercialize our product candidates may be adversely affected.

The development and commercialization of drugs is highly competitive. We compete with a variety of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will develop product candidates and processes competitive with our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop product candidates. We are aware of multiple companies that are working in the field of CF therapeutics, including major pharmaceutical companies such as Vertex Pharmaceuticals Inc., F. Hoffmann-LaRoche Ltd., Novartis International AG, Gilead Sciences, Inc., Abbott Laboratories and Pfizer Inc.

If our lead product candidate, QR-010, is approved for the indications we are currently pursuing, it will compete with a range of therapeutic treatments that are either in development or currently marketed. For example, Vertex's Kalydeco is approved for use by the FDA and works to improve the function of the defective CFTR protein in CF patients with the G551D mutation and certain other gating mutations. Vertex is currently seeking marketing approval for additional mutations, which would increase Kalydeco's target population to up to 10% of the total CF patient population. Vertex is also developing lumacaftor (VX-809), which is intended for a much broader CF patient population, including patients who are homozygous for the DF508 mutation. In June 2014, Vertex announced that its two Phase 3 clinical trials of lumacaftor, when used in combination with Kalydeco in CF patients homozygous for the DF508 mutation, showed statistically significant improvement in the study's primary endpoint of improved lung function, compared to placebo. Vertex also showed statistically

significant reductions in pulmonary exacerbations in the pooled analysis of both studies. Other signs of clinical improvement were either limited or not statistically different from placebo. We believe these studies validate that DF508 CFTR is a treatable target and indicate there is need for more efficacious therapies. There are also a number of products that are marketed or in clinical development for the treatment of symptoms manifested in CF patients. These treatments include inhaled antibiotics, mucus thinners, pancreatic enzymes and anti-inflammatory drugs.

Many of our competitors possess significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than us. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

Even if we are able to commercialize QR-010 or another of our product candidates, the products may not receive coverage and adequate reimbursement from third-party payors, which could harm our business.

The availability of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of QR-010 or another of our product candidates, if approved, will depend substantially on the extent to which the costs of these product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize QR-010 or any other product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries.

The intended use of a drug product by a physician can also affect pricing. For example, CMS could initiate a National Coverage Determination administrative procedure, by which the agency determines which uses of a therapeutic product would and would not be reimbursable under Medicare. This determination process can be lengthy, thereby creating a long period during which the future reimbursement for a particular product may be uncertain.

Outside the United States, particularly in member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations or the successful completion of health technology assessment procedures with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Certain

countries allow companies to fix their own prices for medicines, but monitor and control company profits. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our RNA repair candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be adversely affected.

Recently enacted and future legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may negatively affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities or affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, established the Medicare Part D program and provided authority for limiting the number of drugs that will be covered in any therapeutic class thereunder. The Medicare Modernization Act, including its cost reduction initiatives, could decrease the coverage and reimbursement rate that we receive for any of our approved products. Furthermore, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

The Healthcare Reform Law, among other things, imposes a significant annual fee on companies that manufacture or import branded prescription drug products. It also contains substantial new provisions intended to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers, and impose additional health policy reforms, any of which could negatively impact our business. A significant number of provisions are not yet, or have only recently become, effective, but the Healthcare Reform Law is likely to continue the downward pressure on pharmaceutical and medical device pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

We expect that the Healthcare Reform Law, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may compromise our ability to generate revenue, attain profitability or commercialize our products.

Even if QR-010 or another of our product candidates receive regulatory approval, they may still face future development and regulatory difficulties and any approved products will be subject to extensive post-approval regulatory requirements.

If we obtain regulatory approval for QR-010 or another of our product candidates, it would be subject to extensive ongoing requirements by the FDA, the EMA and comparable foreign regulatory authorities governing

the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The safety profile of any product will continue to be closely monitored by the FDA, the EMA and comparable foreign regulatory authorities after approval. If the FDA, the EMA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, these regulatory authorities may require labeling changes or establishment of a risk management strategy, impose significant restrictions on a product's indicated uses or marketing, impose ongoing requirements for potentially costly post-approval studies or post-market surveillance or impose a recall.

In addition, manufacturers of therapeutic products and their facilities are subject to continual review and periodic inspections by the FDA, the EMA and other regulatory authorities for compliance with cGMP regulations. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue untitled letters or warning letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical studies;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We intend to operate in a number of jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by U.K., U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

If we receive regulatory approvals, we intend to market QR-010 and our other product candidates in multiple jurisdictions where we have limited or no operating experience and may be subject to increased business and economic risks that could affect our financial results.

If we receive regulatory approvals, we plan to market QR-010 and potentially other product candidates in jurisdictions where we have limited or no experience in marketing, developing and distributing our products. Certain markets have substantial legal and regulatory complexities that we may not have experience navigating. We are subject to a variety of risks inherent in doing business internationally, including:

- risks related to the legal and regulatory environment in non-U.S. jurisdictions, including with respect to privacy and data security, and unexpected changes in laws, regulatory requirements and enforcement;
- burdens of complying with a variety of foreign laws in multiple jurisdictions;
- potential damage to our brand and reputation due to compliance with local laws;
- fluctuations in currency exchange rates;
- political, social or economic instability;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- the potential need to recruit and work through local partners;
- reduced protection for or increased violation of intellectual property rights in some countries;
- inadequate data protection against unfair commercial use;
- difficulties in managing global operations and legal compliance costs associated with multiple international locations;
- compliance with the Bribery Act, the FCPA, the OECD Convention on Combating Bribery of Foreign Public Officials in International Business Transactions, and similar laws in other jurisdictions;
- natural disasters, including earthquakes, tsunamis and floods;
- inadequate local infrastructure;
- compliance with trade control laws;
- the effects of applicable foreign tax structures and potentially adverse tax consequences; and
- exposure to local banking, currency control and other financial-related risks.

If we are unable to manage our international operations successfully, our financial results could be adversely affected.

Recent federal legislation and actions by state and local governments may permit reimportation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results.

We may face competition in the United States for QR-010, if approved, from CF therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act contains provisions that may change U.S. importation laws and expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. These changes to U.S. importation laws will not take effect unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. The Secretary of the HHS has so far declined to approve a reimportation plan. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop, including QR-010, and adversely affect our future revenues and prospects for profitability.

The FDA, the EMA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA, the EMA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as QR-010 if approved. In particular, a product may not be promoted for uses that are not approved by the FDA, the EMA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for QR-010 as a treatment for CF patients with the DF508 mutation, physicians may nevertheless prescribe QR-010 to their patients in a manner that is inconsistent with the approved label, potentially including as a therapy to treat CF patients with mutations other than DF508. If we are found to have promoted such off-label uses, we may become subject to significant liability.

In the United States, engaging in impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that materially restrict the manner in which we promote or distribute those products. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical or medical device company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these False Claims Act lawsuits against pharmaceutical and medical device companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements based on certain sales practices promoting off-label drug uses. This growth in litigation has increased the risk that a company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from the Medicare, Medicaid, and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we are not successful in defending against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations.

Adverse decisions of tax authorities or changes in tax treaties, laws, rules or interpretations could have a material adverse effect on our business, results of operations, financial condition and cash flows.

The tax laws and regulations in the Netherlands, the jurisdiction of our incorporation and our current resident state for tax purposes, may be subject to change and there may be changes in enforcement of tax law. Additionally, European and other tax laws and regulations are complex and subject to varying interpretations. We cannot be sure that our interpretations are accurate or that the responsible tax authority agrees with our views. If our tax positions are challenged by the tax authorities, we could incur additional tax liabilities, which could increase our costs of operations and have a material adverse effect on our business, financial condition, and results of operations.

Risks Related to Our Business and Strategy

Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.

Our success largely depends on the continued service of key management and other specialized personnel, including Daniel de Boer, our chief executive officer, and Noreen Henig, our chief development officer. The loss of one or more members of our management board or other key employees or advisors could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our product candidates and technologies and the specialized nature of the regulatory approval process. Because our management board and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management board or officers or key employees. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

As QR-010 advances into clinical trials, if ever, we may experience difficulties in managing our growth and expanding our operations.

We have limited experience in drug development and have not begun clinical trials for any of our product candidates. As our product candidates enter and advance through pre-clinical studies and any clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

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

Despite the implementation of security measures, our information technology and other internal infrastructure systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions in our collaborations with our partners and delays in our research and development work. For instance, the loss of pre-clinical data or data from any future clinical trial involving our product candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

Our current operations are concentrated in one location and any events affecting this location may have material adverse consequences.

Our current operations are located in our facilities in Leiden, the Netherlands. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage,

telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize the facilities may have a material adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Additionally, the lease agreement covering our current laboratories is scheduled to expire on December 31, 2014. To the extent that we are unable to find new facilities for our current operations or we are delayed in finding new facilities, any business interruption could have a material adverse effect on our business, financial position, results of operations and prospects.

The investment of our cash, cash equivalents and fixed income marketable securities is subject to risks which may cause losses and affect the liquidity of these investments.

As of December 31, 2013, we had approximately €4,129,000 in cash and cash equivalents. To date, our cash and cash equivalents have been deposited primarily in savings and deposit accounts with original maturities of three months or less. Savings and deposit accounts generate a small amount of interest income. We intend to invest the net proceeds of this offering in a variety of capital preservation investments, which may include term deposits, short-term, investment-grade, interest-bearing instruments and government securities, all in accordance with our investment policy. These investments are subject to general credit, liquidity, market and interest rate risks, including the impact of U.S. sub-prime mortgage defaults that have affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our condensed financial statements.

In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

Our business entails a significant risk of product liability and our ability to obtain sufficient insurance coverage could have a material effect on our business, financial condition, results of operations or prospects.

The continued use of QR-010 in pre-clinical studies, our planned use of QR-010 in clinical trials and the sale of QR-010, if approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with QR-010. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for QR-010 or any future product candidates following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;

- increased FDA or EMA warnings on product labels;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- the inability to successfully commercialize QR-010 or any future product candidates, if approved.

We will need to obtain product liability insurance coverage for our clinical trials. We may not be able to obtain such coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our share price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

Our ability to use our net operating losses, or NOLs, in the Netherlands, is currently limited and may be further limited. There is also a risk that due to regulatory changes such as suspensions on the use for NOLs, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. For these reasons, we may not be able to use a material portion of the NOLs, even if we attain profitability.

Changes in accounting rules and regulations, or interpretations thereof, could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for biopharmaceutical companies, including policies governing revenue recognition, research and development and related expenses and accounting for share-based compensation, are subject to review, interpretation and guidance from relevant accounting authorities, including the SEC. Changes to accounting methods or policies, or interpretations thereof, may require us to reclassify, restate or otherwise change or revise our financial statements, including those contained in this prospectus.

Risks Related to this Offering and Ownership of our Ordinary Shares

An active, liquid and orderly trading market may not develop for our ordinary shares and we cannot predict what the market price of our ordinary shares will be. As a result it may be difficult for you to sell your ordinary shares at or above the initial public offering price.

Prior to this offering there has been no market for our ordinary shares. An active trading market for our shares may never develop or be sustained following this offering. The initial public offering price for our ordinary shares was determined through negotiations with the underwriters, and the negotiated price may not be indicative of the market price of our ordinary shares after this offering. The market value of our ordinary shares may decrease from the initial public offering price. As a result of these and other factors, you may be unable to resell your shares of our ordinary shares at or above the initial public offering price. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Further, an inactive market may also impair our ability to raise capital by selling our ordinary shares and may impair our ability to enter into strategic partnerships or acquire companies or products by using our ordinary shares as consideration. The market price of our shares may be volatile, and you could lose all or part of your investment.

The trading price of our ordinary shares following this offering is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this prospectus, these factors include:

- the presentation of data at industry conferences by us and/or our competitors, including at the North American Cystic Fibrosis Conference in October 2014;
- the filing of our IND with the FDA, the filing of our CTA with the EMA and the initiation of our first clinical trial of QR-010, all of which is intended for the fourth quarter of 2014;
- the response to our IND application with the FDA and our CTA application with the EMA;
- any current pre-clinical or future clinical trials of our product candidates, including any delays in enrollment rates or timing of these trials;
- regulatory actions with respect to our products or our competitors' products;
- the recruitment or departure of key personnel;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- results of clinical trials of our competitors;
- the success of competitive products or technologies;
- actual or anticipated changes in our growth rate relative to our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the level of expenses related to any of our product candidates or pre-clinical or clinical development programs;
- 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;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our ordinary shares by us, our insiders or our other shareholders;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

In addition, the stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have sometimes been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our ordinary shares, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in these "Risk Factors," could have a dramatic and material adverse impact on the market price of our ordinary shares.

If securities or industry analysts do not publish research, publish inaccurate or unfavorable research or cease to publish research about our business, our share price and trading volume could decline.

The trading market for our ordinary shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our ordinary shares would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our ordinary shares, publish inaccurate or unfavorable research about our business, or cease publishing about us, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our ordinary shares could decrease, which might cause our share price and trading volume to decline.

Sales of a substantial number of our ordinary shares in the public market could cause our share price to fall.

Sales of a substantial number of our ordinary shares in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our ordinary shares. After this offering, we will have outstanding ordinary shares based on the number of shares outstanding as of assuming no exercise of the underwriters' option to purchase additional ordinary shares. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. Of the remaining shares, of our ordinary shares will be restricted as a result of securities laws or lock-up agreements but will be able to be sold after the offering as described in the "Shares Eligible for Future Sale" section of this prospectus. Moreover, after this offering, holders of an aggregate of of our ordinary shares will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include the ordinary shares in registration statements that we may file for ourselves or other shareholders. We also intend to register all of our ordinary shares that we may issue under our equity incentive plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the ''Underwriting'' section of this prospectus.

Members of our management board and supervisory board and our principal shareholders and their affiliates will continue to exercise significant control over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Immediately following the completion of this offering, the existing holdings of the members of our management board and supervisory board and our principal shareholders and their affiliates, including Mr. de Boer, Mr. Termeer, investment funds affiliated with Sofinnova Capital VII and investment funds affiliated with Fidelity will represent beneficial ownership, in the aggregate, of approximately % of our outstanding ordinary shares, assuming no exercise of the underwriters' option to acquire additional ordinary shares in this offering. As a result, these shareholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our shareholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. These shareholders acquired their ordinary shares for substantially less than the price of the ordinary shares being acquired in this offering, and these shareholders may have interests, with respect to their ordinary shares, that are different from those of investors in this offering and the concentration of voting power among these shareholders may have an adverse effect on the price of our ordinary shares. In addition, this concentration of ownership might adversely affect the market price of our ordinary shares by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Please see “Principal Shareholders” in this prospectus for more information regarding the ownership of our outstanding ordinary shares by our management board and supervisory board and our principal shareholders and their affiliates.

If you purchase our ordinary shares in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The initial public offering price is substantially higher than the net tangible book value per share of our ordinary shares. Investors purchasing ordinary shares in this offering will pay a price per share that substantially exceeds the book value of our tangible assets after subtracting our liabilities. As a result, investors purchasing ordinary shares in this offering will incur immediate dilution of $ per share, based on an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, investors purchasing ordinary shares in this offering will contribute approximately % of the total amount invested by shareholders since our inception, but will own, as a result of such investment, only approximately % of the shares of ordinary shares outstanding immediately following this offering. For a further description of the dilution that you will experience immediately following this offering, see “Dilution.”

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively or may use them in a way investors do not approve.

Although we currently intend to use the net proceeds from this offering in the manner described in “Use of Proceeds” elsewhere in this prospectus, 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. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the market price of our ordinary shares to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value. If we do not invest the net proceeds from this offering in ways that enhance shareholder value, we may fail to achieve expected financial results, which could cause the price of our ordinary shares to decline.

Because we do not anticipate paying any cash dividends on our ordinary share in the foreseeable future, capital appreciation, if any, will be your sole source of potential gain.

We have never declared or paid cash dividends on our ordinary shares. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our ordinary shares will be your sole source of gain for the foreseeable future.

We are an “emerging growth company” and we intend to take advantage of reduced disclosure and governance requirements applicable to emerging growth companies, which could result in our ordinary shares being less attractive to investors.

We are an “emerging growth company,” as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our ordinary shares less attractive because we will rely on these exemptions. We may take advantage of these reporting exemptions until we are no longer an emerging growth company, which could be for up to five years. See “Prospectus Summary—Implications of Being an Emerging Growth Company.”

If investors find our ordinary shares less attractive as a result of our reduced reporting requirements, there may be a less active trading market for our ordinary shares and our share price may be more volatile. We may also be unable to raise additional capital as and when we need it.

Prior to this offering, we operated as a private company and therefore, have no experience operating as a public company and complying with public company obligations. Complying with these requirements will increase our costs, require additional management resources and qualified accounting and financial personnel, and we may fail to meet all of these obligations.

We will face increased legal, accounting, administrative and other costs and expenses as a public company. Compliance with the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act of 2010, as well as rules of the SEC and NASDAQ and the Dutch Corporate Governance Code, for example, will result in significant initial cost to us as well as ongoing increases in our legal, audit and financial compliance costs, particularly after we are no longer an "emerging growth company." The Securities Exchange Act of 1934, as amended, or the Exchange Act, requires, among other things, that we file certain periodic reports with respect to our business and financial condition. Our management board, officers and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and require us to incur substantial costs to maintain the same or similar coverage. We expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404 of the Sarbanes-Oxley Act of 2002 once we lose our status as an "emerging growth company." We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and maintain such personnel. Implementing any appropriate changes to our internal controls may require specific compliance training for our directors, officers and employees, entail substantial costs to modify our existing accounting systems, and take a significant period of time to complete. Such changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business.

If we fail to establish and maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ordinary shares.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ordinary shares.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management board will be required to assess the effectiveness of these controls annually. However, for as long as we are an "emerging growth company" under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an "emerging growth company" for up to five years. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon completion of this offering, we will become subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Risks Related to Investing in a Foreign Private Issuer or a Dutch Company

We will be a foreign private issuer and, as a result, we will not be subject to U.S. proxy rules and will be 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.

Upon consummation of this offering, we will report under 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 SEC 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, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

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.

We are a foreign private issuer and therefore we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. In order to maintain our current status as a foreign private issuer, either:

- a majority of our ordinary shares must be either directly or indirectly owned of record by non-residents of the United States; or
- a majority of our "executive officers" or directors may not be U.S. citizens or residents, more than 50% of our assets cannot be located in the United States and our business must be administered principally outside the United States.

If we lose this 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 costs we would incur as a foreign private issuer. As a result, we expect that a 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 currently report our financial results under IFRS, which differ in certain significant respect from U.S. GAAP.

Currently we report our financial statements under IFRS. There have been and there may in the future be certain significant differences between IFRS and U.S. GAAP, including differences related to revenue recognition, share-based compensation expense, income tax and earnings per share. As a result, our financial information and reported earnings for historical or future periods could be significantly different if they were prepared in accordance with U.S. GAAP. In addition, we do not intend to provide a reconciliation between IFRS and U.S. GAAP unless it is required under applicable law. As a result, you may not be able to meaningfully compare our financial statements under IFRS with those companies that prepare financial statements under U.S. GAAP.

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 then 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:

- the authorization of a class of preferred shares that may be issued against payment of 25% of the nominal value thereof to a protection foundation, for which we expect to grant a perpetual and repeatedly exercisable call option to such protection foundation on or prior to the completion of this offering, for up to such number of preferred shares as we are allowed to issue under our authorized share capital;
- a provision that our management board members and supervisory board members may only be appointed upon a binding nomination by our supervisory board, which can be set aside by a two-thirds majority of our shareholders representing more than half of our issued share capital;
- staggered four-year terms of our supervisory board members, as described below;
- a provision that our management board members and supervisory board members may only be removed by our general meeting of shareholders by a two-thirds majority of votes cast representing more than 50% of our issued share capital (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.

As indicated above, we expect to adopt an anti-takeover measure on or prior to completion of the offering by granting a perpetual and repeatedly exercisable call option to the protection foundation, which confers upon the protection foundation the right to acquire, under certain conditions, such number of preferred shares as we are allowed to issue under our articles of association. The issuance of such preferred shares will occur upon the protection foundation's exercise of the call option and will not require shareholder consent. Such a measure has the effect of making a takeover of us more difficult or less attractive and as a result, our shareholders may be unable to benefit from a change of control and realize any potential change of control premium which may materially and adversely affect the market price of our ordinary shares.

We are not obligated to and do not comply with all the best practice provisions of the Dutch Corporate Governance Code. This may affect your rights as a shareholder.

As a Dutch company we are subject to the Dutch Corporate Governance Code, or DCGC. The DCGC contains both principles and best practice provisions that regulate relations between the management board, the supervisory board and the shareholders (i.e. the general meeting of shareholders). The DCGC is based on a "comply or explain" principle. Accordingly, companies are required to disclose in their annual reports, filed in the Netherlands, whether they comply with the provisions of the DCGC. If they do not comply with those provisions (e.g., because of a conflicting NASDAQ requirement), the company is required to give the reasons for such non-compliance.

The DCGC applies to all Dutch companies listed on a government-recognized stock exchange, whether in the Netherlands or elsewhere, including NASDAQ. We do not comply with all the best practice provisions of the DCGC. See "Description of Share Capital and Articles of Association—Dutch Corporate Governance." This may affect your rights as a shareholder and you may not have the same level of protection as a shareholder in a Dutch company that fully complies with the DCGC.

We intend to rely in certain cases 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 your rights as a shareholder will differ from the rights you would have as a shareholder of a domestic U.S. issuer.

As a foreign private issuer whose ordinary shares are listed on The NASDAQ Global 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 SEC each such requirement that it does not follow and describe the home country practice followed instead of any such requirement. We intend to 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 intend to 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 cannot assure you that we will not 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.

Generally, if, for any taxable year, at least 75% of our gross income is passive income, or at least 50% of the value of our assets is attributable to assets that produce passive income or are held for the production of passive

income, including cash, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. For purposes of these tests, passive income includes dividends, interest, and gains from the sale or exchange of investment property and rents and royalties other than rents and royalties which are received from unrelated parties in connection with the active conduct of a trade or business. If we are characterized as a PFIC, our U.S. shareholders may suffer adverse tax consequences, including having gains realized on the sale of our ordinary shares treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on our ordinary shares by individuals who are U.S. holders, and having interest charges apply to distributions by us and the proceeds of share sales. See "Taxation—Certain Material U.S. Federal Income Tax Considerations—Passive Foreign Investment Company Considerations."

Our status as a PFIC may also depend, in part, on how quickly we utilize the cash proceeds from this offering in our business. Since PFIC status depends on the composition of our income and the composition and value of our assets (which, assuming we are not a "controlled foreign corporation" under Section 957(a) of the Code for the year being tested, may be determined in large part by reference to the market value of our ordinary shares, which may be volatile) from time to time, there can be no assurance that we will not be considered a PFIC for any taxable year. Although the matter is not free from doubt, we believe that we were not a PFIC during our 2013 taxable year and may not be a PFIC during our 2014 taxable year.

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

We are incorporated under the laws of the Netherlands. We currently have only limited operations in the United States. Most of our assets are currently located in the Netherlands. The majority of our management board, supervisory board and officers reside outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce 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 Code of Civil Procedure.

Based on the lack of a treaty as described above, U.S. investors 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 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, our internal rules and by the laws governing companies incorporated in the Netherlands. The rights of our shareholders and the responsibilities of members of our supervisory board under Dutch law are different than under the laws of some U.S. jurisdictions. In the performance of their duties, our management board and our supervisory board are required by Dutch law to consider the interests of ProQR Therapeutics, its shareholders, its employees and other stakeholders and not only those of our shareholders. Also, as a Dutch company, we are not required to solicit proxies or prepare proxy statements for general meetings of shareholders. Dutch law does not have a regulatory regime for U.S.-style proxy solicitations and, even though Dutch law accommodates voting by proxy, the solicitation of proxies is not a widely used business practice in the Netherlands. 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—Differences in Corporate Law."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements contained in this prospectus, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “aim,” “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this prospectus include, among other things, statements about:

- the timing of commencement of our planned clinical trials for QR-010, including our planned initiation of a Phase 1b clinical trial in the fourth quarter of 2014;
- our expectations regarding the timing or likelihood of regulatory filings and approvals for our product candidates, including our plan to file an IND with the FDA and a MMA with the EMA for QR-010, in the fourth quarter of 2014;
- the potential benefits, effectiveness or safety of QR-010, including as compared to currently-available treatments or treatments in development;
- the accuracy of our estimates of the size of the CF market and the rate and degree of QR-010’s market acceptance, if any;
- our intention to seek a breakthrough therapy designation as well as a fast track designation for QR-010;
- the progress, timing and amount of expenses associated with our development of QR-010;
- our ability to obtain regulatory approval for QR-010 and any of our other product candidates;
- our ability to develop an internal sales and marketing infrastructure and our intention to develop and commercialize QR-010 on our own;
- our ongoing and planned discovery and development of product candidates;
- our ability to obtain and maintain intellectual property protection for QR-010 and our product candidates without infringing on the intellectual property rights of others;
- our estimates regarding expenses, future revenues, capital requirements, future losses and needs for additional financing;
- our ability to establish and maintain collaborations; and
- our ability to compete with other companies that are, or may be, developing or selling products that may compete with QR-010, if approved.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

This prospectus includes statistical and other industry and market data that we obtained from the medical literature, industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Although we believe these industry publications and third party research, surveys and studies are reliable, we have not independently verified such data.

USE OF PROCEEDS

We estimate that we will receive net proceeds from this offering of $ million (€ million), based upon an assumed initial public offering price of $ per ordinary share (the midpoint of the estimated price range set forth on the cover page of this prospectus), after deducting underwriting discounts and any offering expenses payable by us. If the underwriters exercise their option to purchase additional shares, we estimate that the net proceeds of the offering will be $ million. As of December 31, 2013, we had cash and cash equivalents of approximately €4,129,000 ($5,615,000).

A $1.00 increase (decrease) in the assumed initial public offering price of $ per ordinary share would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming the number of ordinary shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of one million ordinary shares in the number of ordinary shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming the assumed initial public offering price remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations and development of QR-010, to establish a public market for our ordinary shares and to facilitate our future access to the public capital markets. We estimate that we will use the net proceeds from this offering and our existing cash as follows:

- approximately $ million (€ million) to fund development costs associated with our planned Phase 1b clinical trial and POC trial for QR-010;
- approximately $ million (€ million) to fund development costs associated with our planned Phase 2a clinical trials for QR-010;
- approximately $ million (€ million) to fund development costs associated with pre-clinical studies and related activities for QR-110; and
- the remainder for discovery and other pipeline projects, as well as for working capital and other general corporate purposes and potentially for acquisitions or investments in other businesses, technologies or product candidates.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, 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. As a result, our management board retains broad discretion over the allocation of the net proceeds from this offering. We have no current agreements, commitments or understandings for any material acquisitions or licenses of any products, businesses or technologies.

We intend to invest the net proceeds of this offering in a variety of capital preservation investments, which may include term deposits, short-term, investment-grade, interest-bearing instruments and government securities, all in accordance with our investment policy.

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

to the extent that 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. Subject to such restriction, a proposal for the payment of cash dividends on our ordinary shares 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, 2013:

- on an actual basis;
- on a pro forma basis after giving effect to (i) the issuance of 81,187 preferred shares on April 17, 2014 and (ii) the receipt of €41,998,000 in gross proceeds from the issuance of preferred shares on April 17, 2014; and
- on a pro forma as adjusted basis to give further effect to (i) the sale of ordinary shares by us in this offering, assuming an initial public offering price of $ per ordinary share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and (ii) the conversion of our outstanding preferred shares into an aggregate of 81,187 ordinary shares upon the closing of this offering.

This table should be read with our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	As of December 31, 2013		
	Actual	Pro Forma	Pro Forma As Adjusted
	(In Thousands, Except Share And Per Share Data)		
Cash and cash equivalents	€ 4,129	€	€
Total debt:			
Convertible loan	2,514		
Finance lease liability	83		
Borrowings	943		
Total debt	3,540		
Shareholders' equity:			
Ordinary shares	60		
Preferred shares	—		
Share premium	3,481		
Other reserves	41		
Accumulated deficit	(3,671)		
Total shareholders' equity	(89)		
Total capitalization	€ 3,451	€	€

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

The table above excludes:

- 3,726 ordinary shares issuable upon the exercise of options outstanding as of December 31, 2013 at a weighted average exercise price of €113.34 per share; and
- ordinary shares reserved for future issuance under our equity incentive plans following this offering.

DILUTION

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

Our net tangible book value as of December 31, 2013 was a deficit of €128,000 ($174,000), or €2.01 ($2.73) per ordinary share. Net tangible book value per ordinary share represents our total tangible assets less our total tangible liabilities, divided by the number of ordinary shares outstanding on December 31, 2013.

Net tangible book value dilution per share to new investors represents the difference between the amount per ordinary share paid by purchasers in this offering and the pro forma net tangible book value per ordinary share immediately after the completion of this offering. After giving effect to the sale of ordinary shares in this offering, assuming an initial public offering price of $ per share, the mid-point of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of December 31, 2013 would have been € ($), or € ($) per ordinary share. This amount represents an immediate increase in pro forma net tangible book value of € per share to our existing shareholders and an immediate dilution in pro forma net tangible book value of approximately € ($) per ordinary share to new investors purchasing ordinary shares in this offering. We determine dilution by subtracting the pro forma net tangible book value per share after the 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 initial public offering price per ordinary share		
Tangible book value per ordinary share as of December 31, 2013		
Increase per ordinary share attributable to new investors in this offering		
Pro forma net tangible book value per ordinary share as of December 31, 2013 after giving effect to this offering		
Dilution per ordinary share to new investors		

A $1.00 increase (decrease) in the assumed initial public offering price of $ per ordinary share would increase (decrease) the pro forma net tangible book value by $ per ordinary share and increase (decrease) the dilution to new investors by $ per ordinary share, assuming the number of ordinary shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting underwriting discounts and commissions and estimated expenses payable by us. If the underwriters exercise their option to purchase additional ordinary shares from us in full, the pro forma net tangible book value per ordinary share, as adjusted to give effect to this offering, would be $ per ordinary share, and the dilution in pro forma net tangible book value per ordinary share to investors in this offering would be $ per ordinary share.

The table below summarizes, as of the date of this prospectus, the number of ordinary shares purchased from us, the total consideration paid to us and the average price per ordinary share paid to us by existing shareholders and to be paid to us by new investors purchasing our ordinary shares in this offering at an assumed initial public offering price of $ per ordinary share, the midpoint of the estimated price range set forth on the cover page of this prospectus, before deducting underwriting discounts and commissions and estimated offering expenses.

	Ordinary Shares Purchased		Total Consideration			Average Price Per Ordinary Share	
	Number	Percent	Amount		Percent		
			$	€		$	€
Existing shareholders	63,528	%			%		
New investors							
Total		100.0%			100.0%		

The total number of ordinary shares reflected in the discussion and tables above is based on (i) 63,528 ordinary shares issued and outstanding as of December 31, 2013 and (ii) 81,187 ordinary shares into which the preferred shares issued on April 17, 2014 will be converted prior to the closing of this offering, and excludes:

- 3,726 ordinary shares issuable upon the exercise of options outstanding as of December 31, 2013 at a weighted average exercise price of €113.34 per share; and
- ordinary shares reserved for future issuance under our 2014 Stock Option Plan following this offering.

If the underwriters exercise their option to purchase additional shares in full, the number of ordinary shares beneficially owned by existing shareholders would decrease to approximately , or approximately % of the total number of ordinary shares outstanding after this offering, and the number of shares held by new investors will be increased to ordinary shares, or approximately % of the total number of ordinary shares outstanding after this offering.

To the extent options are exercised and awards are granted under these 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.

SELECTED FINANCIAL DATA

The following table sets forth selected financial data for ProQR Therapeutics B.V. for the periods presented below. The selected financial data for the period from February 21, 2012 (inception) through December 31, 2012 and the year ended December 31, 2013 have been derived from our audited financial statements included elsewhere in this prospectus.

Our historical results for any prior period are not necessarily indicative of results to be expected in any future period. The information set forth below should be read in conjunction with "Capitalization", "Management's Discussion and Analysis of Financial Condition and Results of Operations" and with our financial statements and notes thereto included elsewhere in this prospectus.

	Period From February 21, 2012 (Inception) Through December 31, 2012	Year Ended December 31, 2013
Statement of comprehensive loss data:	€ in thousands (except share and per share data)	
Other income	€ 23	€ 116
Research and development costs	(285)	(2,550)
General and administrative costs	(157)	(764)
Share-based compensation	—	(41)
Operating loss	**(419)**	**(3,239)**
Financial income and expense	1	(14)
Net loss and comprehensive loss	€ (418)	€ (3,253)
Net loss per share		
Basic and diluted	€ (17.04)	€ (60.01)
Weighted average shares outstanding	24,556	54,199

	As of December 31,	
	2012	2013
Statement of financial position data:	(€ in thousands)	
Cash and cash equivalents	€ 249	€ 4,129
Total assets	338	4,504
Total debt	239	4,593
Total shareholders' equity (deficit)	99	(89)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the information under "Selected Financial Information" and our audited financial statements, including the notes thereto, included elsewhere in this prospectus. The following discussion is based on our financial statements prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB, which might differ in material respects from generally accepted accounting principles in the United States. The following discussion includes forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those described under "Risk Factors".

Overview

We are an innovative biopharmaceutical company engaged in the discovery and development of RNA-based therapeutics for the treatment of severe genetic disorders. Utilizing our unique, proprietary RNA repair technologies, we believe we will be able to treat genetic disorders in which a single protein is defective due to certain types of genetic mutations. We design our therapeutic candidates to specifically target and repair the defective messenger RNA, or mRNA, that is a product of a mutated gene in order to restore the expression and function of normal, or wild-type, protein. Our primary focus is on the development of a disease modifying therapy for the treatment of cystic fibrosis, or CF, a genetic disease that affects an estimated 70,000 to 100,000 patients worldwide and causes early morbidity and mortality. We are also developing a treatment for Leber's Congenital Amaurosis, or LCA, the leading genetic cause of blindness in childhood. Further, based on our own research and initial selection criteria, we believe that our RNA repair technologies can potentially be used to treat a broad range of other severe genetic diseases that are currently untreatable or have limited effective treatment options and have to date identified approximately 50 potential target indications.

To date, we have financed our operations primarily through private placements of equity securities, and to a lesser extent from funding from patient organizations and governmental bodies. From our inception on February 21, 2012 through December 31, 2013, we raised gross proceeds of approximately €3,523,000 from private placements of equity securities, €2,500,000 in convertible loans from existing shareholders, €922,000 in loans from a governmental body and approximately €139,000 in grants from patient organizations. As of December 31, 2013, we had cash and cash equivalents of €4,129,000. In April 2014, we raised gross proceeds of approximately €41,998,000 from the private placement of our equity securities, including the conversion of the €2,559,000 in outstanding convertible loans. To date, we have not generated any revenues from royalties or product sales. Based on our current plans, we do not expect to generate royalty or product revenues for the foreseeable future.

We have generated losses since our formation in February 2012. For the period from February 21, 2012 (inception) through December 31, 2012 and for the year ended December 31, 2013, we incurred net losses of approximately €418,000 and approximately €3,253,000, respectively. As of December 31, 2013, we had an accumulated deficit of €3,671,000. We expect to continue incurring losses for the foreseeable future as we continue our pre-clinical studies of our lead product candidate, QR-010, initiate our clinical development program for QR-010, apply for marketing approval of QR-010 and, if approved, build a sales and marketing infrastructure for the commercialization of QR-010.

Financial Operations Overview

Other Income

Other income is incidental by nature. In 2012, we received a grant from a patient organization, the Cystic Fibrosis Foundation, for a specific research project that we conducted in 2012 and 2013. This grant was recorded as other income.

Research and Development Expense

Research and development expense consists principally of:

- salaries for research and development staff and related expenses, including social security costs;
- costs for production of pre-clinical compounds and drug substances by contract manufacturers;
- fees and other costs paid to contract research organizations, or CROs, in connection with additional pre-clinical testing;
- costs of related facilities, materials and equipment;
- costs associated with obtaining and maintaining patents and other intellectual property; and
- depreciation of tangible fixed assets used to develop our product candidates.

We expect that our total research and development expense in 2014 will be approximately €15-17 million. Our research and development expenses primarily relate to the following key programs:

- *QR-010 for the treatment of CF*

  The research and development costs relating to our lead product candidate, QR-010, primarily consist of salaries, costs for production of the compound for pre-clinical and toxicology studies, costs for production of the compound for clinical testing, and costs paid to CROs in conjunction with pre-clinical studies and will include costs for our clinical trials. Other significant costs are our internal laboratory costs, including the materials used in the labs and rent allocated to the lab space, as well as consultancy costs in the support of our research and development activities.

- *Other development programs*

  Other research and development expenses mainly relate to our other product candidate, QR-110, as well as other early research projects. These expenses primarily consist of salaries, costs for production of the pre-clinical compounds and costs paid to CROs in conjunction with pre-clinical studies.

For the period from February 2012 (inception) through December 31, 2012, we spent €285,000 on research and development and for the year ended December 31, 2013, we spent €2,550,000 on research and development.

Our research and development expense may vary substantially from period to period based on the timing of our research and development activities. Research and development expense is expected to increase as we advance QR-010 into clinical trials and advance QR-110 and any other product candidates in pre-clinical studies. The successful development of our product candidates is highly uncertain. At this time we cannot reasonably estimate the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from, any of our product candidates. This is due to numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our research and development activities;
- clinical trials and early-stage results;
- the terms and timing of regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; and
- the ability to market, commercialize and achieve market acceptance for QR-010 or any other product candidate that we may develop in the future.

Any of these variables with respect to the development of QR-010 or any other product candidate that we may develop could result in a significant change in the costs and timing associated with the development of QR-010 or such product candidate. For example, if the FDA, EMA or other regulatory authority were to require us to conduct pre-clinical and clinical studies beyond those which we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of our clinical development programs.

General and Administrative Expense

Our general and administrative expense consists principally of:

- salaries for employees other than research and development staff;
- professional fees for auditors and other consulting expenses not related to research and development activities;
- professional fees for lawyers not related to the protection and maintenance of our intellectual property;
- cost of facilities, communication and office expenses;
- IT expenses; and
- amortization and depreciation of tangible and intangible fixed assets not related to research and development activities.

We expect that our general and administrative expense will increase in the future as our business expands and we incur additional costs associated with operating as a public company. These public company-related increases will likely include costs of additional personnel, additional legal fees, accounting and audit fees, directors' and officers' liability insurance premiums and costs related to investor relations. In addition, we expect to grant share-based compensation awards to key management personnel and other employees.

Share-Based Compensation

Share-based compensation reflects the costs of our equity-settled, employee share option plan, which are measured at the fair value of the options at the grant date, and which are spread in line with the vesting period of the options involved. The share-based compensation is recognized in the income statement, with a corresponding entry to the equity-settled employee benefits reserve, which is part of equity. We expect that our share-based compensation costs will increase in the future as the number of outstanding options increases. See "Management's Discussion and Analysis—Critical Accounting Policies and Significant Judgments and Estimates—Share-Based Compensation" for additional information on share-based compensation.

Finance Income

To date, our cash and cash equivalents have been deposited primarily in savings and deposit accounts with original maturities of three months or less. Savings and deposit accounts generate a small amount of interest income. We intend to invest the net proceeds of this offering in a variety of capital preservation investments, which may include term deposits, short-term, investment-grade, interest-bearing instruments and government securities, all in accordance with our investment policy.

Results of Operations

	Period From February 21, 2012 (Inception) Through December 31, 2012	Year Ended December 31, 2013
	(€ in thousands)	
Other income	€ 23	€ 116
Research and development costs	(285)	(2,550)
General and administrative costs	(157)	(764)
Share-based compensation	—	(41)
Total operating costs	(442)	(3,355)
Operating result	(419)	(3,239)
Finance (expense)/income, net	1	(14)
Net loss	€ (418)	€ (3,253)

Other income

For the period from February 21, 2012 (inception) through December 31, 2012 and the year ended December 31, 2013, we had other income of €23,000 and €116,000, respectively. These amounts reflects a single grant we received from the Cystic Fibrosis Foundation.

Research and development costs

Research and development costs increased from €285,000 for the period from February 21, 2012 (inception) through December 31, 2012 to €2,550,000 for the year ended December 31, 2013. These costs were primarily related to our lead project, QR-010, the development of which also formed the basis for other pipeline projects. Our research and development expense is highly dependent on the development phases of our research projects and therefore fluctuate significantly from year to year. We expect that our total research and development costs in 2014 will be in the range of €15-17 million.

The variances in research and development costs between 2012 and 2013 are mainly due to:

- increased staff working on QR-010 pre-clinical studies, as the number of full-time equivalent employees working on such studies increased from 3 in 2012 to 12 in 2013;
- increased laboratory costs, including purchases of compounds and laboratory materials used by the research and development staff in proportion to the increase in the number of employees, and increased costs for the use of laboratories, which we pay on a per capita basis;
- increased costs for externally conducted studies, including various *in vivo* studies, proof of concept studies and dose ranging and toxicity studies conducted in connection with the development of QR-010;
- costs for the production of QR-010 compound, including the costs of comparative production batches of QR-010 in support of selecting our preferred contract manufacturer; and
- increased project-related consultancy costs, including regulatory and intellectual property support.

General and administrative costs

General and administrative costs increased from €157,000 for the period from February 21, 2012 (inception) through December 31, 2012 to €764,000 for the year ended December 31, 2013. The increase was primarily related to:

- increased staff costs associated with the increase of our general and administrative staff from 2 full-time equivalent employees to an average of 5.2 full-time equivalent employees in 2013;

- increased office and general costs, including office rent, IT and communication costs, travel costs and office consumables; and
- increased costs for legal support, accounting and other consultancy costs.

We expect that general and administrative expense will increase in the future as our business expands and we incur additional costs associated with operating as a public company.

Share-based compensation

Share-based compensation amounted to zero for the period from February 21, 2012 (inception) through December 31, 2012, as compared to €41,000 for the year ended December 31, 2013, reflecting the grant of 3,736 share options. We adopted our Option Plan in 2013.

Finance income and expense

We had net finance income of €1,000 for the period from February 21, 2012 (inception) through December 31, 2012, as compared to a net finance expense of €14,000 for the year ended December 31, 2013. The 2013 financial expense mainly results from the interest costs related to borrowings from governmental bodies.

Liquidity and Capital Resources

To date, we have financed our operations through private placements of equity securities, a convertible loan and funding from governmental bodies and patient organizations.

Cash Flows

The table below summarizes our statement of cash flows for the period from February 21, 2012 (inception) through December 31, 2012 and the year ended December 31, 2013.

	Period From February 21, 2012 (Inception) Through December 31, 2012	Year Ended December 31, 2013
	(€ in thousands)	
Net cash used in operating activities	€(325)	€(2,332)
Net cash used in investing activities	(39)	(137)
Net cash generated by financing activities	613	6,349
Net increase in cash and cash equivalents	249	3,880
Cash and cash equivalents at the beginning of the period	€ —	€ 249
Cash and cash equivalents at the end of the period	€ 249	€ 4,129

Net cash used in operating activities increased from €325,000 in the period from February 21, 2012 (inception) through December 31, 2012 to €2,332,000 in the year ended December 31, 2013. This increase was primarily due to the increased loss from operating activities, partially offset by a change in working capital.

Net cash used in investing activities increased from €39,000 in the period from February 21, 2012 (inception) through December 31, 2012 to €137,000 in the year ended December 31, 2013. This increase was primarily due to our investments in laboratory equipment and office equipment in support of our growing operation.

Net cash generated by financing activities increased from €613,000 in the period from February 21, 2012 (inception) through December 31, 2012 to €6,349,000 in the year ended December 31, 2013. This increase was primarily a result of private placements of ordinary shares to investors in 2013 for total net proceeds of €3,023,000. In 2013, we also received gross proceeds in the amount of €2,500,000 from the issuance of a convertible loan to existing shareholders, as well as loans totaling €826,000 from a governmental body.

Cash and Funding Sources

The table below summarizes our sources of financing for the period from February 21, 2012 (inception) through December 31, 2012 and the year ended December 31, 2013.

	Equity Capital	Convertible Loan	Government Borrowing	Total
		(€ in thousands)		
Period from February 21, 2012 (inception) through December 31, 2012	€ 518	€ —	€ 95	€ 613
Year ended December 31, 2013	3,023	2,500	826	6,349
Total	€3,541	€ 2,500	€ 921	€6,962

Our sources of financing in 2013 were private placements of equity securities providing total net proceeds of €3,023,000, a convertible loan from existing shareholders of €2,500,000 and funding from a governmental body amounting to €826,000. Our sources of financing in 2012 were private placements of equity securities amounting to €518,000 and funding from a governmental body of €95,000.

As of December 31, 2013, we had non-current liabilities of €991,000, which consisted of borrowings from a government body in the amount of €943,000 and finance lease liabilities in the amount of €48,000.

On April 17, 2014, we completed a financing round of €41,998,000 in gross proceeds, which included the conversion of an existing convertible loan with existing and new shareholders against the issuance of 81,187 preferred shares to investors.

For a description of our financial commitments, see “Management’s Discussion and Analysis—Contractual obligations and commitments” below.

Funding Requirements

We expect that the net proceeds of this offering, together with our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements for at least the next months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our present and future funding requirements will depend on many factors, including, among other things:

- the progress, timing and completion of pre-clinical testing and clinical trials for our current or any future product candidates;
- the number of potential new product candidates we identify and decide to develop;
- the costs involved in growing our organization to the size needed to allow for the research, development and potential commercialization of our current or any future product candidates;
- the costs involved in filing patent applications and maintaining and enforcing patents or defending against claims or infringements raised by third parties;

- the time and costs involved in obtaining regulatory approval for our product candidates and any delays we may encounter as a result of evolving regulatory requirements or adverse results with respect to any of these product candidates;
- any licensing or milestone fees we might have to pay during future development of our current or any future product candidates;
- selling and marketing activities undertaken in connection with the anticipated commercialization of our current or any future product candidates and costs involved in the creation of an effective sales and marketing organization; and
- the amount of revenues, if any, we may derive either directly or in the form of royalty payments from future sales of our product candidates, if approved.

For more information as to the risks associated with our future funding needs, see "Risk Factors."

Capital Expenditures

The following table sets forth our capital expenditures for the period from February 21, 2012 through December 31, 2012 and the year ended December 31, 2013:

	Period From February 21, 2012 (Inception) through December 31, 2012	Year ended December 31, 2013
	(€ in thousands)	
Investments in tangible fixed assets	€ —	€ 137
Investments in intangible assets	39	—
Total	€ 39	€ 137

We plan to make investments in laboratory and office facilities and equipment, including IT equipment. Our budgeted capital expenditures for the full year 2014 are approximately €1.5 million, and we anticipate that they will be funded from existing cash balances.

Contractual Obligations and Commitments

The table below summarizes our undiscounted liabilities at December 31, 2013:

	Payments Due by Period				
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
	(€ in thousands)				
Other non-current liabilities	€ 943	€ —	€ —	€ 629	€ 314
Convertible loan	2,514	2,514	—	—	—
Finance lease liabilities	83	35	48	—	—
Trade payables	745	745	—	—	—
Other current liabilities	308	308	—	—	—
Total	€4,593	€ 3,602	€ 48	€ 629	€ 314

Commitments

Rent

We have entered into rental agreements for laboratory space and offices with MicroSafe Laboratories and Pharming Group N.V., respectively. These agreements run until December 31, 2014 and July 22, 2015, respectively. The current annual obligation amounts to €194,000, while the 2013 rent expense amounted to €113,000 (2012:€13,000). We expect a material increase in rent obligations as we expand our operations.

Patent license agreement

We have entered into an Exclusive Patent License Agreement with MGH, pursuant to which we may have certain royalty obligations to MGH based on the development or commercialization of QR-010. See "Business—Intellectual Property—License Agreement with MGH."

We have also entered into additional license agreements with other third parties that may require us to pay royalties or milestone fees if certain defined development milestones are achieved.

Research and development commitments

We have commitments related to the development of QR-010 amounting to €953,000 in the aggregate, all of which is due in 2014.

Quantitative and Qualitative Disclosures About Market Risk

We are exposed to a variety of financial risks: market risk (including foreign exchange risk and interest rate risk), credit risk and liquidity risk. Our overall risk management program focuses on the unpredictability of financial markets.

Our cash policy is focused on optimizing the net interest result of funds invested in deposits while accepting limited risk (minimum ratings of P2 or A3 for short-term and long-term, respectively by Moody's and A2 or A- for short-term and long-term, respectively, by Standard and Poor's). Individual commitments exceeding a defined threshold in foreign currencies may be hedged against our functional currency, the euro, to avoid foreign currency exposure affecting the income statement in comparison to budget.

Market Risk

Foreign exchange risk arises from future commercial transactions and recognized assets and liabilities in foreign currencies. In 2013, we had no significant outstanding receivables, but had expenditures in various currencies, predominately €1,258,000 in U.S. dollars. We have exposure associated with the time delay between entering into a contract, budget or forecast and the realization thereof. The impact of fair value measurements on the financial statements is limited. As of December 31, 2013, there was outstanding a net amount of trade payables denominated in US dollars of €339,000.

The majority of the proceeds from the offering in U.S. dollars will be converted to our functional currency, the euro.

Our interest rate risk exposure is limited due to the use of loans with fixed rates. We had two loans and a financial lease with fixed interest, totaling €3,575,000 at December 31, 2013.

Credit Risk

Credit risk represents the risk of financial loss caused by default of the counterparty. We have no large receivables balances with external parties. Our principal financial assets are cash and cash equivalents which are, in line with our cash policy, placed at ABN Amro and Rabobank which meet our defined minimum credit ratings.

Liquidity Risk

We believe that the net proceeds of this offering, together with our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements for at least the next months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with IFRS as issued by the IASB. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our financial statements appearing elsewhere in this prospectus, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Research and Development Expense

Research expenses are recognized as expenses when incurred. Costs incurred on development projects are recognized as intangible assets as of the date as of which it can be established that it is probable that future economic benefits attributable to the asset will flow to us considering its technological and commercial feasibility. This is generally the case when regulatory approval for commercialization is achieved and costs can be measured reliably. Given the current stage of the development of our products, no development expenditures have yet been capitalized. Intellectual property-related costs for patents are part of the expenditure for the research and development projects. Therefore, registration costs for patents are expensed when incurred as long as the research and development project concerned does not meet the criteria for capitalization.

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

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

Share-Based Compensation

Stock options

In September 2013, we adopted our Stock Option Plan, or the Option Plan. Under the Option Plan, the management board or the supervisory board may grant options to eligible individuals. Upon exercise of options, Stichting ProQR Therapeutics Participation, a Dutch foundation that we utilize to facilitate the administration of share-based compensation awards and refer to as the Foundation, issues to such individuals non-voting

depository receipts representing the underlying ordinary shares, against payment of the option exercise price. We have issued 12,218 ordinary shares to the Foundation for the issuance of options (which includes 601 ordinary shares for which depository receipts have been issued in respect of option exercises to date). The voting rights associated with the ordinary shares remain with the Foundation and are controlled by our chief executive officer as chairman of the Foundation.

We amended and restated our Option Plan on , 2014 as our 2014 Stock Option Plan to, among other things, provide for the grant of options to purchase ordinary shares instead of non-voting depository receipts and to terminate the involvement of the Foundation in the Option Plan. See "Management—Option Plan."

The management board may determine the number of ordinary shares to be covered by each option, the exercise price of each option and the conditions and limitations applicable to the exercise of each option, including conditions relating to applicable securities laws, as it considers necessary or advisable. The supervisory board approves the grant of options to members of the management board. The Option Plan provides for the grant of options with service-based vesting conditions that can be combined with vesting conditions subject to performance conditions. With respect to options with service-based vesting conditions, the options vest in four annual equal tranches of 25%, beginning on the first anniversary of the date of grant.

The option exercise price of each option is specified in the applicable notice of grant. For purposes of the Option Plan, the fair market value per ordinary share is determined by (or in a manner approved by) the supervisory board and is currently set equal to the fair market value per ordinary share as determined at the date of grant. Each option is exercisable at such times and subject to such terms and conditions as specified in the applicable notice of grant. We may, in the event of a change of control of our company, decide to exchange, cancel and settle in cash and/or accelerate the vesting of the outstanding options or the supervisory board may take whatever step considered appropriate with respect to the outstanding options.

The outstanding options can be exercised after the respective vesting date up to 10 years following the grant date and then expire.

Share-based compensation reflects the compensation expenses of our equity-settled Option Plan granted to employees or others providing similar services, which are measured at the grant date fair value of the options. The compensation expenses are spread over the vesting period in accordance with each separate vesting tranche of the options granted, taking in consideration actual and expected forfeitures at each reporting date and at the respective vesting dates. The share-based compensation is recognised in the income statement, with a corresponding entry to the equity-settled employee benefits reserve, which is part of equity. We expect that our share-based compensation costs will increase in the future as the number of outstanding options increases.

Fair value options

The grant date fair value of the options is estimated based the Black-Scholes option-pricing formula using the following assumptions:

	2012	2013
Option exercise price (in EUR)	—	113.34
Risk-free interest rate	—	0.942%
Expected volatility	—	93.8%
Expected dividend yield	—	0%
Expected life (in years)	—	5

The weighted average grant date fair value of the options amounts to €80.78.

The risk-free interest rate is derived from the implied yield on AAA rated government bond loans in the euro zone as determined by the European Central Bank at the grant date of the options based on the expected option life.

The expected volatility is estimated using historical daily share price return data from a group of comparable listed companies measured over a period equal to the expected term since we have been a private company and therefore we have no historical or implied volatility information available. We will continue to do so until sufficient historical market data is available for estimating the volatility of our ordinary shares. The group of comparable listed companies are publicly traded entities active in the business of developing RNA based therapeutics, treatments and drugs and are selected taking into consideration the availability of meaningful trading data history and market capitalization.

We consider the expected life of the options to be five years. We have determined this expected life based on economic exercise behavior of vested options by participants and also considering and allowing for the time needed to reach important milestones.

Valuation of our ordinary shares

The fair value of our ordinary shares is determined by our management board and supervisory board, and takes into account our most recently available valuation of ordinary shares performed by an independent valuation firm and our assessment of additional objective and subjective factors we believe are relevant and which may have changed from the date of the most recent valuation through the date of the grant.

Our management board and supervisory board consider numerous objective and subjective factors to determine their best estimate of the fair value of our ordinary shares as of each grant date, including:

- the progress of our research and development programs;
- achievement of enterprise milestones, including our entering into collaboration and licensing agreements, as well as funding milestones;
- contemporaneous third-party valuations of our ordinary shares as of 2014;
- our need for future financing to fund operations;
- the rights and preferences of our preferred shares and our preferred shares relative to our ordinary shares;
- the likelihood of achieving a discrete liquidity event, such as a sale of our company or an initial public offering given prevailing market conditions; and
- external market and economic conditions impacting our industry sector.

In determining the fair values of our ordinary shares as of each award grant date, we considered three generally accepted approaches: income approach, market approach and cost approach. Based on the information available, external transactions of company shares and external rounds of financing, we have determined that the market approach is the most appropriate method. We have employed the prior sale of company stock method to estimate our aggregate enterprise value. In addition, we have taken into consideration the guidance prescribed by the American Institute of Certified Public Accounts Audit and Accounting Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

The prior sale of company stock method considers any prior arm’s length sales of our equity securities. Considerations factored into the analysis include: the type and amount of equity sold, the estimated volatility, the estimated time to liquidity, the relationship of the parties involved, the timing compared to the ordinary shares valuation date and our financial condition and structure at the time of the sale. As such, we have benchmarked the value per share to the external transactions of our shares and external financing rounds.

All option grants in 2013 rely on the prior sale of company stock method. In order to estimate the value of ordinary shares for grants in 2013, we relied on the pricing from a round of financing for our ordinary shares which closed in February 2013 at €113.34 per share. In May 2013, further ordinary shares were issued at the

same price per share as extension of the February 2013 round. Lastly, in November 2013, one of our existing shareholders purchased ordinary shares from another existing shareholder at a price of €113.34 per share. Given that all transactions of our ordinary shares in 2013 took place with independent third party investors, we believe these represent strong and reliable indications of fair value and therefore the basis for estimating the fair value of ordinary shares at €113.34 per share for IFRS 2.

We have granted the following options through December 31, 2013:

Grant Date	Number of Options Granted	Option Price	Estimated Fair Value for Each Ordinary Share	Estimated Fair Value for Each Option
September 26, 2013	2,677	€ 113.34	€ 113.34	€ 80.78
December 1, 2013	1,059	€ 113.34	€ 113.34	€ 80.78

Corporate Income Taxes

We are subject to income taxes in the Netherlands. Significant judgment is required in determining the use of tax loss carry forwards. We recognize deferred tax assets arising from unused tax losses or tax credits only to the extent that we have sufficient taxable temporary differences or there is convincing evidence that sufficient taxable profit will be available against which the unused tax losses or unused tax credits can be utilized by us. Management's judgment is that such convincing evidence is currently not sufficiently available and a deferred tax asset is therefore not yet recognized.

Under Dutch income tax law, tax loss carry-forwards are subject to a time limitation of nine years. As of December 31, 2013, we had a total of approximately €3,700,000 tax loss carry-forwards available for offset against future taxable profits. The first amount of the tax loss carry-forwards will expire in 2021.

Recent Accounting Pronouncements

There are no IFRS standards as issued by the IASB or interpretations issued by the IFRS interpretations committee that are effective for the first time for the financial year beginning on or after January 1, 2014 that would be expected to have a material impact on our financial position.

JOBS Act Exemptions

The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an emerging growth company, we are electing to take advantage of the following exemptions:

- not providing an auditor attestation report on our system of internal controls over financial reporting;
- not providing all of the compensation disclosure that may be required of non-emerging growth public companies under the U.S. Dodd-Frank Wall Street Reform and Consumer Protection Act;
- not disclosing certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation; and
- not complying 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 (auditor discussion and analysis).

The JOBS Act permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We are

choosing to “opt out” of this provision and, as a result, we will comply with new or revised accounting standards as required when they are adopted. This decision to opt out of the extended transition period under the JOBS Act is irrevocable. These exemptions will apply for a period of five years following the completion of our initial public offering or until we no longer meet the requirements of being an “emerging growth company,” whichever is earlier. We would cease to be an emerging growth company if we have more than $1.0 billion in annual revenue, have more than $700 million in market value of our ordinary shares held by non-affiliates or issue more than $1.0 billion of non-convertible debt over a three-year period.

BUSINESS

Overview

We are an innovative biopharmaceutical company engaged in the discovery and development of RNA-based therapeutics for the treatment of severe genetic disorders. Utilizing our unique proprietary RNA repair technologies, we believe we will be able to treat rare genetic disorders in which a single protein is defective due to certain types of genetic mutations. We design our therapeutic candidates to specifically target and repair the defective messenger RNA, or mRNA, that is transcribed from a mutated gene in order to restore the expression and function of normal, or wild-type, protein. We believe that targeting the mRNA to restore the production of normal protein is a unique approach that offers advantages compared with small molecule, gene therapy and other therapeutic approaches. Our initial focus is on the development of a disease-modifying therapy for the treatment of cystic fibrosis, or CF, a genetic disease that affects an estimated 70,000 to 100,000 patients worldwide and causes early morbidity and mortality. We are also developing a treatment for Leber's Congenital Amaurosis, or LCA, the leading genetic cause of blindness in childhood. Further, based on our own research and initial selection criteria, we believe that our RNA repair technologies can potentially be used to treat a broad range of other severe genetic diseases with high unmet medical need, and to date we have identified approximately 50 potential targets.

CF is a genetic disease that currently has no cure. The median age of death for CF patients is 29, and more than 90% of CF patients die from respiratory failure. To date, all but one of the therapies approved to treat CF patients are designed to treat the symptoms of CF rather than address the underlying cause. CF is caused by mutations in the gene that encodes for a protein called cystic fibrosis transmembrane conductance regulator, or CFTR. Although there are more than 1,900 different genetic mutations that cause CF, the DF508 mutation that we are targeting is the most prevalent and is present in approximately 70% of all CF patients. In CF patients, this mutated gene and the resulting defective protein lead to the dysfunction of multiple organ systems, including the lungs, pancreas and gastrointestinal tract. In the lung airways, absence of functional CFTR protein leads to unusually thick, sticky mucus that clogs the lungs and increases vulnerability to chronic, life-threatening lung infections.

Our lead product candidate, QR-010, which we believe is a first-in-class RNA-based oligonucleotide, is designed to address the underlying cause of the disease by repairing the mRNA defect encoded by the DF508 mutation in the CFTR gene of CF patients. The DF508 mutation is a deletion of three of the coding base pairs, or nucleotides, in the CFTR gene, which results in the production of a misfolded CFTR protein that does not function normally. QR-010 is designed to bind to the defective CFTR mRNA and guide the insertion of the three missing nucleotides, thus repairing the mRNA and subsequently producing wild-type, or normal CFTR protein. QR-010 is designed to be self-administered through a small, handheld aerosol delivery device, or nebulizer, in the form of a mist inhaled into the lungs. We believe this method will allow maximum exposure of QR-010 to the primary target organ, the lung, as well as significant exposure to other affected organs through systemic absorption into the blood. To date, we have conducted extensive pre-clinical studies that have shown significant activity of QR-010 in restoring the expression of fully functional CFTR protein in cell and animal models that bear the DF508 mutation. We believe this activity in pre-clinical models of CF provides support for the clinical development and therapeutic potential of QR-010. QR-010 has been granted orphan drug designation in the United States and the European Union.

In the fourth quarter of 2014, we plan to file an Investigational New Drug application, or IND, with the U.S. Food and Drug Administration, or FDA, and a Clinical Trial Application, or CTA, with the European Medicines Agency, or EMA, for QR-010. We have had a pre-IND meeting with the FDA and scientific advice and protocol assistance meetings with the EMA, and we intend to initiate our first clinical trial directly in CF patients. This clinical trial will be a Phase 1b, randomized, double-blind, placebo-controlled, 28-day dose-escalation study to evaluate the safety, tolerability and pharmacokinetics of QR-010 in CF patients who have two copies of the DF508 mutation. We will also assess exploratory outcome measures that could be indicative of the potential efficacy of QR-010. In parallel with our Phase 1b trial, we will also conduct a proof-of-concept, or POC, study

designed to demonstrate restoration of CFTR function in the nasal lining of CF patients with the DF508 mutation. We expect to report top-line data from our Phase 1b trial and our POC study in the fourth quarter of 2015.

ProQR was formed in February 2012 by Daniel de Boer, Gerard Platenburg, Henri Termeer and Dinko Valerio. Mr. de Boer is a passionate and driven entrepreneur and advocate for CF patients, and has assembled an experienced team of successful biotech executives as co-founders and early investors. ProQR's team has extensive experience in discovery, development and commercialization of CF treatments and RNA therapeutics. To date, we have raised €45,521,000 from private placements of equity securities. In addition, we have received grants and loans from CF-focused patient organizations and government institutions supporting our program for CF. ProQR is located in Leiden, the Netherlands.

Our Strategy

We are dedicated to improving the lives of patients through the development of RNA-based therapies for severe genetic diseases and have an initial focus on patients with CF. Key elements of our strategy include:

- ***Rapidly advance QR-010 for the treatment of CF.*** Our lead product candidate, QR-010, has generated compelling data in pre-clinical studies, which we believe support its potential as a disease-modifying therapy for CF patients. We intend to advance QR-010 into clinical trials in CF patients with the DF508 mutation, which affects approximately 70% of all CF patients. In the fourth quarter of 2014, we plan to file our IND with the FDA, file our CTA with the EMA and initiate our first clinical trials directly in CF patients. We are also studying applications of our RNA repair technologies for mutations other than DF508 that could potentially be used to treat an additional 10% of CF patients, including those with the G551D mutation.
- ***Utilize our proprietary RNA repair technologies and know-how to develop additional product candidates targeting genetic diseases with high unmet medical need.*** We aim to develop a product pipeline targeting severe genetic diseases with no or limited effective treatments caused by mutations that we believe can be treated with our RNA repair technologies. Based on our own research and initial selection criteria, we have to date identified approximately 50 potential target indications. As our first non-CF therapeutic program, we are developing QR-110 to treat patients with the most common mutation causing Leber's Congenital Amaurosis, the leading genetic cause of blindness in childhood.
- ***Independently commercialize QR-010 and any other CF product we successfully develop.*** We intend to commercialize QR-010 independently, if approved, and retain all commercial rights in major markets. There are extensive CF patient registries, and CF patients are treated in centralized, specialized care centers. Because of this well-organized CF community, we believe we will be able to market effectively QR-010, if approved, with an initially small, targeted sales force of approximately 35 representatives in the United States and Europe.
- ***Consider collaborative partnerships to develop and commercialize our RNA repair technologies or programs in specific indications outside of CF.*** We will consider collaborative partnerships with pharmaceutical companies and others to leverage our core technologies in therapeutic areas beyond CF depending on the attractiveness of the opportunities. These partnerships may provide us with further validation of our RNA repair technologies, funding to advance our product candidates and access to development, manufacturing and commercial expertise and capabilities.

Our RNA Repair Approach

Genes are the specific sequences of DNA that provide the blueprint used by the human body's cells to make proteins, which are enzymes or other large molecules in cells that serve a functional purpose. Each gene consists of a specific sequence of nucleotides that leads to the production of a specific protein. The gene's coding DNA sequence is transcribed into mRNA, which is subsequently translated into the specific protein. A mutation, or defect, in a specific gene can result in the transcription of abnormal mRNA, which then can produce a defective, misfolded or truncated protein that is unable to carry out its normal function.

Unlike other approaches in the RNA therapeutics field, such as RNAi and antisense, our RNA repair approach aims to treat genetic disorders by repairing the basic defect in the mRNA, thus resulting in fully-functional, wild-type protein. This approach employs single-stranded RNA-based oligonucleotides, which act as guide sequences to repair the targeted abnormal mRNA. The repaired mRNA then acts as a template to generate wild-type protein. We believe this RNA repair approach will allow us to develop novel therapies for genetic disorders that are currently untreatable or have limited effective treatment options.

In the CF field, which is our initial focus, QR-010 is designed to repair the defective mRNA by guiding the insertion of the three nucleotides missing in the DF508 mutation, thus resulting in the production of wild-type CFTR protein with the same functionality as CFTR protein in healthy individuals. We believe we are the only company currently pursuing this RNA repair approach for CF patients.

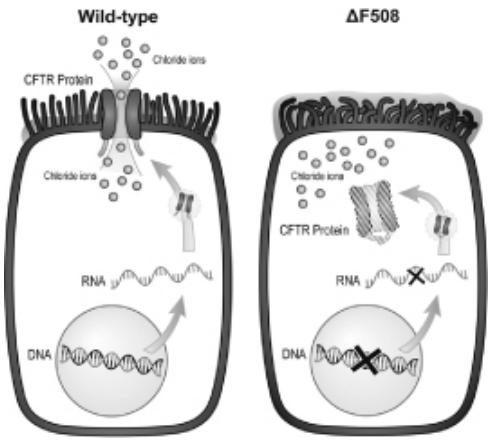
Cystic Fibrosis

Cystic Fibrosis Background

CF is the most common fatal inherited disease in the western world and affects an estimated 70,000 to 100,000 patients worldwide. There is no cure for CF. CF patients require lifelong treatment with multiple daily medications, frequent hospitalizations and ultimately lung transplants, which can extend life for five years on average. The quality of life for CF patients is compromised by approximately four hours of self-care per day and frequent outpatient doctor visits and hospitalizations.

CF is caused by mutations in a gene that encodes the CFTR protein. The CFTR protein channel regulates the movement, or efflux, of specific ions in and out of the cells of organs like the lungs, pancreas and gastrointestinal tract. Through regulation of these ions, the amount of salts in the fluid both inside and outside the cell remains balanced. In CF patients, however, the CFTR protein is defective and cannot perform its normal function of transporting ions across the cell membrane, and this results in an environment characterized by thick mucus in vital organs such as the lung, the pancreas and the gastrointestinal tract. The figure below illustrates a defective CFTR protein hampering the efflux of chloride in lung epithelial cells.

Chloride Ion Flow by Wild-Type CFTR and DF508 CFTR



The lack of functional CFTR in CF patients is particularly problematic in the lungs, where the build-up of thick mucus obstructs parts of the lung, allows bacteria to grow unfettered and impairs the functionality of the local immune system. Of all the manifestations of CF, lung disease is the most critical and is characterized by a combination of airway obstruction, infection and inflammation such that more than 90% of all CF patients die of

respiratory failure. In the pancreas, the buildup of mucus prevents the release of digestive enzymes that help the body break down food and absorb important nutrients. In the GI tract, the thick mucus leads to impaired ability to absorb nutrients. The median age of death for all CF patients is 29 years.

According to the medical literature, restoration of as little as approximately 15% of wild-type CFTR function in CF patients should result in a therapeutic benefit.

Cystic Fibrosis Genetics

CF is an autosomal recessive disease. A normal, healthy gene has two alleles that encode for a given protein. In an autosomal recessive disease such as CF, a patient has a mutation in both alleles. Non-affected carriers have a mutation in only one of the alleles. CF patients have a defect in the gene encoding for the CFTR protein, and they either have two copies of the same mutation, referred to as homozygotes, or one copy of two different mutations, referred to as compound heterozygotes. Although over 1,900 CF-causing gene mutations have been identified, approximately 70% of all CF patients are affected by the DF508 mutation. Among all CF patients, approximately 50% are homozygous for the DF508 mutation and approximately 20% are heterozygous for the DF508 mutation.

In the DF508 mutation, the genetic defect is a deletion of three of the coding base pairs, or nucleotides, in the CFTR gene that results in the transcription of defective mRNA, which results in the production of CFTR protein that is misfolded and can neither migrate to its normal location on the surface of epithelial cells nor perform its normal function. The figure below illustrates the missing three nucleotide sequence.

Cystic Fibrosis Incidence and Diagnosis

CF affects one out of 3,500 live births in the United States and one out of 2,500 live births in Western Europe. Many individuals are also non-affected carriers of a mutated CFTR gene. Carrier results across ethnic groups in the United States are well established, and reports from the American College of Obstetricians and Gynecologists indicate rates of one out of 25 in non-Hispanic Caucasians, one out of 58 in Hispanic Caucasians, one out of 61 in African Americans, and one out of 94 in Asian Americans. While the life expectancy of CF patients has improved over the last three decades, the median age of death is still only 29 years.

Most CF patients in the United States, the European Union, Canada and Australia are now diagnosed at birth through newborn screening, and more than 75% of CF patients are diagnosed by the age of two. CF can be diagnosed by conducting a Nasal Potential Difference, or NPD, test that measures CFTR activity in the nose, or a sweat test, which measures the amount of salt in a person’s sweat. A genetic test is also often used to confirm a CF diagnosis and/or identify the disease-causing mutations. In a genetic test, a blood sample or cells from the inside of the cheek are taken and sent to a laboratory that specializes in genetic testing.

Approaches to the Treatment of Cystic Fibrosis

Treatment overview

There is no cure for CF, and to date, all but one of the therapies approved to treat CF patients have been designed to treat the symptoms rather than address the underlying cause. CF patients require lifelong treatment with multiple daily medications, frequent hospitalizations and ultimately lung transplant, which is life-extending but not curative. In the United States, the average CF patient incurs approximately $50,000 per year in expenses for outpatient medications and services and substantial additional costs for frequent hospitalizations. As the

median age of death for CF patients is 29, this results in an average lifetime cost per CF patient in the U.S. of $1,450,000 in outpatient expenses alone. CF patients who can be treated with Vertex's Kalydeco have additional annual costs of approximately $300,000. Standards of care are generally similar across Western European nations.

Palliative treatments

The current standard of care for CF patients is palliative treatment to manage the symptoms of the disease. In CF patients, the thick mucus that builds up in the lungs and other vital organs such as the pancreas and gastrointestinal tract hampers mucus clearance and leads to airway obstruction and difficulty absorbing nutrients, leading to poor growth and development. Primary treatment options include inhaled therapies such as rhDNase, marketed as Pulmozyme, which thins the mucus in the lungs, as well as pancreatic enzyme replacement therapy, which improves absorption of nutrients. Due to the proliferation of bacteria on the mucus build-up, CF patients often develop chronic lung infections that require inhaled antibiotics treatments, such as TOBI or Cayston, to suppress the infections. CF patients also take a number of other prescribed and over-the-counter medications to alleviate the symptoms of CF and reduce complications, including bronchodilators, inhaled corticosteroids, and ursodeoxycholic acid for biliary tree dysfunction.

Potentiators for certain non-DF508 mutations

For a subset of patients who suffer from the G551D and other gating mutations of the CFTR gene, Vertex Pharmaceuticals has developed a so-called "potentiator" molecule marketed under the trade name Kalydeco (ivacaftor). This product was approved by the FDA in 2012 to treat patients with the G551D CFTR mutation and, in 2014, the label was expanded to include eight additional gating mutations. Vertex has estimated that approximately 2,400 CF patients in the U.S., Europe and Australia have a G551D or a non-G551D gating mutation. Gating mutations are characterized by the presence of CFTR at the cell surface that does not open and close the ion channels properly. Kalydeco is believed to keep the ion channels open for longer. For this population of CF patients, medication costs are approximately $300,000 per year for Kalydeco prescriptions. Kalydeco is an exciting development as it provides a proof of concept that it is possible to target the defective CFTR protein that causes CF and improve key symptoms of the disease.

The DF508 mutation affects approximately 70% of all CF patients. Unlike the "gating" mutations, DF508 is a "processing" mutation, and as such, CFTR with the DF508 mutation is not expressed at the cell surface and cannot be potentiated by Kalydeco.

Gene therapy

Gene therapy is a process in which a functional gene is introduced into a cell to override the effects of a defective gene. The CFTR gene was first identified in 1989. Since that time, several academic consortia and drug-development companies have attempted to develop therapies targeting mutations in the CFTR gene. These companies aimed to permanently correct the CFTR gene at the DNA level by delivering full length CFTR genes to lung epithelial cells to express wild-type CFTR protein. However, these programs encountered limitations faced by gene therapy in general as well as limitations specific to the CFTR gene. These barriers included safety concerns, challenges to delivery of the gene therapy constructs to target cells in the lungs, challenges of both delivery and incorporation into the genome given the size and complexity of the CFTR gene, and immunologic responses to the gene therapy vectors. We believe that, due to these limitations, all commercial gene therapy approaches for the treatment of CF were terminated in the late 1990's and that gene therapy is not currently considered a viable therapeutic option for CF patients.

Protein correctors

Small molecule "corrector" approaches aim to transport the non-functional DF508 CFTR protein to the cell membrane, often in connection with a second agent, such as a potentiator, to enable the abnormally-folded

protein to achieve some level of activity without repairing the actual protein. Companies currently developing small molecule "correctors" include Vertex, Pfizer, Genzyme and Abbvie. To date, however, there are no approved "corrector" molecules on the market. Lumacaftor (VX-809), which is being developed by Vertex, is a small molecule corrector studied in patients homozygous for the DF508 mutation for use in combination with Kalydeco. In June 2014, Vertex announced that its two Phase 3 clinical trials of lumacaftor, when used in combination with Kalydeco in CF patients homozygous for the DF508 mutation, showed statistically significant improvement in the study's primary endpoint of improved lung function, compared to placebo. Vertex also showed statistically significant reductions in pulmonary exacerbations in the pooled analysis of both studies. Other signs of clinical improvement were either limited or not statistically different from placebo. We believe these studies validate that DF508 CFTR is a treatable target and indicate there is need for more efficacious therapies.

Our solution—RNA repair

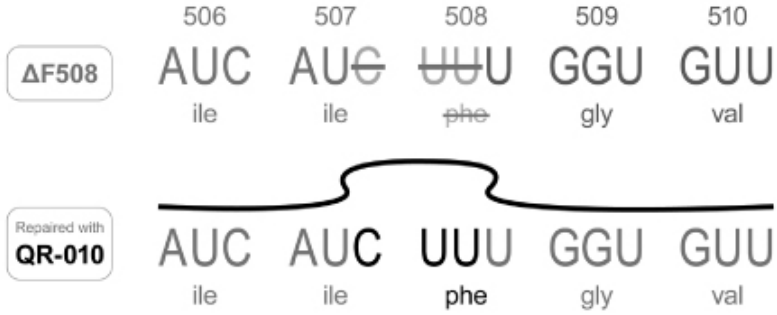
Our approach, RNA repair, aims to repair the basic defect in the CFTR mRNA and subsequently restore expression of wild-type CFTR protein that can normalize the ion transport in the key organs affected by CF, particularly the lung. We believe we are currently the only company pursuing this novel approach for CF patients.

QR-010 for Treatment of CF

We are developing QR-010 as a treatment for CF patients. QR-010 is an oligonucleotide designed to restore wild-type CFTR expression in CF patients with the DF508 gene mutation. QR-010 is 33 nucleotides long and is designed to bind to the CFTR mRNA sequences that are adjacent to the deleted F508 region of the mRNA.

The figure below illustrates wild-type mRNA, the site of the DF508 mRNA deletion and where QR-010 binds on either side of the mutated area and introduces the template to insert the three deleted nucleotides.

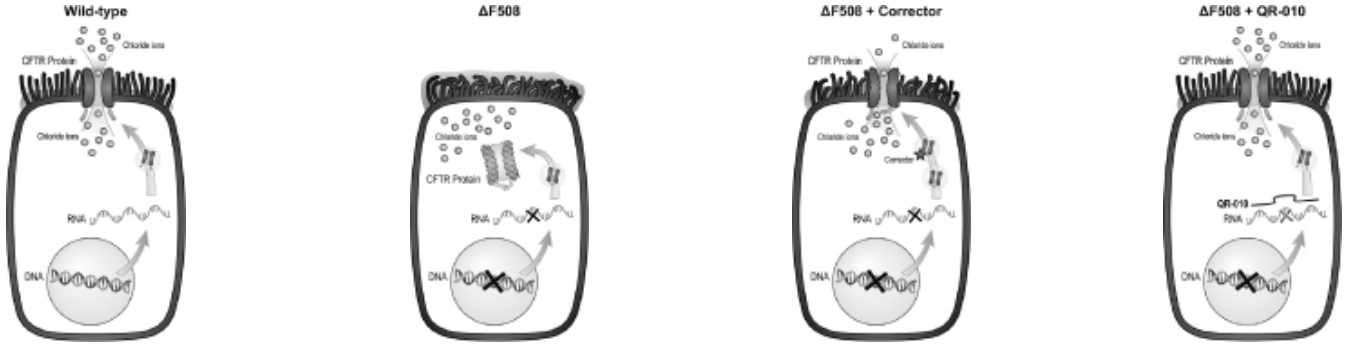
QR-010 Binds to mRNA and Guides Insertion of Deleted Nucleotides



The resulting wild-type CFTR protein will be expected to be processed as any other wild-type CFTR protein and result in an increase in the cell surface density of wild-type CFTR protein and restoration of wild-type CFTR functions, including chloride transport, chloride-bicarbonate exchange and regulation of the epithelial sodium channel, or ENaC.

The figure below shows, from left to right, wild-type CFTR function in a normal cell, impaired CFTR function in a cell with a DF508 mutation, a DF508 mutated cell treated with a protein corrector molecule, which shows limited restoration of chloride efflux, and a DF508 mutated cell treated with QR-010, which shows restoration to wild-type levels of chloride efflux.

Chloride Ion Flow: Partial Restoration through Protein Corrector and Full Restoration through QR-010



We intend to deliver QR-010 through inhalation by means of a small handheld nebulizer, a method of drug delivery used to administer medication in the form of a mist inhaled into the lungs. We believe this method will allow maximum exposure of QR-010 to the primary target organ, the lung, as well as significant exposure to other affected organs through systemic absorption into the blood. This device rapidly and efficiently processes a therapeutic agent through the microscopic holes of a mesh and creates a mist to provide rapid and consistent delivery to the lungs. Commercially-available nebulizers are currently used for other CF therapies and in other clinical studies involving inhaled oligonucleotides.

Clinical Development Plan for QR-010

In the fourth quarter of 2014, we plan to file our IND with the FDA and file our CTA with EMA for QR-010. We have had a pre-IND meeting with the FDA and scientific advice and protocol assistance meetings with the EMA, and we intend to initiate our first clinical trial directly in CF patients. The clinical trial will consist of two clinical studies—a single ascending dose, multiple ascending dose trial, which we refer to as the SAD/MAD trial, and a POC study. We intend to conduct the two studies in parallel, with the POC study being initiated a few months after the SAD/MAD trial. Assuming the results of these two studies are positive, we plan to conduct a Phase 2a trial for QR-010.

SAD/MAD trial

The first clinical trial with QR-010 will be a Phase 1b, randomized, double-blind, placebo-controlled, 28-day dose-escalation trial to evaluate the safety, tolerability and pharmacokinetics of QR-010. QR-010 will be given as a nebulized solution to the lower airways after chest physiotherapy, which is a standard procedure used with other currently administered inhaled medications. This method of drug administration is common in CF patients and has been used with oligonucleotides in development in other indications. The primary outcome measures will characterize safety, tolerability and pharmacokinetics. We will also assess exploratory outcome measures, which we believe could be indicative of the potential efficacy of QR-010. We intend to enroll the first patient in the fourth quarter of 2014. The study will include CF patients that are homozygous DF508 and age 18 years and above with normal, mild or moderately compromised lung function. Pharmacokinetics will be assessed with serum measurements over time. Exploratory clinical measurements, including evaluation of early changes in lung function, reduction in symptoms and weight gain will also be performed to inform the design of future trials.

The trial will be conducted at approximately 20 sites in the United States and selected EU countries and will enroll 72 patients. Randomization will be 3:1, meaning 25% of patients will receive placebo. We anticipate that top-line data will be available in the fourth quarter of 2015.

Dosing will start with four single ascending dose cohorts and continue with up to five multiple ascending dose cohorts. Each cohort will enroll eight patients of which six will receive QR-010 and two will receive placebo. The multiple dose regimens will be for a maximum of 28 days. Dosing will occur as frequently as once daily and as infrequently as once every two weeks. Safety will be monitored throughout by an independent data safety monitoring committee.

POC NPD study

We also plan to conduct a parallel clinical study to demonstrate the ability of QR-010 in improving NPD. NPD is a standard test for detection and quantification of CFTR function in the airways in CF patients. The NPD assay has been used extensively and is standardized to assess the ability of new therapeutics to restore defective ion transport in CF patients and several pre-clinical animal models. This POC study will evaluate QR-010 applied directly to the nasal mucosa in 10 CF patients who are homozygous for DF508 and 10 CF patients who are heterozygous for DF508. This study will be conducted in parallel to our Phase 1b trial.

This POC study is designed to demonstrate the restoration of CFTR function by QR-010 in patients, as was observed in pre-clinical NPD studies in mouse models. The primary outcome measures will be the normalization of NPD as well as normalization of responses to standard challenges. Nasal mucosal samples will be obtained at baseline, Day 14 and Day 28 to assess the proposed mechanism of action of QR-010 including through assays for the presence of repaired CFTR mRNA and wild-type CFTR. The nasal passages are not the intended target site for QR-010. However, the nasal epithelium is the most accessible site for measuring CFTR function in humans and provides a human model of epithelial cell uptake and restoration of CFTR function.

The study hypothesis is that QR-010 will restore CFTR function as assessed by NPD in both homozygous and heterozygous CF patients. If our hypothesis proves to be true and no differences are identified between homozygous and heterozygous patients, we intend to include both groups of CF patients in our future Phase 2 and Phase 3 clinical trials. We anticipate that top-line data from our POC study will be available in the fourth quarter of 2015.

Pre-Clinical Data to Support QR-010

We have conducted extensive *in vitro* and *in vivo* pre-clinical studies that support the development and therapeutic potential of QR-010. In our pre-clinical studies, we demonstrated repair of CFTR mRNA, and activity of wild-type protein through improved chloride ion efflux. We measured *in vitro* activity in certain cell lines with the DF508 mutation, including differentiated primary human CF HBE, or human bronchial epithelial, cells. We also evaluated *in vivo* activity of inhaled QR-010 in DF508 mice and detected increased amounts of repaired mRNA and CFTR function in multiple organs.

On the functional level, QR-010 has also been shown to increase the function of CFTR as demonstrated by enhancing chloride efflux *in vitro* and *in vivo*. Most notably, in two independent *in vivo* activity assays that are similar to human diagnostic tests, QR-010 restored CFTR function. The first was a study of NPD in DF508-CFTR mice in which QR-010 restored both the NPD and response to specific stimuli. The second was a salivary secretion assay, a mouse equivalent of the sweat chloride test, in which QR-010 restored saliva secretion to normal levels in female mice.

Overview of Pre-clinical Data to Support QR-010

Safety

Oligonucleotides with similar chemistry to that of QR-010 have been studied extensively in large groups of patients with different indications. Through these studies, a detailed safety profile of these molecules has been described, indicating that these molecules are generally well tolerated even after several years of chronic treatment. We believe the results from these studies reduce the risk of our development program.

Our pre-clinical studies evaluated QR-010 in two animal safety models—mice and monkeys. We selected the mouse because of the well-characterized homozygous mouse model of the DF508 /DF508 CFTR gene mutation that exists with homology to the human mRNA transcript in the region where QR-010 binds. Since QR-010 is 100% homologous to the complementary portion of the antisense strand of the CFTR gene for both mice and humans, it is expected that binding of QR-010 to the target mRNA in humans will be identical to that observed in the mouse model. We selected cynomolgus monkeys as the non-rodent species for toxicology studies because these monkeys are a well characterized model for human toxicology studies. The cynomolgus monkey has a specific advantage over other non-rodent species because there is sequence identity with humans in the targeted region of wild-type CFTR mRNA.

Pharmacology

To date, we have conducted pre-clinical studies in CFPAC-1 cells, in a DF508 patient derived cell-line, in CF HBE cells, and in mice homozygous for the DF508 mutation. *In vitro* results demonstrated QR-010 activity in cell lines and primary epithelial cells from DF508 CF patients. *In vivo* studies with mice homozygous for the DF508 mutation demonstrated QR-010 activity by restoration of transepithelial NPD responses to standard challenges. In addition, we observed functional CFTR activity, repair of CFTR mRNA and detection of CFTR protein.

QR-010 demonstrated improved CFTR function in several distinct *in vitro* and *in vivo* assays, including:

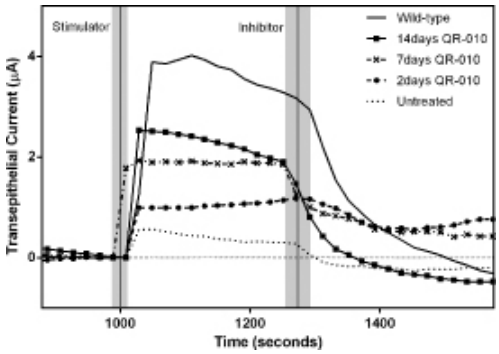
- a Ussing Chamber assay using CF HBE cells affected with DF508 mutations, in which we observed changes in potential difference consistent with increased CFTR function;
- a mouse NPD assay, in which we gave DF508 mice QR-010 intranasally and observed normalization of NPD as well as responses to specific challenges; and
- a mouse saliva secretion assay, in which we gave DF508 mice QR-010 orotracheally and observed changes in saliva volume consistent with improved CFTR function.

QR-010 Increases CFTR Activity in Ex Vivo Primary Lung Cells from CF Patients

The Ussing Chamber assay measures the electrical current over a monolayer of epithelial cells and is a well-established pre-clinical assay to measure the chloride efflux resulting from CFTR activity. This assay has been used extensively to test the effect of a variety of agents on CFTR activity in cells and is performed using fully differentiated HBE cells with the DF508 mutation grown in a manner to resemble the lung epithelium with an airway liquid interface. As reduced efficiency of transfection, or delivery of oligonucleotides into a cell, is predicted in this model, we investigated the effect of QR-010 in CF HBE cultures following repeated treatments over 14 days. The figure below shows the results of the Ussing Chamber assay and the efficacy of QR-010 treatment on CFTR activity over different QR-010 treatment periods. After the addition of a cAMP stimulator, Forskolin, to activate the CFTR protein, we observed an increase in ion current across the cell membrane that represents CFTR activity. To confirm that the observed result was due to restored CFTR function and not an alternative pathway, a CFTR inhibitor was administered and the effect on ion current was extinguished in a selective manner.

As shown in the figure below, we observed a small effect after just two days of treatment with QR-010. After 14 days of treatment, we observed a four- to five-fold, or approximately 60%, increase in the CFTR-specific response, compared to control. As we did not observe a plateau of effect at 14 days of treatment, longer treatment periods may increase the CFTR response even further.

QR-010 Increases CFTR Function and is Dose Dependent (*in vitro*)

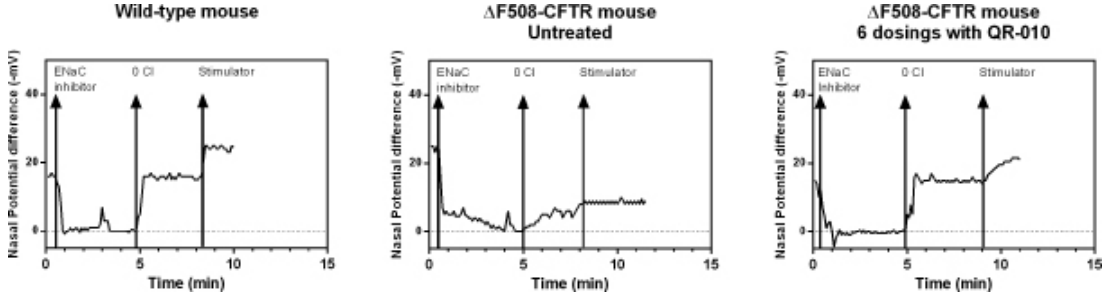


NPD Measurements in* D*F508-CFTR Mice

NPD is a standard test for detection and quantification of CFTR function in the airways in CF patients. The NPD assay has also served as an important endpoint for the diagnosis of CF since 1981. It has been used extensively and is standardized to assess the ability of new therapeutics to restore defective ion transport in CF patients and several pre-clinical animal models.

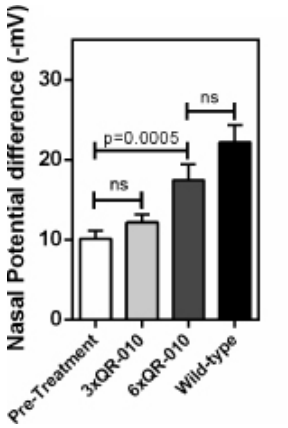
To assess whether or not QR-010 could restore CFTR function *in vivo*, we assessed NPD in DF508-CFTR mice before and after treatment. DF508-CFTR mice were treated with three or six doses of 40 µg per dose per animal of QR-010 intranasally. We then assessed NPD by measuring the current through their nasal epithelial cells. We initially administered amiloride, an ENaC blocker, to block the ENaC signal, drop the signal to baseline and isolate the CFTR signal. Subsequently, we administered chloride-free buffer, or 0Cl, or Forskolin, and a stimulator to activate chloride efflux through CFTR. As chloride flowed, the voltage signal increased over baseline and represents the level of CFTR activity. The figure below shows, from left to right, the results of NPD measurements in wild-type mice, in DF508-CFTR mice receiving no treatment, and in DF508-CFTR mice treated with QR-010. Notably, the pattern of response in the DF508-CFTR mice treated with QR-010 returns the phenotype as measured by this assay to that of a wild-type mouse. The control treated mice did not respond in this fashion.

QR-010 Normalizes NPD Baseline and CFTR Responses (*in vivo*)



As part of the NPD assessment, we treated 18 DF508-CFTR mice with six doses each of QR-010 over 14 days and conducted periodic NPD assessment. As illustrated by the figure below, the level of CFTR activity as measured by chloride response in the treated mice was not significantly increased after 7 days (3 doses), but after 14 days (6 doses), the CFTR activity in the treated mice increased significantly.

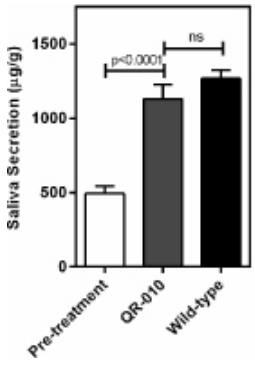
QR-010 Restores CFTR Function to Wild-Type Levels in 6 Doses *(in vivo)*



QR-010 Improves Saliva Secretion in* D*F508-CFTR Mice

The saliva secretion assay in mice is a surrogate for the human sweat test, which is a widely accepted diagnostic tool for CF in humans. Human sweat glands normally respond to stimuli, but CF patients do not demonstrate the same response. Similarly, the saliva glands of wild-type mice respond to these stimuli by producing more saliva, but the saliva glands of DF508 mice do not increase saliva production when stimulated. In an experiment involving nine DF508 mice, we tested whether orotracheal administration of QR-010 would result in increased saliva secretion. A wild-type cohort was also included as a control. The results in saliva secretion (body weight adjusted) are shown in the figure below and demonstrate that saliva secretion increased to wild-type levels after two doses of QR-010. It is well-recognized that male mice do not respond in this assay; therefore, only data from female mice is presented in the figure below. This is a known limitation of the assay and thus, we do not believe that it implies that QR-010 will not work in human males.

QR-010 Restores Saliva Secretion to Wild-Type Levels (*in vivo*)



Other Research and Development

Our innovation unit focuses on the discovery and early development of RNA repair therapeutics in genetic and acute indications. Leveraging our experience with RNA therapeutics, we are screening for therapeutic molecules that can be used to treat severe genetic disorders beyond CF.

We believe that our RNA repair technologies can potentially be applied to treat a broad range of genetic disorders. We use a selection method to identify the most feasible disease targets based on such criteria as disease specific genetics, targeted organ, possible routes of administration, patient population size and clinical development pathway. Based on our own research and selection criteria, we have to date identified approximately 50 other severe genetic diseases with high unmet medical need that we believe may be addressed by our RNA repair technologies. Our most advanced program outside of QR-010 is focused on the most common form of genetic blindness.

Leber's Congenital Amaurosis

LCA is the most severe form of inherited retinal degeneration, affecting 116,000 people worldwide. It is caused by 35 described mutations in 19 different genes. The most common mutation is a change in the centrosome- and cilium-associated gene centrosomal protein 290 or CEP290, which accounts for at least 11,000 of all LCA patients worldwide. The CEP290 mutation accounts consistently for the most severe LCA disease phenotype. Clinical features of CEP290-mediated LCA include congenital or early onset loss of vision, nystagmus, amaurotic pupils and no light response on electroretinography.

We are developing QR-110 to treat patients affected by a specific mutation in the CEP290 gene through repair of the mRNA to enable the production of wild-type protein. In pre-clinical studies to date, QR-110 has demonstrated full restoration of wild-type CEP290 mRNA in cultured lymphoblastoid cells of LCA patients homozygous for the CEP290 mutation. Significantly increased CEP290 protein levels and a complete rescue of ciliation and cilium length to normal levels have been observed. The next steps in the program include compound optimization, chemistry, manufacturing and controls, or CMC, and pre-clinical safety studies. QR-110 is currently in the optimization phase, and, if we choose to advance it into clinical development, we anticipate that we would initiate our first clinical trial in 2016.

Intellectual Property

We strive to protect our technology platforms and our product candidates through variety of approaches, including obtaining and maintaining patent and trade secret protection for our current and future technology platforms, our product candidates as well as their methods of use and processes for their manufacture, and any other inventions or discoveries that are commercially important to our business. We seek to obtain domestic and international patent protection and endeavor to promptly file patent applications or in-license patent rights relating to new, commercially valuable inventions to expand our intellectual property portfolio.

Our commercial success will depend in part upon obtaining and maintaining patent and trade secret protection for our current and future technology platforms and product candidates, as well as successfully defending our patent rights against third-party challenges. Our ability to prevent or stop third parties from making, using, selling, offering to sell or importing our product candidates will depend in part upon whether we have valid and enforceable patent rights that cover the activities of third parties.

We cannot be sure that patents will be granted with respect to any of our own or our in-licensed pending patent applications or with respect to any patents applications we may own or in-license in the future, nor can we be sure that any of our own or in-licensed patents or any patents we may own or license in the future will be useful in protecting our technology. Please see "Risk Factors—Risks Related to Our Intellectual Property" for additional information on the risks associated with our intellectual property strategy and portfolio.

Patent Rights

We have been building and will continue to build our patent portfolio. Where possible, we pursue or plan to pursue multi-tiered patent protection for our technology platforms and our product candidates as well as their manufacture, formulation and use. In addition to the United States, we file, and in the future plan to file, patent applications in various countries and regions where we think such filings are likely to be cost effective.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file or plan to file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. PTO in granting a patent. However, the term of a United States patent may be shortened if a patent is terminally disclaimed by its owner over another patent. In addition, depending upon the circumstances, certain United States patents may be eligible for a patent term extension which compensates a patentee for administrative delays by the FDA in granting marketing approval for a patented product or use of a product.

Patent Rights Relating to Our Cystic Fibrosis Program

With regard to our lead product candidate, QR-010, we own an international patent application filed under the Patent Cooperation Treaty relating to certain aspects of our RNA repair technology platform, including claims relating to the use of certain single stranded oligonucleotides, particularly modified RNA oligonucleotides, for making a change in the sequence of a target RNA molecule in a living cell, as well as claims relating to our QR-010 product candidate. We expect to file national and regional stage patent applications based on this international application in the United States, Europe and in other commercially significant jurisdictions before January 2015. The term of any patents resulting from this application, if issued, would be expected to extend to July 2033.

In addition, in May 2012, we entered into an exclusive license agreement with Massachusetts General Hospital, or MGH, to obtain rights to a patent family with claims directed to an alternative RNA repair platform that uses an RNA oligonucleotide complex rather than a single stranded oligonucleotide. This patent family includes an issued U.S. patent with a claim directed to an RNA oligonucleotide complex containing two specific oligonucleotide sequences for modulating the activity of a CFTR gene product, and an allowed U.S. patent application with claims directed to a method of treating a symptom of cystic fibrosis in a subject by administering to the subject an RNA oligonucleotide complex comprising two oligonucleotides, as well as claims directed to a specific RNA complex for modulating the activity of a CFTR gene product. The issued and allowed claims, however, cover elements of our RNA repair technologies, but may not cover the QR-010 product or its use. The term of the issued U.S. patent is expected to extend to October 2027, and the allowed U.S. application, when and if issued, would be expected to extend to March 2025. In addition, we have rights in a U.S. patent application to be filed in July 2014 with claims relating to QR-010. The term of any patent resulting from this application, if issued, would be expected to extend to March 2025.

Patent Rights Relating to Our LCA Program

With regard to our LCA Program, in April 2014, we entered into an exclusive license agreement with the Radboud University Medical Center to obtain rights in a patent family directed to certain antisense oligonucleotides for treating LCA and a method of modulating the splicing of the CEP290 gene product. Patent applications currently are pending in the U.S. as well as Brazil, Canada, Australia, Europe, Eurasia and Japan. The term of any patents resulting from these applications, if issued, would be expected to extend to 2032.

Trade Secrets

In addition to patent protection, we rely on trade secrets and know-how to develop and maintain our competitive position. Trade secrets and know-how can be difficult to protect. Nevertheless, we seek to protect

our trade secrets and know-how via, among other things, confidentiality and invention assignment agreements with our employees and consultants. We also seek to preserve the confidentiality of our trade secrets and know-how by implementing and maintaining security of our premises and information, and limiting access to our trade secrets and know-how.

License Agreement with MGH

In May 2012, we entered into a license agreement with MGH. Under the terms of this license agreement, we have an exclusive, royalty-bearing license under certain MGH patent rights to make, use and sell any product or process that is covered by the licensed patent rights for use in all therapeutic indications in the field of cystic fibrosis. We may sublicense our rights unless MGH objects to a potential sublicensee because of a conflict of interest. Our sublicensees may not further sublicense nor assign their rights without MGH's consent. MGH retains the right for it, its affiliates and other academic, government and not-for-profit institutions to use the licensed patents rights for internal research and educational purposes. If we ever desire to expand the license field beyond CF, we must provide to MGH a development plan that demonstrates we have sufficient resources to commercially develop a therapeutic indication in that field and MGH would then engage in good faith negotiations with us for a license covering such field on substantially the same terms as those contained in the license agreement.

Pursuant to the terms of the license agreement, in lieu of an upfront license payment to MGH, we are obligated to reimburse MGH, on a pro rata basis based on the number of licensees under the licensed patent rights, the fees and costs incurred by MGH in preparing, filing, prosecuting and maintaining the licensed patent rights. Currently, we are the sole licensee of the MGH patent rights and have paid approximately $65,000 in patent fee reimbursements to MGH. We are also obligated to pay MGH up to $800,000 in milestone payments upon the achievement of certain development and regulatory milestones and, beginning after our first commercial sale of a product covered by the licensed patent rights, a $10,000 annual license fee which is creditable against royalties due to MGH in the same calendar year. In addition, we are obligated to pay MGH 2% of any net sales by us, our affiliates or sublicensees on licensed products made or sold in the United States, as well as a low double-digit percentage of any payments that we may receive from any sublicensee anywhere in the world.

MGH is responsible for the preparation, filing, prosecution and maintenance of the licensed patent rights. MGH has the first right to protect the licensed patent rights from alleged infringement. If MGH declines to prosecute the alleged infringement, we may, at our expense, initiate legal proceedings against the alleged infringer, provided that we must give prior notice to MGH, obtain MGH's prior written consent in some cases, reasonably cooperate with MGH regarding the proposed action and not settle any proceeding without MGH's prior written consent. We must also indemnify MGH against any costs, expenses and liabilities incurred in connection with any such legal proceeding we initiate. Any award recovered from the alleged infringer after we and MGH are reimbursed for our expenses are shared so that we receive an amount equal to our lost profits or a reasonable royalty on the infringing sales, MGH receives an amount equal to the royalties or other payments we would have paid MGH if we had sold the infringing product, and any remainder is shared equally.

We are obligated to use commercially reasonable efforts to develop and make available to the public one or more CF therapeutic products or processes in the United States under the licensed MGH patent rights. We also must achieve certain specified development, regulatory and commercial milestones. If we do not meet the specified milestones, MGH may terminate the license agreement or grant us an extension and require us to pay additional milestone fees and, in some cases, an increased royalty on net sales, depending upon the length of our delay. The license agreement will remain in effect until the date on which all issued patents and filed patent applications under the licensed patent rights have expired or been abandoned. We may terminate the license agreement for any reason by giving MGH 90 days advance written notice of termination. MGH may terminate the license agreement upon our default of certain obligations under the license agreement which is not cured within a specified period of time or if we, our affiliates or sublicensees challenge the validity of the licensed patent rights. If we challenge the validity of the licensed patent rights during the term of the license agreement

and they are found to be valid and enforceable, we must reimburse MGH for its legal costs and expenses in defending the challenge. Upon a termination of the agreement, MGH will allow those of our sublicensees who are in compliance with their sublicense agreement and agree to assume our obligations under the license agreement to retain their rights.

Manufacturing and Supply

We do not currently own or operate manufacturing facilities for the production of preclinical or our planned clinical or commercial quantities of any of our product candidates. We currently contract with only one drug product formulation manufacturer for the production of QR-010 solution for nebulization, and we expect to continue to do so to meet the preclinical and planned clinical requirements of our product candidates. We do not have a long term agreement with this third party.

Currently, each of our drug starting materials for our manufacturing activities are supplied by a single source supplier. We have agreements for the supply of such drug materials with manufacturers or suppliers that we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. However, there is a risk that, if supplies are interrupted, it would materially harm our business. We typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

We do have manufacturing processes developed at a back-up GMP manufacturer. Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. The contract manufacturing organization we currently use manufactures our product candidates under cGMP conditions. cGMP is a regulatory standard for the production of pharmaceuticals that will be used in humans.

Competition

The pharmaceutical industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. Key competitive factors affecting the commercial success of our product candidates are likely to be efficacy, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement. Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA, EMA and other regulatory approvals of products and the commercialization of those products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than we may be in obtaining FDA or EMA approval for therapies and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our therapies obsolete or non-competitive before we can recover development and commercialization expenses.

A number of companies are seeking to identify and develop drug candidates for the treatment of CF, including Vertex, Novartis, Pfizer, Genzyme, which is a division of Sanofi, Insmed, and several private companies. Of these, Vertex's Kalydeco is the only drug approved to treat an underlying cause of CF, rather than the symptoms. Kalydeco was initially approved to treat CF patients with the G551D mutation, which represents approximately 4% of the total CF population, or approximately 2,000 patients worldwide. In 2014, Kalydeco's label was expanded to include eight additional gating mutations. Vertex is currently seeking marketing approval for additional mutations, which would increase Kalydeco's target population to up to 10% of the total CF patient population. Other drugs that have been approved for CF patients are palliative treatments that manage the symptoms of the disease, such as Novartis' TOBI and Gilead's Cayston, which are used to suppress chronic lung infections, and Roche's Pulmozyme, which is an inhaled therapy used to thin mucus.

Among the product candidates that are currently in development for CF patients, Vertex's VX-809 is the most advanced. VX-809 is a small molecule "corrector" that aims to transport non-functional CFTR protein to the cell membrane to achieve some level of activity in the damaged protein. VX-809 is intended for a much broader CF patient population than Kalydeco and includes patients who are homozygous for the DF508 mutation. In June 2014, Vertex announced that its two Phase 3 clinical trials of lumacaftor, when used in combination with Kalydeco in CF patients homozygous for the DF508 mutation, showed statistically significant improvement in the study's primary endpoint of improved lung function, compared to placebo. See "Business—Cystic Fibrosis—Approaches to the Treatment of Cystic Fibrosis" for more information.

Our other competitors have research and development programs directed at identifying and developing CFTR potentiators, CFTR correctors and drug candidates with other mechanisms of action that seek to address the underlying cause of CF. Vertex's success in developing and commercializing Kalydeco and VX-809, if approved, could increase the resources that our competitors allocate to the development of these potential treatments for CF. Other than VX-809, none of the other companies have listed a DF508 specific compound clinical trial on clintrials.gov. Our competitors may also obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. See "Risk Factors—Risks Related to our Business and Strategy—We face competition from entities that have developed or may develop product candidates for our target disease indications, including companies developing novel treatments for CF patients. If these companies develop technologies or product candidates more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected" and elsewhere in this prospectus for more information regarding competitors and competitive products.

Regulatory Matters

Government Regulation and Product Approval

Government authorities in the United States at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of products such as those we are developing. Our product candidates, including QR-010, must be approved by the FDA through the new drug application, or NDA, process before they may legally be marketed in the United States.

Regulation of Combination Products in the United States

Certain products may be comprised of components that would normally be regulated under different types of regulatory authorities, and frequently by different centers at the FDA. These products are known as combination products. Specifically, under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products;
- a drug or device packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug or device where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or
- any investigational drug or device packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

Under the Federal Food, Drug, and Cosmetic Act, or FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. That determination is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a device-drug combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established an Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

U.S. Drug Development Process

The process of obtaining regulatory approvals and compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to GCP to establish the safety and efficacy of the proposed drug for its intended use;
- preparation and submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP; and
- FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort and financial resources and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Once a pharmaceutical product candidate is identified for development, it enters the pre-clinical testing stage. Pre-clinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. An IND sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor must also include a protocol detailing, among other things, the objectives of the initial clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical trial lends itself to an efficacy evaluation. Some pre-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to a proposed clinical trial and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns or non-compliance, and may be imposed on all drug products within a certain class of drugs. The FDA also can impose partial clinical holds, for example, prohibiting the initiation of clinical trials of a certain duration or for a certain dose.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent in writing before their participation in any clinical trial. Further, an IRB must review and approve the plan for any clinical trial before it commences at any institution, and the IRB must conduct continuing review and reapprove the study at least annually. An IRB considers, among other things, whether the risks to individuals participating in the clinical trial are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical trial and the consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

Each new clinical protocol and any amendments to the protocol must be submitted to the IND for FDA review, and to the IRBs for approval. Protocols detail, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety.

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

- *Phase 1.* The product is initially introduced into a small number of healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product is suspected or known to be unavoidably toxic, the initial human testing may be conducted in patients.
- *Phase 2.* Involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage and schedule.
- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit relationship of the product and provide an adequate basis for product labeling.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events. Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

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

U.S. Review and Approval Processes

The results of product development, pre-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the drug proposed labeling and other relevant information, are submitted to the FDA as part of an NDA for a new drug, requesting approval to market the product. The

submission of an NDA is subject to the payment of a substantial user fee, and the sponsor of an approved NDA is also subject to annual product and establishment user fees; a waiver of such fee may be obtained under certain limited circumstances. For example, the agency will waive the application fee for the first human drug application that a small business or its affiliate submits for review.

The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure the product's identity, strength, quality and purity. Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. An advisory committee is a panel of experts, including clinicians and other scientific experts, who provide advice and recommendations when requested by the FDA. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations when making decisions.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies that the FDA identified in the NDA that must be satisfactorily addressed before it can be approved. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post-approval studies, including Phase 4 clinical trials, to further assess a drug's safety and effectiveness after NDA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Fast Track Designation and Accelerated Approval

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug may request the FDA to designate the drug as a Fast Track product concurrently with, or at any time after, submission of an IND, and the FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request.

Under FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. In clinical trials, a surrogate endpoint is a marker, such as a measurement of laboratory or clinical signs of a disease or condition that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of post-approval clinical trials sometimes referred to as Phase 4 trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

In addition to other benefits, such as the ability to use surrogate endpoints and engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of each portion of the NDA and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Designation

The Food and Drug Administration Safety and Innovation Act, or FDASIA, amended the FDCA to require the FDA to expedite the development and review of a breakthrough therapy. A drug product can be designated as a breakthrough therapy if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A sponsor may request that a drug product be designated as a breakthrough therapy concurrently with, or at any time after, the submission of an IND, and the FDA must determine if the drug candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather pre-clinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor, and taking steps to ensure that the design of the clinical trials is as efficient as practicable.

Post-Approval Requirements

Any products for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. Moreover, each component of a combination product retains their regulatory status (as a drug or device, for example) and is subject to the requirements established by the FDA for that type of component. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing

investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Manufacturers and other entities involved in the manufacturing and distribution of approved products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the product. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release. We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution or may require substantial resources to correct.

The FDA may withdraw a product approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidances, and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our product candidates. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration dates, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA; however, there can be no assurance that any such extension will be granted to us.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule

or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the pre-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of exclusivity in the United States. Pediatric exclusivity, if granted, provides an additional six months to an existing exclusivity or statutory delay in approval resulting from a patent certification. This six-month exclusivity, which runs from the end of other exclusivity protection or patent delay, may be granted based on the voluntary completion of a pediatric clinical trial in accordance with an FDA-issued "Written Request" for such a clinical trial.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease or condition with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease or condition, except in limited circumstances, such as if the second applicant demonstrates the clinical superiority of its product to the product with orphan drug exclusivity through a demonstration of superior safety, superior efficacy, or a major contribution to patient care. "Same drug" means, with respect to a drug composed of large molecules (macromolecules), a drug that contains the same principal molecular structural features (but not necessarily all of the same structural features) and is intended for the same use as a previously approved drug, except that if the subsequent drug can be shown to be clinically superior to the first drug, it will not be considered to be the same drug. Orphan drug exclusivity does not prevent FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Pediatric Information

Under the Pediatric Research Equity Act of 2003, NDAs or supplements to NDAs must contain data adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. Recently, the FDASIA amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including

such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of data or full or partial waivers. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from pre-clinical studies, early phase clinical trials, and/or other clinical development programs.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Law, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an

increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval of our products, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order, or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires applicable manufacturers of covered drugs to disclose payments and other transfers of value provided to physicians and teaching hospitals and physician ownership and investment interests;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Healthcare Reform Law broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services

that are false or fraudulent. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to ‘‘cause’’ the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. In addition, private individuals have the ability to bring actions under the federal False Claims Act and certain states have enacted laws modeled after the federal False Claims Act.

Patient Protection and Affordable Health Care Act

In March 2010, the Healthcare Reform Law was enacted, which includes measures that have or will significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the Healthcare Reform Law of greatest importance to the pharmaceutical industry are the following:

- The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services a condition for states to receive federal matching funds for the manufacturer’s outpatient drugs furnished to Medicaid patients. Effective in 2010, the Healthcare Reform Law made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers’ rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of average manufacturer price, or AMP, and adding a new rebate calculation for ‘‘line extensions’’ (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The Healthcare Reform Law also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits, to be phased-in by 2014. The Centers for Medicare & Medicaid Services, or CMS, have proposed to expand Medicaid rebate liability to the territories of the United States as well. In addition, the Healthcare Reform Law provides for the public availability of retail survey prices and certain weighted average AMPs under the Medicaid program. The implementation of this requirement by the CMS may also provide for the public availability of pharmacy acquisition of cost data, which could negatively impact our sales.
- In order for a pharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. Effective in 2010, the Healthcare Reform Law expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children’s hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs when used for the orphan indication. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

- Effective in 2011, the Healthcare Reform Law imposed a requirement on manufacturers of branded drugs to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (i.e., the“donut hole’’).
- Effective in 2011, the Healthcare Reform Law imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.
- The Healthcare Reform Law required pharmaceutical manufacturers to track certain financial arrangements with physicians and teaching hospitals, including any ‘‘transfer of value’’ made or distributed to such entities, as well as any investment interests held by physicians and their immediate family members. Manufacturers were required to begin tracking this information in 2013 and to report this information to CMS beginning in 2014. The reported information will be made publicly available in a searchable format on a CMS website beginning in September 2014.
- As of 2010, a new Patient-Centered Outcomes Research Institute was established pursuant to the Healthcare Reform Law to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.
- The Healthcare Reform Law created the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings.
- The Healthcare Reform Law established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

European Union Drug Review Approval

In the European Economic Area, or EEA (which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations: the Community MA, which is issued by the European Commission through the Centralized Procedure based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, a body of the EMA, and which is valid throughout the entire territory of the EEA; and the National MA, which is issued by the competent authorities of the Member States of the EEA and only authorized marketing in that Member State’s national territory and not the EEA as a whole.

The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or for products which are in the interest of public health in the European Union. The National MA is for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. If the RMS proposes to authorize the product, and the other Member States do not raise

objections, the product is granted a national MA in all the Member States where the authorization was sought. Before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Regulation in the European Union

Product development, the regulatory approval process, and safety monitoring of medicinal products and their manufacturers in the European Union proceed in much the same manner as they do in the United States. Therefore, many of the issues discussed above apply similarly in the context of the European Union. In addition, drugs are subject to the extensive price and reimbursement regulations of the various European Union Member States.

Clinical trials

As is the case in the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. The Clinical Trials Directive 2001/20/EC, as amended, (and which will be replaced as from 28 May 2016 or later by Regulation (EU) No 536/2014) provides a system for the approval of clinical trials in the European Union via implementation through national legislation of the Member States. Under this system, approval must be obtained from the competent national authorities of the European Union Member States in which the clinical trial is to be conducted. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application, which must be supported by an investigational medicinal product dossier with supporting information prescribed by the Clinical Trials Directive and corresponding national laws of the Member States and further detailed in applicable guidance documents. The sponsor of a clinical trial, or its legal representative, must be based in the European Economic Area. European regulators and ethics committees also require the submission of adverse event reports during a study and a copy of the final study report.

Marketing approval

Marketing approvals under the European Union regulatory system may be obtained through a centralized or decentralized procedure. The centralized procedure results in the grant of a single marketing authorization that is valid for all—currently 28—European Union Member States.

Pursuant to Regulation (EC) No. 726/2004, as amended, the centralized procedure is mandatory for drugs developed by means of specified biotechnological processes, advanced therapy medicinal products as defined in Regulation (EC) No. 1394/2007, drugs for human use containing a new active substance for which the therapeutic indication is the treatment of specified diseases, including but not limited to acquired immune deficiency syndrome, neurodegenerative disorders, auto-immune diseases and other immune dysfunctions, as well as drugs designated as orphan drugs pursuant to Regulation (EC) No. 141/2000. The CHMP also has the discretion to permit other products to use the centralized procedure if it considers them sufficiently innovative or they contain a new active substance. Given the fact that QR-010 has been granted orphan designation in the EU, it qualifies for the centralized procedure.

In the marketing authorization application, or MAA, the applicant has to properly and sufficiently demonstrate the quality, safety and efficacy of the drug. Under the centralized approval procedure, the CHMP, possibly in conjunction with other committees, is responsible for drawing up the opinion of the EMA on any matter concerning the admissibility of the files submitted in accordance with the centralized procedure, such as an opinion on the granting, variation, suspension or revocation of a marketing authorization, and pharmacovigilance.

The CHMP and other committees are also responsible for providing guidelines and have published numerous guidelines that may apply to our products. These guidelines provide additional guidance on the factors

that the EMA will consider in relation to the development and evaluation of drug products and may include, among other things, the preclinical studies required in specific cases; and the manufacturing and control information that should be submitted in a MAA; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions. Although these guidelines are not legally binding, we believe that our compliance with them is likely necessary to gain approval for any of our product candidates.

The maximum timeframe for the evaluation of an MAA by the CHMP under the centralized procedure is 210 days after receipt of a valid application. This period will be suspended until such time as the supplementary information requested by the CHMP, has been provided by the applicant. Likewise, this time-limit will be suspended for the time allowed for the applicant to prepare oral or written explanations. When an application is submitted for a marketing authorization in respect of a drug which is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure. If the CHMP accepts such request, the time-limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time-limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

If the CHMP concludes that the quality, safety and efficacy of the product is sufficiently proven, it adopts a positive opinion. This is sent to the European Commission which drafts a decision. After consulting with the Member States, the European Commission adopts a decision and grants a marketing authorization, which is valid for the whole of the European Union. The marketing authorization may be subject to certain conditions, which may include, without limitation, the performance of post-authorization safety and/or efficacy studies.

European Union legislation also provides for a system of regulatory data and market exclusivity. According to Article 14(11) of Regulation (EC) No. 726/2004, as amended, and Article 10(1) of Directive 2001/83/EC, as amended, upon receiving marketing authorization, new chemical entities approved on the basis of complete independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder, or MAH, obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator is able to gain the period of data exclusivity, another company nevertheless could also market another version of the drug if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical test, pre-clinical tests and clinical trials. However, products designated as orphan medicinal products enjoy, upon receiving marketing authorization, a period of 10 years of orphan market exclusivity—see also *Orphan Drug Regulation*. Depending upon the timing and duration of the EU marketing authorization process, products may be eligible for up to five years' supplementary protection certification, or SPC, pursuant to Regulation (EC) No. 469/2009. Such SPCs extend the rights under the basic patent for the drug.

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

Orphan drug regulation

In the European Union, Regulation (EC) No. 141/2000, as amended, states that a drug will be designated as an orphan drug if its sponsor can establish:

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

Regulation (EC) No. 847/2000 sets out further provisions for implementation of the criteria for designation of a drug as an orphan drug. An application for the designation of a drug as an orphan drug must be submitted at any stage of development of the drug before filing of a marketing authorization application. A designation of QR-010 as an orphan drug has been granted by the European Commission (EU orphan designation number: EU/3/13/1195).

If a European Union-wide community marketing authorization in respect of an orphan drug is granted pursuant to Regulation (EC) No. 726/2004 or if all the European Union Member States have granted marketing authorizations in accordance with the procedures for mutual recognition, the European Union and the Member States will not, for a period of 10 years, accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect of a similar drug. This period may however be reduced to six years if, at the end of the fifth year, it is established, with respect to the drug concerned, that the criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity. Notwithstanding the foregoing, a marketing authorization may be granted, for the same therapeutic indication, to a similar drug if:

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

Regulation (EC) No. 847/2000 lays down definitions of the concepts ‘similar drug’ and ‘clinical superiority’. Other incentives available to orphan drugs in the European Union include financial incentives such as a reduction of fees or fee waivers and protocol assistance. Orphan drug designation does not shorten the duration of the regulatory review and approval process.

Manufacturing and Manufacturers’ License

Pursuant to Directive 2003/94/EC, as transposed into the national laws of the Member States, the manufacturing of investigational medicinal products and approved drugs is subject to a separate manufacturer’s license and must be conducted in strict compliance with cGMP requirements, which mandate the methods, facilities, and controls used in manufacturing, processing, and packing of drugs to assure their safety and identity. Manufacturers must have at least one qualified person permanently and continuously at their disposal. The qualified person is ultimately responsible for certifying that each batch of finished product released onto the

market has been manufactured in accordance with cGMP and the specifications set out in the marketing authorization or investigational medicinal product dossier. cGMP requirements are enforced through mandatory registration of facilities and inspections of those facilities. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties.

Advertising

In the European Union, the promotion of prescription medicines is subject to intense regulation and control, including EU and national legislation as well as self-regulatory codes (industry codes). Advertising legislation inter alia includes a prohibition on direct-to-consumer advertising. All prescription medicines advertising must be consistent with the product's approved summary of products characteristics, and must be factual, accurate, balanced and not misleading. Advertising of prescription medicines pre-approval or off-label is not allowed. Some jurisdictions require that all promotional materials for prescription medicines be subjected to either prior internal or regulatory review and approval.

Other Regulatory Requirements

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

The obligations of an MAH include:

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

Pharmacovigilance. MAHs are obliged to establish and maintain a pharmacovigilance system, including a qualified person responsible for oversight, submit safety reports to the regulators and comply with the good pharmacovigilance practice guidelines adopted by the EMA.

Advertising and promotion. MAHs remain responsible for all advertising and promotion of its products, including promotional activities by other companies or individuals on their behalf and in some cases must conduct internal or regulatory pre-approval of promotional materials. Regulation in this area also covers interactions with healthcare practitioners and/or patient groups, and in some jurisdictions obligations to disclose such interactions exist.

Medical affairs/scientific service. MAHs are required to disseminate scientific and medical information on its medicinal products to healthcare professionals, regulators and patients.

Legal representation and distributor issues. MAHs are responsible for regulatory actions or inactions of their distributors and agents.

Preparation, filing and maintenance of the application and subsequent marketing authorization. MAHs must maintain appropriate records, comply with the marketing authorization's terms and conditions, fulfill reporting obligations to regulators, submit renewal applications and pay all appropriate fees to the authorities.

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

Reimbursement

In the European Union, the pricing and reimbursement mechanisms by private and public health insurers vary largely by country and even within countries. The public systems reimbursement for standard drugs is determined by guidelines established by the legislator or responsible national authority. The approach taken varies by Member State. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. Other Member States allow companies to fix their own prices for medicines, but monitor and control company profits and may limit or restrict reimbursement. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products and some of EU countries require the completion of studies that compare the cost-effectiveness of a particular product candidate to currently available therapies in order to obtain reimbursement or pricing approval. Special pricing and reimbursement rules may apply to orphan drugs. Inclusion of orphan drugs in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any drug. Acceptance of any medicinal product for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. In addition, results based rules of reimbursement may apply.

Employees

As of June 30, 2014, we had 34 full-time employees and 4 part-time employees. 13 of our employees have Ph.D. or M.D. degrees or foreign equivalents. 27 of our employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreements. Geographically, all employees are located in the Netherlands. We consider our relationship with our employees to be good.

Facilities

Our corporate headquarters are located in Leiden, Netherlands, where we lease 362 square meters of office and laboratory space. The lease agreement for our laboratory space is currently scheduled to expire on December 31, 2014. The lease for our office space automatically renews for one-year periods pursuant to its terms.

We believe that our existing facilities are adequate for our near-term needs. When our leases expire, we may exercise renewal options or look for additional or alternate space for our operations. We believe that suitable additional or alternative space would be available if required in the future on commercially reasonable terms.

Legal Proceedings

We are not currently a party to any material legal proceedings.

MANAGEMENT

General

Below is a summary of relevant information concerning our supervisory board, management board and our officers, as well as a brief summary of certain significant provisions of Dutch corporate law, the articles of association that will be in effect upon the closing of this offering and the Dutch Corporate Governance Code, or DCGC, in respect of our management board and supervisory board.

Members of Our Supervisory Board, Management Board and Our Officers

Supervisory Board

The following table sets forth information with respect to each of our supervisory board members and their respective ages as of the date of this prospectus. The terms of office of all our supervisory board members expire according to a rotation schedule drawn up by our supervisory board. The business address of our supervisory board members is our registered office address at Darwinweg 24, 2333 CR Leiden, the Netherlands.

Our supervisory board is currently composed of the following members, all of whom will be independent under applicable NASDAQ standards immediately following the closing of this offering:

Name	Age	Position	Member Since	Term expires
Dinko Valerio	58	Member of the Supervisory Board (Chairman)	January 1, 2014	
Henri Termeer	68	Member of the Supervisory Board	January 1, 2014	
Antoine Papiernik	48	Member of the Supervisory Board	January 1, 2014	

The following sets forth biographical information regarding our supervisory board members.

Dinko Valerio is one of our founders and currently serves as the chairman of our supervisory board. Mr. Valerio has served on our board since January 2014. Mr. Valerio is a scientist and an experienced biotech entrepreneur with experience in both public and private companies as CEO and board member. Mr. Valerio is founder and former CEO of Crucell N.V., a Dutch biotech company, and founder and general partner of Aescap Venture, a life sciences venture capital firm. In 1999, Mr. Valerio was one of the founders of Galapagos Genomics N.V., a spinout from Crucell N.V. which develops novel mode of action medicines. Adding to his corporate experience, Mr. Valerio is a professor in the field of gene therapy of the hematopoietic system at the University of Leiden. He received his Master of Science degree in Biology from the University of Amsterdam in 1982 and completed his Ph.D. in Molecular Genetics with Honors at the University of Leiden in 1986. Mr. Valerio also was a visiting scientific specialist at Genentech Inc., San Francisco in 1985 and a postdoctoral fellow at the Salk Institute, San Diego from 1986 to 1987. He is an author on more than 100 articles in peer-reviewed Journals and an inventor on 11 patent-families. We believe that Mr. Valerio's experience in the venture capital industry, particularly with biopharmaceutical companies, and his experience serving on the boards of directors of a number of biopharmaceutical companies provide him with the qualifications and skills to serve as chairman of our supervisory board.

Henri Termeer has served on our supervisory board since January 2014. From October 1983 to June 2011, Mr. Termeer served as chairman, president and chief executive officer of Genzyme Corporation. For ten years prior to joining Genzyme, Mr. Termeer worked for Baxter International Laboratories, Inc., a manufacturer of human health care products. Mr. Termeer resigned from Genzyme in June 2011 following the acquisition of Genzyme by Sanofi. Widely acknowledged for his contributions to the biotechnology industry and health care field, Mr. Termeer is active in the areas of humanitarian assistance, policy issues, and innovation in providing access to health care. He is a member of the board of each of Massachusetts General Hospital and Partners HealthCare and a member of the board of fellows of Harvard Medical School. Mr. Termeer is also a member of

the board of the Massachusetts Institute of Technology and serves on its Executive Committee and a board member of the Biotechnology Industry Organization (BIO). He is chairman emeritus of the New England Healthcare Institute, a nonprofit, applied research health policy organization he was instrumental in founding. Mr. Termeer is currently a board member of Abiomed Inc., Aveo Pharmaceuticals, Verastem, Inc. and Medical Simulation. In 2008, he was appointed to Massachusetts Governor Deval Patrick's Council of Economic Advisors, and he is a co-chair of the Leadership Council of the Massachusetts Life Sciences Collaborative. Mr. Termeer was chairman of the Federal Reserve Bank of Boston's board of directors from 2010-2011. Mr. Termeer studied economics at the Economische Hogeschool (Erasmus University, The Netherlands) and earned an MBA from the Darden School at the University of Virginia. We believe that Mr. Termeer's experience in the pharmaceutical and biotechnology industries and his experience serving on the boards of directors of a number of biopharmaceutical companies provide him with the qualifications and skills to serve as member of our supervisory board.

Antoine Papiernik has served on our supervisory board since January 2014. Mr. Papiernik is managing partner at Sofinnova Partners, which he joined in 1997. Mr. Papiernik has been an initial investor and active board member in public companies like Actelion, Addex, Orexo, NovusPharma (then sold to CTI), Movetis (then sold to Shire), Mainstay, Pixium and Stentys, which went public respectively on the Zürich stock exchange, the Stockholm stock exchange, the Milan Nuovo Mercato, the Belgium Stock Exchange, the Dublin Stock Exchange and EuroNext Paris, in Cotherix (initially NASDAQ listed, then sold to Actelion), CoreValve (sold to Medtronic), Fovea (sold to Sanofi Aventis) and Ethical Oncology Science (EOS, sold to Clovis Oncology). Mr. Papiernik has also invested in and is a board member of private companies Auris Medical, MD Start, ReCor, Shockwave Medical, Reflexion Medical. Mr. Papiernik has an MBA degree from the Wharton School of Business, University of Pennsylvania. We believe that Mr. Papiernik's experience in the venture capital industry, particularly with biopharmaceutical companies, and his experience serving on the boards of directors of a number of biopharmaceutical companies provide him with the qualifications and skills to serve as member of our supervisory board.

Management Board

The following table sets out information with respect to each of our management board members, their respective ages and their positions at the company as of the date of this prospectus. The business address of our management board members is our registered office address at Darwinweg 24, 2333 CR Leiden, the Netherlands.

Name	Age	Position	Date of Appointment
Daniel de Boer	31	Chief Executive Officer	February 21, 2012
René Beukema	50	Chief Corporate Development Officer and General Counsel	April 17, 2014

The following sets forth biographical information regarding our management board members.

Daniel de Boer is our founding chief executive officer and has served as such since our incorporation in February 2012. Mr. de Boer has been a serial entrepreneur in IT who has led a number of other companies through phases of growth, initiating development and launch of several IT related products in several European countries. Prior to joining us, Mr. de Boer served as a founder and Chief Executive Officer of RNA Systems from 2009 to 2011. From 2007 to 2008, he was a founder and Chief Executive Officer of PC Basic, and from 2005 to 2011, he served as a founder and Chief Executive Officer of Running IT. Mr. de Boer is responsible for the overall strategy and general business in the company.

René Beukema has served as our chief corporate development officer and general counsel since April 2014. Mr. Beukema joined us in September 2013 and is a seasoned in-house corporate lawyer in the Dutch biotechnology arena. Prior to joining us, Mr. Beukema served as general counsel and corporate secretary of Crucell N.V. for twelve years, following his experience as a senior legal counsel at GE Capital / TIP Europe and

legal counsel at TNT Express Worldwide. Mr. Beukema was also a venture partner of Aescap Venture, a life sciences venture capital firm. As of today, Mr. Beukema is the co-founder and advisor of Mytomorrows N.V., a Dutch life sciences company, and a member of the VU Medical Cancer Center children in Amsterdam. He holds a post-doctoral degree in corporate law from the University of Nijmegen in co-operation with the Dutch Association of In-house Counsel (*Nederlands Genootschap van Bedrijfsjuristen*) and a Master's degree in Dutch law from the University of Amsterdam.

Officers

Our management board is supported by our officers. The following table sets forth information with respect to each of the officers, their respective ages and their positions as of the date of this prospectus. The business address of our officers is our registered office address at Darwinweg 24, 2333 CR Leiden, the Netherlands.

Name	Age	Position
Noreen Henig	49	Chief Development Officer
Gerard Platenburg	50	Chief Innovation Officer

Noreen Henig has served as our chief development officer since March 2014. Prior to joining us, Dr. Henig was Senior Director, Global Respiratory, from 2011 to 2014 and Director, Respiratory Therapeutics, from 2008 to 2011, at Gilead Sciences, Inc. Dr. Henig is a board certified physician in Pulmonary, Critical Care and board eligible in Allergy and Immunology and has over 15 years of experience in the cystic fibrosis field and as a director of Adult Cystic Fibrosis Care Centers from 1999 to 2008. Dr. Henig has basic, translational and clinical trial expertise and clinical experience in advanced lung disease including cystic fibrosis, pulmonary arterial hypertension, idiopathic pulmonary fibrosis and lung transplantation. Dr. Henig's experience at Gilead Sciences, Inc. in drug development includes building and leading a global medical affairs organization, strategic development of clinical trials Phase 2-4, regulatory strategy, corporate development, leadership of key alliances and commercial strategy. Dr. Henig received her medical degree from Albert Einstein College of Medicine of Yeshiva University in 1991 with a distinction in immunology. She also has a bachelor's degree in History of Art from Yale University.

Gerard Platenburg has served as our chief innovation officer since February 2014. Mr. Platenburg is a co-founder of our company and also served as the sole member of our supervisory board between August 2012 and December 2013. Mr. Platenburg has an extensive background in RNA modulation and orphan drug discovery and development and is in charge of our innovation unit. Mr. Platenburg has more than twenty years of senior managerial experience, which he gained during his different operational and leadership roles in growing biotech companies. Prior to joining our company, Mr. Platenburg worked at Isa Pharmaceuticals B.V. from June 2009 to January 2014. Mr. Platenburg co-founded Prosensa Holding N.V., growing it to become a well-known RNA modulation clinical stage company**,** and held various positions between April 2002 and May 2009, including Chief Executive Officer and Chief Development Officer. Mr. Platenburg also worked at Pharming B.V. from April 1990 to March 2002. He is a passionate and driven pioneer of early stage technologies. Mr. Platenburg has a master degree in chemistry and molecular biology from Leiden University in 1987 and pursued PhD work at Leiden University.

Board Structure

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

Supervisory Board

Our supervisory board is responsible for the supervision of the activities of our management board and our company's general affairs and business. Our supervisory board may also, on its own initiative, provide the

management board with advice and may request any information from the management board that it deems appropriate. In performing its duties, the supervisory board is required to act in the interests of our company (including its stakeholders) and its associated business as a whole. The members of the supervisory board are not authorized to represent us in dealings with third parties.

Pursuant to Dutch law, members of the supervisory board must be natural persons. Under our articles of association, the number of supervisory board members is determined by our supervisory board itself, provided there will be at least three supervisory board members. Our articles of association provide that members of the supervisory board are appointed by the general meeting of shareholders upon a binding nomination by the supervisory board. Our general meeting of shareholders may at all times deprive such a nomination of its binding character by a resolution passed by at least two-thirds of the votes cast representing more than 50% of our issued share capital, following which our supervisory board shall draw up a new binding nomination.

Our supervisory board rules provide that members of our supervisory board will serve for a maximum duration of three four-year terms. Our articles of association provide that the supervisory board members must retire periodically in accordance with a rotation schedule to be adopted by the supervisory board. Subject to the rotation schedule, a retiring supervisory board member can be reappointed immediately. The members of our supervisory board that were appointed by our general meeting of shareholders held on , 2014 were appointed for different terms as a result of which only approximately one-fourth of our supervisory board members will be subject to election in any one year and which has the effect of creating a staggered board (which may in turn deter a takeover attempt). The supervisory board appoints a chairman from among its members.

Under our articles of association, the general meeting of shareholders may suspend or remove supervisory board members at any time. A resolution of our general meeting of shareholders to suspend or remove a supervisory board member may be passed by a simple majority of the votes cast, provided that the resolution is based on a proposal by our supervisory board. In the absence of a proposal by our supervisory board, a resolution of our general meeting of shareholders to suspend or remove a supervisory board member shall require a majority of at least two-thirds of the votes cast representing more than 50% of our issued share capital.

In a meeting of the supervisory board, each supervisory board member is entitled to cast one vote. A supervisory board member may grant a written proxy to another supervisory board member to represent him at a meeting of the supervisory board. All resolutions by our supervisory board are adopted by a simple majority of the votes cast unless our supervisory board rules provide otherwise. In case of a tie vote in any vote of the supervisory board, the chairman of the supervisory board shall have the casting vote. Our supervisory board may also adopt resolutions outside a meeting, provided that such resolutions are adopted in writing, all supervisory board members are familiar with the resolution to be passed and provided that no supervisory board member objects to such decision-making process.

Management Board

Our management board is responsible for the day-to-day management of our operations under the supervision of the supervisory board. The management board is required to

- keep the supervisory board informed in a timely manner in order to allow the supervisory board to carry out its responsibilities;
- consult with the supervisory board on important matters; and
- submit certain important decisions to the supervisory board for its approval, as more fully described below.

Our management board may perform all acts necessary or useful for achieving our corporate purposes, other than those acts that are prohibited by law or by our articles of association, as more fully discussed below. The management board as a whole and any management board member individually, are authorized to represent us in dealings with third parties.

Under our articles of association, the number of management board members is determined by the supervisory board, and the management board must consist of at least one member. The supervisory board appoints a CEO from among the members of the management board.

Members of the management board are appointed by the general meeting of shareholders upon a binding nomination of the supervisory board. Our general meeting of shareholders may at all times deprive such a nomination of its binding character by a resolution passed by at least two-thirds of the votes cast representing more than 50% of our issued share capital, following which our supervisory board shall draw up a new binding nomination.

Our management board rules provide that, unless the resolution appointing a management board member provides otherwise, members of our management board will serve for a maximum term of four years and may be reappointed immediately for a term of not more than four years at a time.

The general meeting of shareholders may suspend or remove members of the management board at any time. A resolution of our general meeting of shareholders to suspend or remove a management board member may be passed by a simple majority of the votes cast, provided that the resolution is based on a proposal by our supervisory board. In the absence of a proposal by our supervisory board, a resolution of our general meeting of shareholders to suspend or remove a management board member shall require a majority of at least two-thirds of the votes cast representing more than 50% of our issued share capital. The supervisory board may also suspend members of the management board at any time. A suspension of a management board member is discontinued if the general meeting of shareholders does not resolve to dismiss him within three months.

In a meeting of the management board, each management board member is entitled to cast one vote. A management board member may grant a written proxy to another management board member to represent him at a meeting of the management board. All resolutions by our management board are adopted by a simple majority of the votes cast unless our management board rules provide otherwise. Where there is a tie in any vote of the management board, the CEO shall have a casting vote in case the management board consists of at least three managing board members and in case the management board consists of two management board members, the supervisory board shall decide the matter. Our management board may also adopt resolutions outside a meeting, provided that such resolutions are adopted in writing, all management board members are familiar with the resolution to be passed and provided that no management board member objects to such decision-making process.

Our articles of association and Dutch law provide that resolutions of our management board concerning a material change in the identity or character of the company or our business are subject to the approval of the general meeting of shareholders. Such changes include in any event:

- a transfer of all or materially all of our business to a third party;
- the entry into or termination of a long-term alliance of the company or of a subsidiary either with another entity or company, or as a fully liable partner of a limited partnership or partnership, if this alliance or termination is of significant importance for the company; and
- the acquisition or disposition of an interest in the capital of a company by the company or by a subsidiary with a value of at least one third of the value of the assets, according to the balance sheet with explanatory notes or, if the company prepares a consolidated balance sheet, according to the consolidated balance sheet with explanatory notes in the company’s most recently adopted annual accounts.

The absence of approval of the general meeting of shareholders does not affect the power of our management board or its members to represent us in dealings with third parties.

Under our articles of association, the following decisions of our management board must be approved by our supervisory board:

- the making of a proposal to the general meeting of shareholders concerning:
  - the issuance of shares or the granting of rights to subscribe for shares;
  - the limitation or exclusion of pre-emption rights;
  - the granting of an authorization with respect to the issuance of shares;
  - the granting of an authorization with respect to the limitation or the exclusion of pre-emption rights;
  - the granting of an authorization to acquire fully paid up shares in our own capital for no consideration;
  - a decrease in our issued share capital;
  - the granting of an approval of the general meeting of shareholders for resolutions concerning a material change to the identity or character of the company or our business;
  - the making of a distribution from our reserves or profits;
  - the determination that all or part of a distribution, instead of being made in cash, shall be made in the form of shares in our capital or in the form of assets;
  - the amendment of our articles of association;
  - the entering into of a merger or demerger;
  - the instruction of our management board to apply for our bankruptcy; and
  - our dissolution;
- calling for payment on preferred shares that have not already been paid in full;
- the acquisition of shares in our own capital, including the determination of the value of a non-cash consideration for such an acquisition;
- the granting of an approval for the transfer of preferred shares;
- the election or removal of the CEO;
- the drawing up or amendment of our management board rules;
- the performance of certain legal acts as described in our articles of association;
- the charging of amounts to be paid on shares against our reserves;
- the making of an interim distribution of profits;
- the determination of our strategy, including those resolutions that may have a material impact on our strategy;
- the adoption of our business plan or budget, as well as any material amendment to or material deviation from the prevailing business plan or budget;
- the sale or disposition of all, or an essential part of, our assets;
- the issuance and acquisition of shares and of debentures chargeable against us or chargeable against a limited partnership (*commanditaire vennootschap*), or a general partnership (*vennootschap onder firma*) of which we are a fully liable partner;
- the application for quotation, or withdrawal of quotation, of our shares or debt on any stock exchange;
- our entry into or termination of any long-term, material cooperation by us or our subsidiary with another legal entity or partnership;

- our investment in the capital of another company in an amount equal to at least one-fourth of our issued capital plus our reserves, as reflected on our most recent balance sheet, as well as a material change to such investment;
- the termination of a significant number of our employees simultaneously or within a short period of time; and
- a significant change in the employment conditions of our employees.

Our supervisory board may also require that certain resolutions by the management board, beyond those listed above, require the supervisory board's approval. Such board resolutions requiring approval must be clearly specified by the supervisory board to the management board in writing. The absence of approval of the supervisory board does not affect the power of our management board or its members to represent us in dealings with third parties.

Independence of Supervisory Board Members

As a Dutch company that lists its ordinary shares on a government-recognized stock exchange, we are subject to the DCGC. The DCGC, became effective on January 1, 2009, and applies to all Dutch companies listed on a government-recognized stock exchange, whether in the Netherlands or elsewhere, including the NASDAQ. The DCGC is based on a "comply or explain" principle. We may not always comply with all the provisions of the DCGC on independence criteria for our supervisory board members where such provisions conflict with or are inconsistent with the corporate governance rules with respect to independence of the NASDAQ and U.S. securities laws that apply to us. We will therefore apply the NASDAQ criteria on independence of members of the supervisory board. At the date of this offering, we are in compliance with the provisions of the DCGC on independence of supervisory board members, because _____, _____ and _____ comply with the independence criteria of the DCGC.

Corporate Governance Practices

The Sarbanes-Oxley Act of 2002, as well as related rules subsequently implemented by the SEC, requires foreign private issuers, including our company, to comply with various corporate governance practices. As a foreign private issuer, subject to certain exceptions, the NASDAQ listing standards permit a foreign private issuer to follow its home country practice in lieu of the NASDAQ listing standards. A foreign private issuer that elects to follow a home country practice instead of the NASDAQ listing standards 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 SEC each such requirement that it does not follow and describe the home country practice followed instead of any such requirement.

The home country practices followed by our company in lieu of NASDAQ rules are described below:

- We do not intend to follow NASDAQ's quorum requirements applicable to meetings of shareholders. In accordance with Dutch law and generally accepted business practice, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders.
- We do not intend to follow NASDAQ's requirements regarding the provision of proxy statements for general meetings 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. We do intend to provide shareholders with an agenda and other relevant documents for the general meeting of shareholders and shareholders will be entitled to give proxies and voting instructions to us and/or third parties.

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act of 2002, the rules adopted by the SEC and NASDAQ's listing standards.

Certain NASDAQ corporate governance requirements are not reflected in the Dutch Corporate Governance Code or other Dutch law. Accordingly, our shareholders may not be afforded the same protection as provided under NASDAQ corporate governance rules to the extent Dutch law does not provide similar protections. Furthermore, as a foreign private issuer, we will be exempt from the rules and regulations under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders will be exempt from the reporting and short swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as domestic companies whose securities are registered under the Exchange Act.

Committees of the Supervisory Board

Upon the completion of this offering, we will have an audit committee, a compensation committee and a nominating and corporate governance committee. We have adopted a charter for each of these committees.

Audit Committee

Upon the completion of this offering, our audit committee will consist of Antoine Papiernik (chairman), Henri Termeer and . Each member satisfies the independence requirements of the NASDAQ listing standards / Rule 10A-3(b)(1) under the Exchange Act as well as the criteria for independence set forth in best practice III.2.2 of the DCGC, and qualifies as an "audit committee financial expert," as defined by the SEC in Item 16A of Form 20-F and as determined by our supervisory board. The audit committee will oversee our accounting and financial reporting processes and the audits of our financial statements. The audit committee will be responsible for, among other things:

- making recommendations to our supervisory board regarding the appointment by the general meeting of shareholders of our independent auditor(s);
- overseeing the work of our independent auditor(s), including resolving disagreements between the management board, the officers and the independent auditors relating to financial reporting;
- pre-approving all audit and non-audit services permitted to be performed by the independent auditor(s);
- reviewing the independence and quality control procedures of the independent auditor(s);
- discussing material off-balance sheet transactions, arrangements and obligations with the management board and the independent auditor(s);
- reviewing and approving all proposed related-party transactions;
- discussing the annual audited statutory financial statements with the management board;
- annually reviewing and reassessing the adequacy of our audit committee charter;
- meeting separately with the independent auditors to discuss critical accounting policies, recommendations on internal controls, the auditor's engagement letter and independence letter and other material written communications between the independent auditors and the management board and the officers; and
- attending to such other matters as are specifically delegated to our audit committee by our supervisory board from time to time.

Compensation Committee

Upon the completion of this offering, our compensation committee will consist of Henri Termeer (chairman), Dinko Valerio and . Each member satisfies the independence requirements of the NASDAQ listing standards as well as the criteria for independence set forth in best practice III.2.2 of the DCGC. The

compensation committee will assist our supervisory board in reviewing and approving or recommending our compensation structure, including all forms of compensation relating to our supervisory board members, our management board members and our officers. Members of our management board may not be present at any compensation committee meeting while their compensation is deliberated. Subject to and in accordance with the terms of the compensation policy approved by our general meeting of shareholders from time to time, as required by Dutch law, the compensation committee will be responsible for, among other things:

- reviewing and making recommendations to the supervisory board with respect to compensation of our management board and supervisory board members;
- reviewing and approving the compensation, including equity compensation, change-of-control benefits and severance arrangements, of our chief financial officer and our officers (not part of our management board or supervisory board) as it deems appropriate;
- overseeing the evaluation of our management board members and our officers;
- reviewing periodically and making recommendations to our supervisory board with respect to any incentive compensation and equity plans, programs or similar arrangements;
- exercising the rights of our supervisory board under any equity plans, except for the right to amend any such plans unless otherwise expressly authorized to do so;
- attending to such other matters as are specifically delegated to our compensation committee by our supervisory board from time to time;
- approving the compensation package for the officers; and
- periodically reviewing, in consultation with our CEO, our management board and our officers succession planning.

Nominating and Corporate Governance Committee

Upon the completion of this offering, our nominating and corporate governance committee will consist of Dinko Valerio (chairman), Antoine Papiernik and . Each member satisfies the independence requirements of the NASDAQ listing standards as well as the criteria for independence set forth in best practice III.2.2 of the DCGC. The nominating and corporate governance committee will assist our supervisory board in selecting individuals qualified to become our supervisory board members and management board members and in determining the composition of the management board, supervisory board and its committees and officers. The nominating and corporate governance committee will be responsible for, among other things:

- recommending to the supervisory board persons to be nominated for election or re-election to the supervisory board and the management board at any meeting of the shareholders;
- overseeing the supervisory board's annual review of its own performance and the performance of its committees; and
- considering, preparing and recommending to the supervisory board a set of corporate governance guidelines.

Code of Business Conduct and Ethics

We expect to adopt a Code of Business Conduct and Ethics applicable to all of our management board and supervisory board members and our employees, including our CEO, chief financial officer, controller or principal accounting officer, or other persons performing similar functions, which is a "code of ethics" as defined in Item 16B of Form 20-F promulgated by the SEC. Upon the effectiveness of the registration statement of which this prospectus forms a part, the full text of the Code of Business Conduct and Ethics will be posted on our website at .

If we make any amendment to the Code of Business Conduct and Ethics or grant any waivers, including any implicit waiver, from a provision of the Code of Business Conduct and Ethics, we will disclose the nature of such amendment or waiver on our website to the extent required by the rules and regulations of the SEC. Under Item 16B of Form 20-F, if a waiver or amendment of the Code of Business Conduct and Ethics applies to our principal executive officer, principal financial officer, principal accounting officer or controller and relates to standards promoting any of the values described in Item 16B(b) of Form 20-F, we are required to disclose such waiver or amendment on our website in accordance with the requirements of Instruction 4 to such Item 16B.

The Code of Business Conduct and Ethics will include the whistleblower policy as contemplated in the DCGC.

Rules on Insider Trading

Pursuant to the rules contained in the Dutch Financial Markets Supervision Act (*Wet op het financieel toezicht*, or FMSA) intended to prevent market abuse, prior to the completion of this offering we will adopt an internal code on inside information in respect of the holding of and carrying out of transactions by management board members, supervisory board members, any other person who has (co)managerial responsibilities in respect of us and employees in our shares or in financial instruments the value of which is based on the value of our shares.

Because we are a foreign private issuer, our management board members, supervisory board members and our officers are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the Exchange Act. They will, however, be subject to the obligations to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules.

Insurance and Indemnification of Management Board and Supervisory Board Members

Under Dutch law, management board members, supervisory board members 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 for infringement of the articles of association or of certain provisions of the Dutch Civil Code. They may also be liable towards third parties for infringement of certain provisions of the Dutch Civil Code. In certain circumstances they may also incur additional specific civil and criminal liabilities.

Our articles of association provide that we will indemnify our management board members, supervisory board members, former management board members and former supervisory board members (each an “Indemnified Person”) against (i) any financial losses or damages incurred by such Indemnified Person and (ii) any expense reasonably paid or incurred by such Indemnified Person in connection with any threatened, pending or completed suit, claim, action or legal proceedings, whether civil, criminal, administrative or investigative and whether formal or informal, in which he becomes involved, to the extent this relates to his position with the company, in each case to the fullest extent permitted by applicable law. No indemnification shall be given to an Indemnified Person (a) if a Dutch court has established, without possibility for appeal, that the acts or omissions of such Indemnified Person that led to the financial losses, damages, suit, claim, action or legal proceedings result from either an improper performance of his duties as an officer of the company or an unlawful or illegal act and (b) to the extent that his financial losses, damages and expenses are covered by an insurance and the insurer has settled these financial losses, damages and expenses (or has indicated that it would do so). Our supervisory board may stipulate additional terms, conditions and restrictions in relation to such indemnification.

Compensation of Supervisory Board Members, Management Board Members and Officers

Under Dutch law and our articles of association, the general meeting of shareholders must upon the proposal of our supervisory board adopt the compensation policy for the management board, which includes the outlines of the compensation of any members who serve on our management board. The supervisory board determines the

compensation of the management board members in accordance with the compensation policy. A proposal by the supervisory board with respect to compensation 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 or changes to such grants. The general meeting of shareholders, may determine the compensation of supervisory directors. The supervisory directors will be reimbursed for their expenses.

Supervisory Board Compensation

In 2013, the aggregate compensation paid to our supervisory directors was as follows:

	Share-Based Payments(1)	Board Fee	2013 Total
		(€ in thousands)	
Gerard Platenburg	€ 12(2)	€—	€ 12
Antoine Papiernik(3)	—	—	—
Henri Termeer(3)	—	—	—
Dinko Valerio(3)	—	—	—
Total	€ 12	€—	€ 12

(1) The share-based payment reflects the fair value of share options granted under our Option Plan during the year, as required by and determined in accordance with IFRS 2 - Share based payment.
(2) Represents a share option to purchase 1,059 ordinary shares granted on September 26, 2013 at an exercise price of €113.34 per ordinary share, which option expires on September 26, 2023.
(3) Appointed to our supervisory board on January 1, 2014.

The members of our supervisory board receive board fees of € per year. The chairman receives board fees of € per year. In addition, members receive € for attendance in person at each supervisory board meeting and € for attendance by telephone.

Management Board Compensation

The table below sets out a breakdown of the compensation in 2013 of each current member of the management board:

	Short Term Employee Benefits	Share-Based Payments(1)	Post-Employment Benefits	Total
		(€ in thousands)		
Daniel de Boer	€ 180	€ 7(2)	€ 8	€195
René Beukema(3)	32	12(4)	3	47
Total	**€ 212**	**€ 19**	**€ 11**	**€242**

(1) The share-based payment reflects the fair value of share options granted under our Option Plan during the year, as required by and determined in accordance with IFRS 2 - Share based payment.
(2) Represents the share-based payment expenses recognized for 3,529 shares acquired on November 15, 2013 by Mr. de Boer for which he received a loan from the company. As part of the agreement, Mr. de Boer has a put option to return the shares to the company under certain conditions. Therefore, the company recognized a share-based payment expense for these shares.
(3) Mr. Beukema joined our company on September 1, 2013 and was appointed to our management board on April 17, 2014.
(4) Represents a share option to purchase 1,059 ordinary shares granted on September 26, 2013 at an exercise price of €113.34 per ordinary share, which option expires on September 26, 2023.

Employment Agreements

We have entered into employment agreements with both of our management board members. The employment agreements contain a termination notice period of one month. Both employment agreements may be terminated in the event of an urgent reason (*dringende reden*) at any time, without advance notice. The employment agreements with Daniel de Boer and René Beukema provides for a lump-sum payment following a change in control subject to certain conditions. Such payment is equal to 24 months of the individual's monthly gross fixed salary in effect at the time of the change in control. This offering is not expected to constitute a change of control under the agreements. The employment agreements also contain certain restrictive covenants, including post termination non-competition and non-solicitation covenants, which survive for a period of 12 months post-termination. Our employment agreement with Mr. de Boer includes a non-competition covenant during the term of his employment with us and for a non-solicitation covenant that survives for a period of 12 months post-termination.

Option Plan

In September 2013, we adopted our Stock Option Plan, or the Option Plan. We amended and restated the Option Plan on , 2014 as our 2014 Stock Option Plan to provide for the grant of options to purchase ordinary shares instead of non-voting depository receipts and the termination of the involvement of the Foundation in the Option Plan, among other things. On , 2014 all depository receipts issued under the Option Plan were cancelled and exchanged for ordinary shares. As of , 2014, options to purchase up to an aggregate of ordinary shares have been granted under the Option Plan.

Plan administration. The plan is administered by our supervisory board.

Eligibility. The management board may grant options to eligible individuals which have been selected by the management board, not being a member of the management board. The supervisory board may grant options to eligible individuals who are members of the management board. The management board or the supervisory board, as the case may be, may grant options to purchase ordinary shares and determine the number of ordinary shares to be covered by each option, the exercise price of each option and the conditions and limitations applicable to the exercise of each option, including conditions relating to applicable securities laws, as it considers necessary or advisable.

Vesting. The Option Plan provides for the grant of options with service-based vesting conditions that can be combined with vesting conditions subject to performance conditions. Currently we only grant options with only service-based vesting conditions. Generally, the options granted vest in four annual equal tranches of 25% starting for the first time as from the first anniversary of the date of grant. Vesting of the options may be subject to other conditions or in exceptional cases, options may vest immediately, which is specified in the notice of grant. The company may in the event of a change of control of the company decide to exchange, cancel and settle in cash and/or accelerate the vesting of the outstanding options or the supervisory board may take whatever step considered appropriate with respect to the outstanding options.

Option Exercise price. The supervisory board or the management board, as the case may be, establish the exercise price of each option and specify the exercise price in the applicable notice of grant, which may be less than, equal to, or greater than the fair market value per ordinary share on the date the option is granted. For purposes of the Option Plan, the fair market value per ordinary share is determined by (or in a manner approved by) the supervisory board.

Option Exercise. Each option is exercisable at such time and subject to such terms and conditions as the supervisory board or the management board, as the case may be, as specified in the Option Plan or in the applicable option agreement.

RELATED PARTY TRANSACTIONS

Since February 21, 2012, we have engaged in the following transactions with our managing directors and supervisory directors and the holders of more than 5% of our ordinary shares, which we refer to as our related parties.

Placements of Securities

2012 Seed Loan Agreement; 2012 Subscription Agreement and Shareholders Agreement

On April 21, 2012, we entered into a seed loan agreement with certain investors and the chairman of our supervisory board, Dinko Valerio, in the principal amount of €300,000 at 4% interest per annum. The seed loan agreement provided that all principal and interest outstanding would be converted into shares upon a closing of a preferred share financing in accordance with the terms of the seed loan agreement.

On August 21, 2012, we entered into a subscription agreement and a shareholders agreement with several of the seed loan investors and certain other investors, including supervisory board members Henri Termeer and Dinko Valerio, as well as with Stichting Administratiekantoor Endavit, a foundation owned and controlled by Dinko Valerio, pursuant to which we agreed to issue and sell an aggregate of 17,293 ordinary shares in exchange for a contribution of €501,765 by means of conversion of the seed loan agreement and/or cash payment in accordance with the terms of the subscription agreement. The April 21, 2012 loan was repaid and the seed loan agreement has terminated pursuant to its terms.

February 2013 Issuance of Ordinary Shares

On February 6, 2013, we raised €1,472,601 in proceeds through the issuance of 19,371 ordinary shares to certain investors, including our chairman of the supervisory board, Dinko Valerio, Stichting Administratiekantoor Endavit, a foundation owned and controlled by by Dinko Valerio, supervisory board member Henri Termeer and René Beukema, a member of our management board.

May 2013 Issuance of Ordinary Shares

On May 3, 2013, we raised an additional €1,559,770 in proceeds through the issuance of 15,920 ordinary shares to certain investors, including Sofinnova Capital VII FCPR, of which Antoine Papiernik, a member of our supervisory board, is a managing partner.

November 2013 Loan to Appel B.V.

On November 15, 2013, we provided a loan in the principal amount of €399,977 at an annual interest of 4% to Appel B.V., an entity owned and controlled by Daniel de Boer, our chief executive officer, for the purpose of acquiring 3,529 ordinary shares from Stichting ProQR Therapeutics Participation. On June 20, 2014, Appel B.V. repaid the loan by transferring 792 ordinary shares to Stichting ProQR Therapeutics Participation at a price of €517.30 per share. On June 20, 2014, the total amount of principal and interest outstanding under the loan was €409,532.

November 2013 Issuance of Convertible Notes

On November 27, 2013, we issued convertible notes in the aggregate principal amount of €2,500,000 at an annual interest rate of 6% to certain investors and directors, including management board member René Beukema and two members of our supervisory board, Dinko Valerio and Henri Termeer as well as J.H.J. Voskamp Participaties B.V., Sofinnova Capital VII FCPR, Stichting Administratiekantoor the Invisible Hand At Work and Vogelgezang B.V. On April 17, 2014, these convertible notes were converted into preferred shares, in connection with the April 2014 preferred stock financing, as described below.

April 2014 Preferred Shares Financing

On April 17, 2014, we issued an aggregate of 81,187 preferred shares, at a price of €525.18 per share, for aggregate consideration of €41,998,000 in cash and in the conversion of the amount of principal and interest outstanding under convertible notes to certain existing and new shareholders, including René Beukema, Henri Termeer, Dinko Valerio, J.H.J. Voskamp Participaties B.V., Sofinnova Capital VII FCPR, Vogelgezang B.V., Stichting Administratiekantoor The Invisible Hand at Work, Fidelity Advisor Series VII Fidelity Advisor Biotechnology Fund, Fidelity Select Portfolios: Biotechnology Portfolio, Jennison Global Healthcare Master Fund, Ltd., Coöperatieve Gilde Healthcare III Sub-Holding 2 U.A., ATP III GP, Ltd., Sabby Healthcare Volatility Master Fund, Ltd., Sabby Volatility Warrant Master Fund, Ltd, Redmile Capital Fund, LP, Redmile Capital Offshore Fund, Ltd., Redmile Capital Offshore Fund II, Ltd., Redmile Special Opportunities Fund, Ltd., Leerink Holdings LLC, Leerink Swann Co-Investment Fund, LLC, Thomas Malley, El Chichon Partners, LLC, Foresite Capital Fund II, L.P. and Stichting Administratiekantoor Friends of ProQR. In connection with the April 2014 preferred shares financing, the 2013 convertible notes were converted in preferred shares and terminated.

Advisory Fees

Mr. Platenburg, who is currently our chief innovation officer, served as chairman of our supervisory board from August 21, 2012 to December 1, 2013. In that capacity, Progress Therapeutics B.V., Mr. Platenburg's holding company, received advisory fees of €8,000 in 2012 and €22,000 in 2013.

Registration Rights Agreement

Effective upon consummation of this offering, we intend to enter into a registration rights agreement with certain of our existing shareholders pursuant to which we will grant them customary registration rights for the resale of their ordinary shares.

Shareholders' Agreement

We and all of our then-existing shareholders entered into a shareholders agreement on August 21, 2012, which was subsequently amended on each of February 3, 2013, May 3, 2013 and April 17, 2014, which, as amended and restated, we refer to as the shareholders' agreement. Upon consummation of this offering, the shareholders' agreement will terminate automatically.

Stichting ProQR Therapeutics Participation

Our Option Plan utilized a Dutch foundation called Stichting ProQR Therapeutics Participation, or the Foundation. The purpose of the Foundation was to facilitate administration of share-based compensation awards and pool the voting interests of the underlying shares. We issued an aggregate of 12,218 ordinary shares to the Foundation for stock option grants. Upon the exercise to the grantee of an option under the Option Plan, the Foundation issues a depository receipt for each issued ordinary shares acquired upon exercise. The depository receipt holder is entitled to any dividends or other distributions paid on the shares for which the depository receipts are granted. The voting rights attached to the shares are exercised by the Foundation. The depository receipt holders do not have meeting rights and they are not entitled to attend a general meeting of shareholders or to cast a vote. The voting rights attached to the shares are exercised by the board of the Foundation at its own discretion. The Option Plan is administered by the members of our supervisory board. Our chief executive officer is the only member of the board and accordingly has sole voting power over all ordinary shares held by the Foundation.

On August 21, 2012, February 6, 2013, May 3, 2013 and April 17, 2014, we issued 1,765, 6,435, 2,385 and 4,370 ordinary shares, respectively, to the Foundation for the benefit of our Option Plan.

On August 21, 2012, February 6, 2013, May 3, 2013, April 17, 2014 and June 20, 2014, we provided loans to the Foundation in the aggregate principal amount of €2,371,055 at a rate of 4% per individual loan for the purpose of acquiring an aggregate of 15,747 of our ordinary shares.

On June 30, 2014, these individual loans were consolidated into one amended and restated loan agreement between us and the Foundation. We intend to buy back the ordinary shares issued to the Foundation prior to the completion of this offering and terminate the Foundation's involvement in administering share-based compensation awards. In connection with the share buy-back, the Foundation intends to repay the total amount outstanding under the loan agreement, including accrued interest, through a set-off of the purchase price.

PRINCIPAL SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of June 30, 2014, giving effect to the conversion of our preferred shares into ordinary shares prior to the completion of this offering, by:

- each of the members of our supervisory board and management board; and
- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares.

The column entitled "Percentage of Shares Beneficially Owned—Prior to this Offering" is based on a total of 144,524 ordinary shares outstanding as of June 30, 2014 and excludes 11,617 ordinary shares held by our Foundation in respect of unexercised options or available for future grant under our Option Plan. With respect to the 11,617 ordinary shares held by the Foundation for which no depository receipts have been issued, 8,805 options have been granted and the remainder of the shares are available for future grants.

The column entitled "Percentage of Shares Beneficially Owned—Upon Completion of this Offering" is based on ordinary shares outstanding immediately after completion of this offering, not including any additional shares issuable upon exercise of outstanding options.

The amounts and percentages of ordinary shares beneficially owned are reported on the basis of regulations of the SEC governing the determination of beneficial ownership of securities. Under the applicable SEC rules, a person is deemed to be a "beneficial owner" of a security if that person has or shares voting power, which includes the power to vote or direct the voting of such security, or investment power, which includes the power to dispose of or to direct the disposition of such security. A person is also deemed to be a beneficial owner of any securities of which that person has a right to acquire beneficial ownership within 60 days. Under these rules, more than one person may be deemed beneficial owner of the same securities and a person may be deemed to be a beneficial owner of securities as to which such person has no economic interest. Except as otherwise indicated, each of the beneficial owners has, to our knowledge, sole voting and investment power with respect to the indicated ordinary shares, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o ProQR Therapeutics B.V., Darwinweg 24, 2333CR, Leiden, the Netherlands.

Name and Address of Beneficial Owner	Number of Ordinary Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Prior to this Offering	Upon Completion of this Offering
5% or Greater Shareholders:			
Sofinnova Capital VII FCPR(1)	25,287	17.50%	%
Entities affiliated with Fidelity Select Portfolios: Biotechnology Portfolio(2)	16,573	11.47%	%
Appel B.V. (3)	12,709	8.25%	%
Vogelgezang B.V. (4)	10,122	7.00%	%
Jennison Global Healthcare Master Fund, Ltd.(5)	9,330	6.46%	%
Progress Therapeutics B.V.(6)	9,177	6.35%	%
J.H.J. Voskamp Participaties B.V.(7)	7,808	5.40%	%
Cooperatieve Gilde Healthcare III Sub-Holding 2 U.A.(8)	7,808	5.40%	%
Supervisory Board Members and Management Board Members			
Henri Termeer(9)	15,527	10.74%	%
Daniel de Boer(10)	12,709	8.25%	
Dinko Valerio(11)	9,267	6.41%	%
Antoine Papiernik	—	—	%
René Beukema	2,561	1.77%	%

(1) Consists of 25,287 ordinary shares issuable upon conversion of preferred shares. Sofinnova Partners SAS, a French corporation and the management company of Sofinnova Capital VII FCPR, may be deemed to have sole voting and investment power, and the managing partners of Sofinnova Partners SAS, Dennis Lucquin, Antoine Papiernik, Dr. Tordjman and Monique Saulnier, may be deemed to have shared voting and investment power with respect to such shares. The address of Sofinnova Capital VII FCPR is 16-18 rue du Quatre-Septembre, Paris 75002, France.

(2) Fidelity Management & Research Company, or Fidelity, 82 Devonshire Street, Boston, Massachusetts 02109, a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of ordinary shares as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940. Consists of (i) 14,236 ordinary shares issuable upon conversion of preferred shares held by Fidelity Select Portfolios: Biotechnology Portfolio; and (ii) 2,337 ordinary shares issuable upon conversion of preferred shares held by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund. Edward C. Johnson 3d and FMR LLC, through its control of Fidelity, and the funds, or Funds, each has sole power to dispose of the shares owned by the Funds. Members of the family of Edward C. Johnson 3d, Chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Funds' Boards of Trustees.

(3) Appel B.V. is owned and controlled by Daniel de Boer, our chief executive officer, and Mr. de Boer exercises sole voting and dispositive power over the shares owned by Appel B.V. The address for Appel B.V. is Archimedesweg 24, 2333 CR, Leiden, the Netherlands.

(4) The address for Vogelgezang B.V. is Eisenhowerlaan 124, 2517 KM, The Hague, the Netherlands.

(5) Jennison Associates, LLC, or Jennison, serves as investment manager with power to direct investments and/or power to vote the shares owned by Jennison Global Healthcare Master Fund, Ltd., or the Jennison Fund, and may be deemed to beneficially own the shares held by the Jennison Fund. Jennison expressly disclaims ownership of such shares, except to the extent of its pecuniary interest therein, if any. Jennison is an indirect wholly-owned subsidiary of Prudential Financial, Inc., which is a publicly traded financial services firm. The Jennison Fund is an exempted investment company incorporated under the laws of the Cayman Islands. By virtue of his position with Jennison, David Chan, Managing Director of Jennison and Portfolio Manager to the Jennison Fund, has authority to vote or dispose of the securities held by the Jennison Fund. David Chan expressly disclaims beneficial interest of such shares, except to the extent of his pecuniary interest therein, if any. The address of the registered office of the Jennison Fund is c/o Intertrust Corporate Services (Cayman) Limited, 190 Elgin Avenue, George Town KY1-9005, Grand Cayman, Cayman Islands.

(6) Progress Therapeutics B.V. is owned and controlled by Gerard Platenburg, our chief innovation officer, and Mr. Platenburg has sole voting and dispositive power over the shares owned by Progress Therapeutics B.V. The address for Progress Therapeutics B.V. is Wijngaardenlaan 56, 2252 XR Voorschoten, the Netherlands.

(7) Jeroen Hendrik-Jan Voskamp has sole voting and dispositive power over the shares as managing director of Stichting Administratiekantoor J.H.J. Voskamp, which serves as managing director of J.H.J. Voskamp Participaties B.V. The address for J.H.J. Voskamp Participaties B.V. is De Beaufortlaan 6, 3743 DS Baarn, the Netherlands.

(8) The manager of Coöperatieve Gilde Healthcare III Sub-Holding 2 U.A. is Gilde Healthcare III Management B.V., or Gilde Management, and Gilde Management is owned by Gilde Healthcare Holding B.V., or Gilde Holding. The address of Coöperatieve Healthcare III Sub-Holding 2 U.A. is Newtonlaan 91, 3584 BP, Utrecht, The Netherlands.

(9) Consists of (i) 15,244 ordinary shares and (ii) 283 depository receipts issued by the Foundation. Daniel de Boer has sole voting power over the ordinary shares underlying the depository receipts as the only member of the board of the Foundation.
(10) Consists of 12,709 ordinary shares held by Appel, B.V., which is owned and controlled by Daniel de Boer, our chief executive officer.
(11) Consists of (i) 4,480 ordinary shares and (ii) 318 depository receipts issued by the Foundation held by Dinko Valerio. Daniel de Boer has sole voting power over the ordinary shares underlying the depository receipts as the only member of the board of the Foundation. Also includes 4,469 shares held by the Valerio family foundation, Stichting Administratiekantoor Endavit, for which Mr. Valerio is the managing director. The address of Stichting Administratiekantoor Endavit is Vlielandstraat 5, 1181 HZ, Amstelveen, the Netherlands.

Holdings by U.S. Shareholders

As of June 30, 2014, approximately 38.4% of our outstanding shares were held by 16 record holders in the United States.

DESCRIPTION OF SHARE CAPITAL

This section of the prospectus includes a description of the material terms of our articles of association as they will be in effect as of the completion of this offering, and of applicable Dutch law. The following description is intended as a summary only and does not constitute legal advice regarding those matters and should not be regarded as such. The description is qualified in its entirety by reference to the complete text of our amended articles of association, which are attached as an exhibit to the registration statement of which this prospectus is a part. We urge you to read the full text of this document.

General

We were incorporated on February 21, 2012 as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) under Dutch law. Prior to completion of this offering, we intend to convert into a public company with limited liability (*naamloze vennootschap*) pursuant to a deed of amendment and conversion, which we refer to as the Deed of Amendment and Conversion, and our legal name will be ProQR Therapeutics 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 Leiden, the Netherlands under number 54600790. Our corporate seat is in Leiden, the Netherlands, and our registered office is at Darwinweg 24, 2333 CR Leiden, the Netherlands.

We refer to our articles of association as of the date of this prospectus as our "current articles." When we refer to our "articles of association" in this prospectus, we mean our articles of association as they will be in force after the execution of the Deed of Amendment and Conversion which is expected to take place prior to the completion of this offering.

Our current articles were last amended by a deed of amendment, executed on April 17, 2014. We intend to further amend our current articles and convert our company into a public company with limited liability (*naamloze venootschap*) effective prior to the completion of this offering. On , 2014 the general meeting of shareholders resolved to amend the current articles and to convert into a public company with limited liability by means of the Deed of Amendment and Conversion. The draft Deed of Amendment and Conversion has been made available to the shareholders in advance of the date of the resolution and remains available for inspection by interested parties at our offices in Leiden, the Netherlands up to and including the completion of this offering.

Set forth below is a summary of relevant information concerning material provisions of our articles of association and applicable Dutch law.

Authorized and Outstanding Share Capital

As of the date of this prospectus, our share capital is divided into ordinary shares and preferred shares, each with a nominal value of € . All of our outstanding preferred shares will be converted into ordinary shares pursuant to the Deed of Amendment and Conversion prior to completion of this offering. Our issued share capital at the date of this prospectus amounts to € .

As of the execution of the Deed of Amendment and Conversion, our authorized share capital will be , divided into ordinary shares, each with a nominal value of € , and preferred shares, each with a nominal value of € . Under Dutch law, our authorized share capital is the maximum capital that we may issue without amending our articles of association.

We intend to apply for the listing of our ordinary shares on the NASDAQ Global Market under the symbol " ".

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 investing in 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 ordinary shares will not be certificated. We have appointed as our agent to maintain our shareholders' subregister and to act as transfer agent, registrar and paying agent for the ordinary shares. Our ordinary shares will be traded on the NASDAQ in book-entry form.

Anti-Takeover Measure

We expect to adopt an anti-takeover measure on or prior to completion of the offering, by granting a perpetual and repeatedly exercisable call option to the protection foundation, Stichting Continuity ProQR Therapeutics. The call option confers on the protection foundation the right to acquire under certain conditions such number of preferred shares as we are allowed to issue under our articles of association. The protection foundation's articles of association will provide that it will act to promote and protect the best interests of us, our business and our stakeholders by opposing any influences that conflict with these interests and threaten to undermine our strategy, continuity, independence and identity. The board of the protection foundation will be independent from us, our stakeholders and our subsidiaries.

Upon exercise of the call option, the preferred shares will be issued to the protection foundation for their nominal value, of which only 25% will be due upon issuance. The voting rights of our shares are based on nominal value and as we expect our shares to trade substantially in excess of nominal value, a foundation acquiring preferred shares issued at 25% of their nominal value can obtain significant voting power for a substantially reduced price and thus be used as a defensive measure. These preferred shares will have both a liquidation and dividend preference over our ordinary shares and will accrue cash dividends at a fixed rate with deficits in a preferred dividend being carried forward. The protection foundation may exercise the call option to acquire preferred shares in order to protect us from influences that do not serve our best interests and threaten to undermine our strategy, continuity, independence and identity. These influences may include a third-party acquiring a significant percentage of our ordinary shares, the announcement of a public offer for our ordinary shares, other concentration of control over our ordinary shares or any other form of pressure on us to alter our strategic policies.

Form of Ordinary Shares

Pursuant to our articles of association, our ordinary shares are registered shares, although our management board may resolve that one or more ordinary shares are bearer shares.

Company's Shareholders' Register

All of our registered shares are registered in our shareholders' register. Subject to Dutch law and our articles of association, we must keep our shareholders' register, accurate and up-to-date. Our shareholders' register shall be kept by our management board and, when it regards the subregister, on behalf of the management board by our agent. In our shareholders' register the names and addresses and other relevant details of all holders of registered shares are recorded, 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 and other relevant details of those with a right usufruct (*vruchtgebruik*) or a right of pledge (*pandrecht*) in respect of such shares. The ordinary shares offered in this offering will be held through DTC, therefore DTC will be recorded in the shareholders register as the holder of those ordinary shares.

Shareholders, usufructuaries and pledgees whose particulars must be recorded in our shareholders' register are required to provide our management board with the necessary particulars in a timely fashion. Upon request, shareholders, usufructuaries and pledgees shall be provided with an extract of our shareholders' register in respect of their right to one or more registered shares.

Issuance of Shares and Preemptive Rights

Under Dutch law, shares are issued and rights to subscribe for shares are granted pursuant to a resolution of the general meeting of shareholders. Our articles of association provide that our general meeting may only adopt such resolution upon a proposal of our management board, which proposal must have been approved by our supervisory board. Our general meeting of shareholders may authorize our management board to issue new shares or grant rights to subscribe for shares. The authorization can be granted and extended, in each case for a period not exceeding five years. For as long as such authorization is effective, our general meeting of shareholders will not have the power to issue shares and rights to subscribe for shares. Pursuant to our articles of association, our management board may only exercise the power to issue shares with the approval of our supervisory board.

Immediately prior to the completion of this offering, our general meeting of shareholders is expected to adopt a resolution pursuant to which our management board will be irrevocably authorized to, following approval of our supervisory board, issue up to ordinary shares for a period of 18 months from the date of such resolution. Also, the call-option for preferred shares is expected to be issued to the protection foundation, as described above under "Anti-Takeover Measure".

Under Dutch law, in the event of an issuance of ordinary shares or granting of rights to subscribe for 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. A holder of ordinary shares does not have a preemptive right with respect to the issuance of—or granting of rights to subscribe for (i) ordinary shares for consideration other than cash, or (ii) ordinary shares to our employees or employees of one of our group companies, or (iii) ordinary shares to persons exercising a previously granted right to subscribe for shares, or (iv) preferred shares.

The preemptive rights in respect of newly issued ordinary shares may be restricted or excluded by a resolution of the general meeting of shareholders. Our articles of association provide that our general meeting may only adopt such resolution upon a proposal of our management board, which proposal must have been approved by our supervisory board. Our general meeting of shareholders may authorize our management board to restrict or exclude the preemptive rights in respect of newly issued ordinary shares. Such authorization for the management board can be granted and extended, in each case for a period not exceeding five years. For as long as such authorization is effective, our general meeting of shareholders will not have the power to limit or exclude preemptive rights and such authorization may not be revoked unless stipulated otherwise in the authorization. A resolution of the general meeting of shareholders to restrict or exclude the preemptive rights or to designate our management board as the authorized body to do so requires at least a two-thirds majority of the votes cast, if less than one half of our issued share capital is represented at the meeting.

Preferred shares do not carry preemptive rights in respect of newly issued ordinary shares or preferred shares, nor do holders of ordinary shares have preemptive rights in respect of newly issued preferred shares. The call option of the protection foundation to acquire newly issued preferred shares of the company, see "Description of Share Capital—Anti-Takeover Measure", shall be construed as an irrevocable and repeatedly exercisable right to subscribe for preferred shares.

Immediately prior to the completion of this offering, our general meeting of shareholders is expected to adopt a resolution pursuant to which our management board will be irrevocably authorized to—following approval of our supervisory board—limit or exclude the preemptive rights of holders of ordinary shares for a period of 18 months from the date of such resolution.

Repurchases of our Shares

Under Dutch law, we may not subscribe for newly issued shares in our own capital. We may acquire our shares, subject to applicable provisions and restrictions of Dutch law and our articles of association, to the extent that:

- such shares are fully paid-up;
- such shares are acquired for no consideration or 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 Dutch law or our articles of association; and
- after the acquisition of shares, we and our subsidiaries would not hold, or would not hold as pledgees, shares having an aggregate nominal value that exceeds 50% of our issued share capital.

Other than shares acquired for no consideration or by universal succession, we may acquire shares only if our general meeting has authorized the management board to do so. An authorization by the general meeting of shareholders for the acquisition of shares can be granted for a maximum period of 18 months. Such authorization must specify the number 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. No authorization of the general meeting of shareholders is required if ordinary shares are acquired by us on NASDAQ with the intention of transferring such ordinary shares to our employees or employees of a group company pursuant to an arrangement applicable to them. Our articles of association further provide that a resolution of our management board to acquire fully paid-up shares in our share capital requires the approval of our supervisory board.

Our general meeting of shareholders is expected to adopt a resolution pursuant to which our management board will be authorized to acquire up to 10 % of our ordinary shares on NASDAQ for an 18-month period from the date of such resolution for a price per share not exceeding 110% of the market price of the ordinary shares on NASDAQ (with the market price deemed to be the average of the closing price on each of the five consecutive days of trading preceding the three trading days prior to the date of acquisition).

Capital Reductions; Cancellation

At a general meeting, our shareholders may resolve to reduce our issued share capital by (i) cancelling shares or (ii) reducing the nominal value of the shares by virtue of an amendment to our articles of association. In either case, this reduction would be subject to applicable statutory provisions. A resolution to cancel shares may only relate (x) to shares held by the company itself or in respect of which the company holds the depository receipts, and (y) to all preferred shares. Our articles of association provide that our general meeting may only adopt such resolution upon a proposal of our management board, which proposal must have been approved by our supervisory board. In order to be adopted by the general meeting of shareholders, a resolution to reduce the capital requires of a simple majority of the votes cast at a general meeting of shareholders if at least half the issued capital is represented at the meeting or at least two-thirds of the votes cast at the general meeting of shareholders if less than half of the issued capital is represented at the general meeting of shareholders.

A reduction of the nominal value of shares without repayment and without release from the obligation to pay up the shares must be effectuated proportionally on shares of the same class (unless all shareholders concerned agree to a disproportional reduction). A resolution that would result in a reduction of capital requires approval of the meeting of each group of holders of shares of the same class whose rights are prejudiced by the reduction. In addition, a reduction of capital involves a two month waiting period during which creditors have the right to object to a reduction of capital under specified circumstances.

In the event that all preferred shares are cancelled, distributions shall be made to the protection foundation as sole holder of such preferred shares.

Corporate Objectives

Under our articles of association, our corporate objectives are:

- the development and exploitation of products and technologies in the field of biotechnology;
- the research and development of (or the commission to research and develop) patents, know-how and intellectual and industrial property;
- to participate in, to finance, to hold any other interest in and to conduct the management or supervision of other entities, companies, partnerships and businesses;
- to furnish guarantees, to provide security, to warrant performance in any other way and to assume liability, whether jointly and severally or otherwise, in respect of obligations of group companies or other parties; and
- to do anything which, in the widest sense of the words, is connected with or may be conducive to the attainment of these objects.

Amendment of Articles of Association

Our general meeting of shareholders, at the proposal of our management board, with the prior approval of our supervisory board, may resolve to amend our articles of association. A resolution taken by the general meeting of shareholders to amend our articles of association requires a simple majority of the votes cast.

General Meetings of Shareholders

General meetings of shareholders are held in Leiden, Amsterdam, Rotterdam, The Hague, or in the municipality of Haarlemmermeer (Schiphol Airport), the Netherlands. 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, either in person or by proxy.

We must hold at least one general meeting of shareholders each year, to be held within six months after the end of our financial year. A general meeting of shareholders shall also be held within three months after our management board has considered it to be likely that the company's equity has decreased to an amount equal to or lower than half of its paid up and called up capital. If the management board and supervisory board have failed to ensure that such general meetings of shareholders as referred to in the preceding sentences are held in a timely fashion, each shareholder and other person entitled to attend shareholders' meetings may be authorized by the Dutch court to convene the general meeting of shareholders.

Our management board and our supervisory board may convene additional extraordinary general meetings of shareholders whenever they so decide. Pursuant to Dutch law, one or more shareholders and/or others entitled to attend general meetings of shareholders, alone or jointly representing at least ten percent of our issued share 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 to it that the applicants have previously requested that the management board or supervisory board convenes a shareholders' meeting and neither the management board nor the supervisory board has taken the necessary steps so that the shareholders' meeting 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 or losses and proposals relating to the composition and filling of any vacancies of the management board or supervisory board. In addition, the agenda for a general meeting of shareholders includes such items as have been included therein by our management board or our supervisory board. Pursuant to Dutch law, one or more shareholders and/or others entitled to attend

general meetings of shareholders, alone or jointly representing at least 3% of the issued share capital have the right to request the inclusion of additional items on the agenda of shareholders' meetings. Such requests must be made in writing, substantiated, or by a proposal for a resolution and received by us no later than the sixtieth day before the day the relevant general meeting is held. No resolutions will be adopted on items other than those which have been included in the agenda.

We will give notice of each general meeting of shareholders by publication on our website and, to the extent required by applicable law, in a Dutch daily newspaper with national distribution, and in any other manner that we may be required to follow in order to comply with Dutch law, applicable stock exchange and SEC requirements. We will observe the statutory minimum convening notice period for a general meeting of shareholders.

Pursuant to our articles of association, our management board may determine a record date (*registratiedatum*) of 28 calendar days prior to a general meeting of shareholders to establish which shareholders and others with meeting rights are entitled to attend and, if applicable, vote in the general meeting of shareholders. The record date, if any, and the manner in which shareholders can register and exercise their rights will be set out in the convocation notice of the general meeting. Our articles of association provide that a shareholder must notify the company in writing of his identity and his intention to attend (or be represented at) the general meeting of shareholders, such notice to be received by us ultimately on the seventh day prior to the general meeting. If this requirement is not complied with or if upon direction of the company to that effect no proper identification is provided by any person wishing to enter the general meeting of shareholders, the chairman of the general meeting of shareholders may, in his sole discretion, refuse entry to the shareholder or his proxy holder.

Pursuant to our articles of association, our general meeting of shareholders is chaired by the chairman of our supervisory board. If the chairman of our supervisory board is absent and has not charged another person to chair the meeting in his place, the supervisory board members present at the meeting shall appoint one of them to be chairman. If no supervisory board members are present at the general meeting of shareholders, the general meeting of shareholders will be chaired by our CEO or, if our CEO is absent, another managing board member present at the meeting and, if none of them is present, the general meeting shall appoint its own chairman. The person who should chair the meeting may appoint another person in his stead.

The chairman of the general meeting may decide at his discretion to admit other persons to the meeting. The chairman of the general meeting shall appoint another person present at the shareholders' meeting to act as secretary and to minute the proceedings at the meeting. The chairman of the general meeting may instruct a civil law notary to draw up a notarial report of the proceedings at the company's expense, in which case no minutes need to be taken. The chairman of the general meeting is authorized to eject any person from the general meeting of shareholders if the chairman considers that person to disrupt the orderly proceedings. The general meeting of shareholders shall be conducted in the English language.

Voting Rights and Quorum Requirements

In accordance with Dutch law and our articles of association, each issued ordinary share and preferred share confers the right on the holder thereof to cast one vote at the general meeting of shareholders. The voting rights attached to any shares held by us or our direct or indirect subsidiaries are suspended as long as they are held in treasury. Dutch law does not permit cumulative voting for the election of management board members or supervisory board members.

Voting rights may be exercised by shareholders or by a duly appointed proxy holder (the written proxy being acceptable to the chairman of the general meeting of shareholders) of a shareholder, which proxy holder need not be a shareholder. Our articles of association do not limit the number of shares that may be voted by a single shareholder.

Under our articles of association, blank votes, abstentions and invalid votes shall not be counted as votes cast. Further, shares in respect of which a blank or invalid vote has been cast and shares in respect of which the person with meeting rights who is present or represented at the meeting has abstained from voting are counted when determining the part of the issued share capital that is present or represented at a general meeting of shareholders. The chairman of the general meeting shall determine the manner of voting and whether voting may take place by acclamation.

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.

Resolutions of the general meeting of shareholders are adopted by a simple majority of votes cast without quorum requirement, except where Dutch law or our articles of association provide for a special majority and/or quorum in relation to specified resolutions.

The chairman of the general meeting of shareholders shall decide on the method of voting and may determine the voting procedure. The determination made by the chairman of the general meeting of shareholders with regard to the results of a vote shall be decisive. However, where the accuracy of the chairman's determination is contested immediately after it has been made, a new vote shall take place if the majority of the general meeting of shareholders so requires or, where the original vote did not take place by response to a roll call or in writing, if any party with voting rights present at the meeting so requires.

Our management board will keep a record of the resolutions passed at each general meeting of shareholders. The record shall be available at our office for inspection by any person entitled to attend general meetings of shareholders and upon request a copy of or extract from the record will be provided to such person at no more than the cost price.

Our articles of association and Dutch law provide that resolutions of our management board concerning a material change in the identity or character of the company or our business are subject to the approval of the general meeting of shareholders. Such changes include in any event:

- a transfer of all or materially all of our business to a third party;
- the entry into or termination of a long-lasting alliance of the company or of a subsidiary either with another entity or company, or as a fully liable partner of a limited partnership or partnership, if this alliance or termination is of significant importance for the company; and
- the acquisition or disposition of an interest in the capital of a company by the company or by a subsidiary with a value of at least one third of the value of the assets, according to the balance sheet with explanatory notes or, if the company prepares a consolidated balance sheet, according to the consolidated balance sheet with explanatory notes in the company's most recently adopted annual accounts.

Adoption of Annual Accounts and Discharge of Management and Supervisory Liability

Pursuant to Dutch law, we are required to publish our annual accounts within eight days after adoption and ultimately within 13 months after the end of our financial year.

Each year within five months after the end of our financial year, save where this period is extended for a maximum of six months by the general meeting of shareholders on account of special circumstances, our management board will prepare the annual accounts. The annual accounts must be accompanied by an auditor's certificate, an annual report and certain other mandatory information and must be made available for inspection by our shareholders at our offices within the same period. Under Dutch law, the general meeting of shareholders

may appoint and remove our independent auditors, as referred to in Section 2:393 Dutch Civil Code, who audit the annual accounts. If the general meeting of shareholders fails to appoint an independent auditor, the auditor will be appointed by the supervisory board or, if the supervisory board fails to do so, the management board. The annual accounts are adopted by our shareholders at the general meeting of shareholders and will be prepared in accordance with Part 9 of Book 2 of the Dutch Civil Code.

The adoption of the annual accounts by our shareholders does not release our management board members and our supervisory board members from liability for acts reflected in those documents. Any such release from liability requires a separate shareholders' resolution.

Our financial reporting will be subject to the supervision of the Dutch regulator AFM. The AFM will review the content of the financial reports and has the authority to approach us with requests for information if, on the basis of publicly available information, it has reasonable doubts as to the integrity of our financial reporting. For a more detailed description we refer to the description below under the heading "—Dutch Financial Reporting Supervision Act."

Dividends and other Distributions

We may only make distributions to our shareholders and other persons entitled to distributable profits, to the extent that 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.

Under our articles of association, a (cumulative) dividend is first paid out of the profit, if available for distribution, on any preferred shares, of which none will be outstanding on completion of this offering. Any amount remaining out of the profit is carried to reserve as the management board determines. After reservation by the management board of any profit, the remaining profit will be at the disposal of the general meeting 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.

Distributions shall be payable in such currency as determined by our management board. We intend that distributions, if any, shall be payable on such date as determined by our management board. Our management board will set the date that will be applied in order to establish which shareholders (or usufructuaries or pledgees, as the case may be) are entitled to the distribution, such date not being earlier than the date on which the distribution was announced. Claims for payment of 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 dividends for the foreseeable future.

Liquidation and Dissolution

The general meeting of shareholders may, based on a proposal by our management board, which proposal has been approved by our supervisory board, resolve to dissolve the company by a resolution passed by a simple majority of the votes cast. In the event of the company being dissolved, the liquidation shall be effected by our management board under the supervision of the supervisory board, unless the general meeting of shareholders decides otherwise.

In the event of a dissolution and liquidation, the assets remaining after payment of all of the company's debts (including any liquidation expenses) are to be distributed (i) firstly to the holders, if any, of preferred shares the nominal value of the preferred shares (to the extent paid-up) plus unpaid accrued dividends and deficits (if any) in preferred dividends, (ii) the balance remaining to the holders of ordinary shares in proportion to the aggregate nominal value of their ordinary shares. The liquidation and all distributions referred to in this paragraph will be made in accordance with the relevant provisions of Dutch law.

Limitations on Non-Residents and Exchange Controls

There are no limits under the laws of the Netherlands or in our articles of association on non-residents of the Netherlands holding or voting our ordinary shares. Under Dutch law, there currently 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.

Netherlands Squeeze-Out Proceedings

Pursuant to Section 2:92a of the Dutch Civil Code, a shareholder who for its own account (or together with its group companies) provides at least 95% of our issued share capital may institute proceedings against our other shareholders jointly for the transfer of their shares to it. The proceedings are held before the Enterprise Chamber of the Amsterdam Court of Appeal (*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 of the shares of the minority shareholders. Once the order to transfer by the Enterprise Chamber of the Amsterdam Court of Appeal becomes final and irrevocable, the majority shareholder that instituted the squeeze-out proceedings shall give written notice of the date and place of payment and the price to the holders of the shares to be acquired whose addresses are known to the majority shareholder. Unless the addresses of all minority shareholders are known to the majority shareholder acquiring the shares, the majority shareholder is required to publish the same in a newspaper with a national circulation.

A shareholder that provides a majority of our issued share capital, but less than the 95% required to institute the squeeze-out proceedings described above, may seek to propose and implement one or more restructuring transactions with the objective to obtain at least 95% of our issued share capital and thus to be allowed to initiate squeeze-out proceedings. Those restructuring transactions could, amongst other things, include a legal merger or demerger involving our company, a contribution of cash and/or assets against issuance of shares involving our company, the issue of new shares to the majority shareholder while excluding any pre-emption rights of minority shareholders in relation to such issuance or an asset sale transaction.

The asset sale transaction has been developed in Dutch public takeover practice and, depending on the circumstances at hand, could also be implemented by any shareholder providing a certain supermajority of our issued share capital to be determined by the circumstances. The asset sale may for instance be implemented after a successful public offer through which the offeror acquired the relevant supermajority. The asset sale transaction comprises of the sale and transfer of all of the assets of our company to a special purpose entity controlled by the relevant majority shareholder against payment of a purchase price that reflects the market value of those assets, followed by the liquidation of our company and the pro-rata payment of the purchase price for the assets to the minority shareholders (and the relevant majority shareholder) as liquidation proceeds.

Under our articles of association, any proposal to sell and transfer all of our assets and to dissolve and liquidate our company is subject to approval by a majority of the votes cast in our general meeting of shareholders which must be preceded by a proposal by our management board, which must be approved by our supervisory board.

Dutch Corporate Governance Code

The DCGC is based on a “comply or explain” principle. Accordingly, companies are required to disclose in their annual report filed in the Netherlands whether or not they are complying with the various rules of the DCGC that are addressed to the management board and supervisory board and, if they do not apply those provisions, to give the reasons for such non-application. The DCGC contains both principles and best practice provisions for the management board, supervisory board, shareholders and general meetings of shareholders, financial reporting, auditors, disclosure, compliance and enforcement standards. The principles and best practice

provisions apply to our management board and supervisory board, for example in relation to its role and composition, conflicts of interest, independence requirements for supervisory board members, supervisory board committees and compensation; shareholders and the general meeting of shareholders, for example, regarding anti-takeover protection and obligations of the company to provide information to our shareholders; and financial reporting, including external auditor and internal audit requirements.

We acknowledge the importance of good corporate governance. However, at this stage, we do not comply with all the provisions of the DCGC, to a large extent because such provisions conflict with or are inconsistent with the corporate governance rules of the NASDAQ and U.S. securities laws that apply to us, or because such provisions do not reflect best practices of global companies listed on the NASDAQ.

The discussion below summarizes the most important differences between our expected governance structure following this offering and the principles and best practices of the DCGC:

- Best practice provisions I.1 and I.2 provide that each substantial change in our corporate governance structure and in our compliance with the DCGC must be submitted to the general meeting of shareholders for discussion under a separate agenda item. As our ordinary shares will be listed on the NASDAQ Global Market only, we intend to comply with the corporate governance rules that apply to companies that are listed on the NASDAQ Global Market and therefore will not comply with these provisions.
- Best practice provision III. 2.1. stipulates that all supervisory board members, with the exception of not more than one person, shall be independent within the meaning of best practice provision III.2.2. As our ordinary shares will be listed on the NASDAQ Global Market only, we intend to comply with the corporate governance rules that apply to companies that are listed on the NASDAQ Global Market, and will therefore only apply the NASDAQ criteria on independence of members of the supervisory board.
- Best practice provision III.7.1 prohibits the granting of shares or rights to shares to members of the supervisory board as compensation. It is common practice for companies listed on the NASDAQ Global Market to grant shares to the members of the supervisory board as compensation, in order to align the interests of the members of the supervisory board with our interests and those of our shareholders.
- Best practice provision IV.1.1 provides that the general meeting of shareholders may pass a resolution to cancel the binding nature of a nomination for the appointment of a member of the management board or of the supervisory board or a resolution to dismiss such member by an absolute majority of the votes cast. It may be provided that such majority should represent a given proportion of the issued capital, but this proportion may not exceed one third. In addition, best practice IV.1.1. provides that if such proportion of the share capital is not represented at the meeting, but an absolute majority of the votes cast is in favor of a resolution to cancel the binding nature of the nomination, a new general meeting of shareholders will be convened where the resolution may be adopted by absolute majority, regardless of the proportion of the share capital represented at the meeting. Our articles of association will provide that these resolutions can only be adopted with at least a 2/3 majority which must represent more than 50% of our issued capital, and that no such second meeting will be convened, because we believe that the decision to overrule a nomination by the management board or the supervisory board for the appointment or dismissal of a member of our management board or of our supervisory board must be widely supported by our shareholders.
- Best practice provision IV.3.1 stipulates that meetings with analysts, presentations to analysts, presentations to investors and institutional investors and press conferences must be announced in advance on the company’s website and by means of press releases. Provision must be made for all shareholders to follow these meetings and presentations in real time, for example by means of webcasting or telephone. After the meetings, the presentations must be posted on the company’s website. We believe that enabling shareholders to follow in real time all the meetings with analysts, presentations to analysts and presentations to investors, would create an excessive burden on our resources. We will ensure that analyst presentations are posted on our website after meetings with analysts.

Market Abuse

The Dutch Financial Markets Supervision Act (*Wet op het financieel toezicht*, or FMSA) contains rules intended to prevent market abuse, such as insider trading, tipping and market manipulation. Such rules on market manipulation may restrict our ability to buy back our shares. In certain circumstances, our investors can also be subject to such rules intended to prevent market abuse.

Pursuant to the FMSA, any member of our management board, any member of our supervisory board and any other person who has managerial or co-managerial responsibilities in respect of us or who has the authority to make decisions affecting our future developments and business prospects and who may have regular 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 all transactions conducted for his own account relating to our shares or in financial instruments the value of which is determined or co-determined by the value of our shares, conducted for its own account.

In addition, in accordance with the FMSA and the regulations promulgated thereunder, certain persons closely associated with members of our management board, supervisory board or any of the other persons as described above, must also notify the AFM of any transactions conducted for their own account relating to our shares or in financial instruments the value of which is determined or co-determined by the value of our shares. The FMSA and the regulations promulgated thereunder cover the following categories of persons: (i) the spouse or any partner considered by national law as equivalent to the spouse, (ii) dependent children of such persons, (iii) other relatives who have shared the same household for at least one year at the relevant transaction date and (iv) any legal person, trust or partnership whose, among other things, managerial responsibilities are discharged by a person referred to under (i), (ii) or (iii) above or by the relevant member of the management board or supervisory board or other person with any authority in respect of us as described above.

These notifications to the AFM must be made no later than on the fifth business day following the transaction date. Under certain circumstances, the notification may be postponed until the moment that the value of the transactions performed for that person's own account, together with the transactions carried out by the persons closely associated with that person, reaches or exceeds an amount of €5,000 in the calendar year in question.

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 accessible 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.

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

Pursuant to the rules intended to prevent market abuse, prior to the completion of this offering we will adopt an internal code on inside information in respect of the holding of and carrying out of transactions by management board members, supervisory board members and employees in our shares or in financial instruments the value of which is determined or co-determined by the value of our shares. 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.

Dutch Financial Reporting Supervision Act

Under the Dutch Financial Reporting Supervision Act (*Wet toezicht financiële verslaggeving*) (the "FRSA"), the AFM supervises the application of financial reporting standards by, among others, companies whose corporate seats are in the Netherlands and whose securities are listed on a regulated market within the EU or in a

non-EU country on a system similar to a regulated market. Since our company has its corporate seat in the Netherlands and our ordinary shares will be listed on the NASDAQ, the FRSA will be applicable to us.

Pursuant to the FRSA, the AFM has an independent right to (i) request an explanation from us regarding our application of the applicable financial reporting standards and (ii) recommend to us that we make available further explanations. If we do not comply with such a request or recommendation, the AFM may request that the Enterprise Chamber order us to (i) make available further explanations as recommended by the AFM, (ii) provide an explanation of the way we have applied the applicable financial reporting standards to our financial reports or (iii) prepare our financial reports in accordance with the Enterprise Chamber's instructions.

Differences in Corporate Law

We are incorporated under the laws of the Netherlands. The following discussion summarizes material differences between the rights of holders of our ordinary shares and the rights of holders of the common stock of a typical corporation incorporated under the laws of the state of Delaware, which result from differences in governing documents and the laws of the Netherlands and Delaware.

This discussion does not purport to be a complete statement of the rights of holders of our ordinary shares under applicable Dutch law and our articles of association or the rights of holders of the common stock of a typical corporation under applicable Delaware law and a typical certificate of incorporation and bylaws.

Delaware	***The Netherlands***
Duties of Directors	
The board of directors of a Delaware corporation bears the ultimate responsibility for managing the business and affairs of a corporation. There is generally only one board of directors.	In the Netherlands, a listed company typically has a two-tier board structure, with a management board comprising the executive directors and a supervisory board comprising the non-executive directors (although a single-tier board system may also be used).
In discharging this function, directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. 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.	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 and the business connected with it. Unlike under Delaware law, 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 and the business connected with it also applies in the event of a proposed sale or break-up of the company, whereby the specific circumstances generally dictate how such duty is to be applied. Any management board resolution concerning a material change in the identity or character of the company or its business requires shareholders' approval. The management

Delaware	*The Netherlands*
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 shareholders.	board may decide in its sole discretion, within the confines of Dutch law and the articles of association, to incur additional indebtedness subject to any contractual restrictions pursuant to our existing financing arrangements.
Director Terms	
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 the certificate of incorporation, an initial bylaw or a bylaw adopted by the shareholders. A director elected to serve a term on a "classified" board of directors may not be removed by shareholders without cause. There is no limit to the number of terms a director may serve.	In contrast to Delaware law, under Dutch law a supervisory board member of a listed company is generally appointed for a maximum term of four years. There is no statutory limit to the number of terms a supervisory board member may serve, although the DCGC recommends that supervisory board members shall serve for a maximum of three four-year terms. It is currently anticipated that our supervisory board members will serve a maximum of three terms of four years. A supervisory board member may be removed at any time, with or without cause, by the general meeting of shareholders. Pursuant to our articles of association, our general meeting of shareholders may only adopt a resolution to suspend or dismiss such supervisory board member 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.
Board Vacancies	
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) or by a sole remaining director unless (a) otherwise provided in the certificate of incorporation or by-laws of the corporation or (b) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.	Under Dutch law, management board members and supervisory board members of a company such as ours are appointed by the general meeting of shareholders, rather than appointed by the board of directors as is typical for a Delaware corporation. Under our articles of association, management board members and supervisory board members are appointed by our 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 our issued share capital, following which our supervisory board shall draw up a new binding nomination.

Delaware	*The Netherlands*
Conflict-of-Interest Transactions	
Under the Delaware General Corporation Law, transactions with directors must be approved by disinterested directors or by the shareholders, or otherwise proven to be fair to the company as of the time it is approved. Such transaction will be void or voidable, unless (1) the material facts of any interested directors' interests are disclosed or are known to the board of directors and the transaction is approved by the affirmative votes of a majority of the disinterested directors, even though the disinterested directors constitute less than a quorum; (2) the material facts of any interested directors' interests are disclosed or are known to the shareholders entitled to vote thereon, and the transaction is specifically approved in good faith by vote of the shareholders; or (3) the transaction is fair to the company as of the time it is approved.	Under Dutch law, a management board member and a supervisory board member with a direct or indirect personal interest that conflicts with the interests of the company or of the business connected with it must abstain from participating in the decision-making process (i.e., the deliberations and the decision-making) with respect to the relevant matter. A board member with such a conflict of interest must promptly notify the other directors of his or her conflict. If it becomes apparent that such member was indeed involved in the decision-making process, then such decision may be nullified. Our articles of association provide that if as a result of conflicts of interest no resolution of the management board can be adopted, the resolution will be adopted by our supervisory board. If as a result of a conflict of interest of supervisory board members no resolution of the supervisory board can be adopted, the resolution can nonetheless be adopted by our 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. Management board members with a conflict of interest remain authorized to represent the company. However, the relevant management board members may under certain circumstances be held personally liable for any damage suffered by the company as a consequence of the transaction. Agreements entered into with third parties contrary to the rules on decision-making in the case of a conflict of interest, may as a rule not be annulled. Only under special circumstances will a company be able to annul an agreement or claim damages, such as when a third party misuses a conflict of interest situation.
Proxy Voting by Directors	
A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.	An absent management board member may issue a proxy for a specific meeting of the management board but only in writing to another management board member. An absent supervisory board member may issue a proxy for a specific meeting of the supervisory board but only in writing to another supervisory board member.

Delaware	*The Netherlands*
Voting Rights	
Under the Delaware General Corporation Law, each shareholder is entitled to one vote per share of stock, unless the certificate of incorporation provides otherwise. Cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation specifically provides for it. Either the certificate of incorporation or the bylaws may specify the number of shares 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, except that, where a separate vote by a class or series or classes or series is required, a quorum will consist of no less than 1/3 of the shares of such class or series or classes or series.	Under Dutch law, shares have one vote per share, provided such shares have the same nominal value. Our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. All resolutions of the general meeting of shareholders are adopted by a simple majority of votes cast without quorum requirement, except where Dutch law or our articles of association provide for a special majority and/or quorum in relation to specified resolutions. Each holder of ordinary shares may cast as many votes as it holds shares. The voting rights attached to any shares held by us or our direct or indirect subsidiaries are suspended as long as they are held in treasury. Dutch law does not permit cumulative voting for the election of management board members and supervisory board members.
Shareholders 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 days nor less than 10 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	Pursuant to our articles of association, our management board may determine a record date (*registratiedatum*) of 28 calendar days prior to a general meeting of shareholders to establish which shareholders and others with meeting rights are entitled to attend and, if applicable, vote in the general meeting of shareholders. The record date, if any, and the manner in which shareholders can register and exercise their rights will be set out in the convocation notice of the general meeting. There is no specific provision in Dutch law for adjournments.
Shareholder Proposals	
Delaware law does not provide shareholders an express right to put any proposal before a meeting of shareholders, but it provides that a corporation's bylaws may provide that if the corporation solicits proxies with respect to the election of directors, it may be required to include in its proxy solicitation materials one or more individuals nominated by a shareholder. In keeping with common law, Delaware corporations generally afford shareholders an opportunity to make proposals and nominations provided that they comply with the notice provisions in the certificate of incorporation or bylaws. Additionally, if a Delaware corporation is subject to the SEC's proxy rules, a shareholder who owns at least $2,000 in market value or 1% of the corporation's securities entitled to vote for a continuous period of one year as of the date he submits a proposal, may propose a matter for a vote at an annual or special meeting in accordance with those rules.	Pursuant to Dutch law, one or more shareholders or others with meeting rights alone or jointly representing at least 10% of the issued share capital may on their application be authorized by the Dutch Court to convene a general meeting if the management board and the supervisory board fail to do so in a timely manner. The agenda for a general meeting of shareholders must contain such items as the management board, supervisory board or the person or persons convening the meeting decide. Pursuant to Dutch law, unlike under Delaware law, the agenda will also include such other items as one or more shareholders and/or others entitled to attend general meetings of shareholders, alone or jointly representing at least 3% of the issued share capital may request of the management board in writing and substantiated or by a proposal for a resolution, received by the company no later than on the 60th day before the date of the meeting.

Delaware	*The Netherlands*
Action by Written Consent	
Unless otherwise provided in the corporation's certificate of incorporation, any action required or permitted to be taken at any annual or special meeting of shareholders of a corporation may be taken without a meeting, without prior notice and without a vote, if one or more consents in writing, setting forth the action to be so taken, are signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted.	Under Dutch law, shareholders' resolutions may be adopted in writing without holding a meeting of shareholders, provided (a) the articles of association expressly so allow, (b) no bearer shares or depository receipts are issued, (c) there are no persons entitled to the same rights as holders of depository receipts issued with the company's cooperation, (d) the management board and supervisory board members have been given the opportunity to give their advice on the resolution, and (e) the resolution is adopted unanimously by all shareholders that are entitled to vote. The requirement of unanimity renders the adoption of shareholder resolutions without a meeting not feasible for publicly traded companies. Our articles of association only expressly allow resolutions of the holders of preferred shares to be adopted without holding a meeting.
Shareholder Suits	
Under the Delaware General Corporation Law, a shareholder 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 shareholders 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 shareholder 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 shareholder not only at the time of the transaction that is the subject of the suit, but also 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.	Unlike under Delaware law, in the event a third party is liable to a Dutch company, only the company itself can bring a civil action against that party. Individual shareholders do not have the right to bring an action on behalf of the 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 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—outside the collective action—institute a civil claim for damages.

Delaware	*The Netherlands*
Repurchase of Shares	
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.	Under Dutch law, a company such as ours may not subscribe for newly issued shares in its own capital. Such company may, however, repurchase its existing and outstanding shares or depository receipts if permitted under its articles of association. We may acquire our shares, subject to applicable provisions and restrictions of Dutch law and our articles of association, to the extent that: (i) such shares are fully paid-up; (ii) such shares are acquired for no consideration or 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 Dutch law or our articles of association; and (iii) after the acquisition of shares, we and our subsidiaries would not hold, or would not hold as pledgees, shares having an aggregate nominal value that exceeds 50% of our issued share capital. Other than shares acquired for no consideration or by universal succession, our management board may acquire shares only if our general meeting of shareholders has authorized the management board to do so. An authorization by the general meeting of shareholders for the acquisition of shares can be granted for a maximum period of 18 months. Such authorization must specify the number 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. No authorization of the general meeting of shareholders is required if listed ordinary shares are acquired by us with the intention of transferring such ordinary shares to our employees under an applicable employee stock purchase plan. Our articles of association further provide that a resolution of our management board to acquire fully paid-up shares in our share capital, requires the approval of our supervisory board. Immediately prior to completion of this offering, our general meeting of shareholders is expected to adopt a resolution pursuant to which our management board will be authorized to acquire up to 10% of the issued outstanding ordinary shares on the NASDAQ for an 18-month period from the date of such resolution for a price per share not exceeding 110% of the market price of the ordinary shares on the NASDAQ (with the market price deemed to be the average of the closing price on each of the five consecutive days of trading preceding the three trading days prior to the date of acquisition).

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Anti-Takeover Provisions

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 shareholder that beneficially owns 15% or more of a corporation's voting stock (or which is an affiliate or associate of the corporation and owned 15% or more of the corporation's outstanding voting stock within the past three years), within three years after the person becomes an interested shareholder, unless:

- the transaction that will cause the person to become an interested shareholder 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 shareholder, the interested shareholder holds at least 85% of the voting stock of the corporation not including shares owned by persons who are directors and also officers of interested shareholders and shares owned by specified employee benefit plans; or
- after the person becomes an interested shareholder, 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 shareholder.

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.

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 authorization of a class of preferred shares that may be issued to a protection foundation, for which we expect to grant a perpetual and repeatedly exercisable call option to such protection foundation on or prior to the completion of this offering;
- staggered four-year terms of our management board members and supervisory board members;
- a provision that our management board members and our supervisory board members may only be appointed upon a binding nomination by our supervisory board, which can be set aside by a two-thirds majority of our shareholders representing more than half of our issued share capital;
- a provision that our management board members and supervisory board members may only be removed by our general meeting of shareholders by at least a two-thirds majority of votes cast representing more than 50% of our issued share capital (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.

Inspection of Books and Records

Under the Delaware General Corporation Law, any shareholder may inspect for any proper purpose the corporation's stock ledger, a list of its shareholders and its other books and records during the corporation's usual hours of business.

Our shareholders' register is available for inspection by the shareholders and usufructuraries and pledgees whose particulars must be registered therein.

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	Our management board and our supervisory board provide our shareholders, at the general meeting of shareholders, with all information that the general meeting of shareholders requests reasonably unless doing so would be contrary to an overriding interest of ours. Our management board or our supervisory board will in principle give reason for electing not to provide such information on the basis of overriding interest.
Removal of Directors	
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 (a) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, shareholders may effect such removal only for cause, or (b) in the case of a corporation having cumulative voting, if less than the entire board of directors 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.	Under our articles of association, the general meeting of shareholders is at all times entitled to suspend or remove a management board member or supervisory board member. The general meeting of shareholders may only adopt a resolution to suspend or remove 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 our supervisory board in which case a simple majority of the votes cast is sufficient.
Preemptive Rights	
Under the Delaware General Corporation Law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.	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, which proposal must have been approved by our supervisory board. Our general meeting of shareholders may authorize our management board, to restrict or exclude the preemptive rights in respect of newly issued ordinary shares. Such authorization for the management board can be granted and extended, in each case 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 our management board as the authorized body to do so requires at least a two-thirds majority of the votes cast, if less than one half of our issued share capital is represented at the meeting. Immediately prior to the completion of this offering, our general meeting of shareholders is expected to adopt a resolution pursuant to which our management

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	board will be irrevocably authorized to—following approval of our supervisory board—limit or exclude the preemptive rights of holders of ordinary shares for a period of 18 months from the date of such resolution. No preemptive rights apply in respect of preferred shares.
Dividends	
Under the Delaware General Corporation Law, a Delaware corporation may, subject to any restrictions contained in its certificate of incorporation, 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 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 ordinary shares, property or cash.	Dutch law provides that dividends may only 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 sum of the paid-up and called-up share capital and the reserves that must be maintained under Dutch 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 paid-up and called-up share capital and the reserves that must be maintained under Dutch law or the articles of association as apparent from an (interim) financial statement. Interim dividends should be regarded as advances on the final dividend to be declared with respect to the financial year in which the interim dividends have been declared. Should it be determined after adoption of the annual accounts with respect to the relevant financial year that the distribution was not permissible, the company may reclaim the paid interim dividends as unduly paid. Under our articles of association, a (cumulative) dividend is first paid out of the profit, if available for distribution, on any preferred shares, of which none will be outstanding on completion of this offering. Any amount remaining out of the profit is carried to reserve as the management board determines. After reservation by the management board of any profit, the remaining profit will be at the disposal of the general meeting of shareholders. Dividends shall be payable in such currency and on such date as determined by the management board. Claims for payment of dividends not made within five years from the date that such dividends became payable, will lapse and any such amounts will be considered to have been forfeited to us.

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Appraisal Rights and Shareholder Vote on Certain Reorganizations

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 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 shareholders of a surviving corporation to a merger is needed; however, unless required by the certificate of incorporation, if (a) the agreement of merger does not amend in any respect the certificate of incorporation of the surviving corporation, (b) the shares of stock of the surviving corporation are not changed in the merger and (c) the number of ordinary shares 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 ordinary shares outstanding immediately prior to the effective date of the merger. In addition, shareholders 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 shareholders will be entitled to appraisal rights.

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.

Under Dutch law, resolutions of the management board concerning a material change in the identity or character of the company or its business are subject to the approval of the general meeting of shareholders. Such changes include in any event:

- a transfer of all or materially all of our business to a third party;
- the entry into or termination of a long-lasting alliance of the company or of a subsidiary either with another entity or company, or as a fully liable partner of a limited partnership or partnership, if this alliance or termination is of significant importance for the company; and
- the acquisition or disposition of an interest in the capital of a company by the company or by a subsidiary with a value of at least one third of the value of the assets, according to the balance sheet with explanatory notes or, if the company prepares a consolidated balance sheet, according to the consolidated balance sheet with explanatory notes in the company's most recently adopted annual accounts.

The concept of appraisal rights does not exist under Dutch law. However, pursuant to Dutch law, a shareholder who for its own account (or together with its group companies) provides at least 95% of the company's issued capital may institute proceedings against the company's other shareholders jointly for the transfer of their shares to that shareholder. The proceedings are held before the Enterprise Chamber of the Amsterdam Court of Appeal *(Ondernemingskamer)*, which 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 of the shares to be transferred.

Furthermore, 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.

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Compensation of Directors	
Under the Delaware General Corporation Law, the shareholders do not generally have the right to approve the compensation policy for the board of directors or the senior management of the corporation, although certain aspects of the compensation policy may be subject to shareholder vote due to the provisions of federal securities and tax law.	In contrast to Delaware law, under Dutch law and our articles of association, the general meeting of shareholders must upon the proposal of our supervisory board adopt the compensation policy for the management board, which includes the outlines of the compensation of any members who serve on our management board. The supervisory board determines the compensation of the management board members in accordance with the compensation policy. A proposal by the supervisory board with respect to compensation 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 compenation of supervisory board members. The supervisory directors will be reimbursed for their expenses.

SHARES ELIGIBLE FOR FUTURE SALE

Upon completion of this offering, we will have outstanding ordinary shares. All of the ordinary shares sold in this offering will be freely transferable by persons other than our "affiliates" without restriction or further registration under the Securities Act. Sales of substantial numbers of our ordinary shares in the public market could adversely affect prevailing market prices of our ordinary shares. Prior to this offering, there has been no public market for our ordinary shares, and while application has been made for the ordinary shares to be quoted on the NASDAQ Global Market, we cannot assure you that a regular trading market will develop in the ordinary shares.

Rule 144

In general, under Rule 144 of the Securities Act, beginning 90 days after the date of this prospectus, an "affiliate" who has beneficially owned our shares for a period of at least six months is entitled to sell within any three-month period a number of shares that does not exceed the greater of either 1% of our then outstanding shares, or approximately shares immediately after this offering, or the average weekly trading volume of our shares on the NASDAQ Global Market during the four calendar weeks preceding the filing with the SEC of a notice on Form 144 with respect to such sale. Such sales under Rule 144 of the Securities Act are also subject to prescribed requirements relating to the manner of sale, notice and availability of current public information about us.

Under Rule 144, a person who is not deemed to have been an affiliate of ours at any time during the 90 days preceding a sale, and who has beneficially owned the shares proposed to be sold for at least six months, including the holding period of any prior holder other than an affiliate, is entitled to sell such shares without restriction, provided we have been in compliance with our reporting requirements under the Exchange Act for the six months following satisfaction of the six-month holding period. To the extent that our affiliates sell their shares, other than pursuant to Rule 144 or a registration statement, the purchaser's holding period for the purpose of effecting a sale under Rule 144 commences on the date of transfer from the affiliate.

Rule 701

In general, under Rule 701 of the Securities Act, each of our employees, consultants or advisors who purchases our ordinary shares from us in connection with a compensatory stock plan or other written agreement executed prior to the completion of this offering is eligible to resell such ordinary shares in reliance on Rule 144, but without compliance with some of the restrictions, including the holding period, contained in Rule 144.

Regulation S

Regulation S under the Securities Act provides generally that sales made in offshore transactions are not subject to the registration or prospectus-delivery requirements of the Securities Act.

Lock-up Arrangements

For a description of the lock-up arrangements that we, the members of our management and supervisory boards and substantially all of our shareholders have entered into in connection with this offering, see "Underwriting."

TAXATION

Taxation in the Netherlands

General

The following is a general summary of certain material Netherlands tax consequences of the holding and disposal of the ordinary shares. This summary does not purport to describe all possible tax considerations or consequences that may be relevant to all categories of investors, some of which may be subject to special treatment under applicable law (such as trusts or other similar arrangements), and in view of its general nature, it should be treated with corresponding caution. Holders should consult with their tax advisors with regard to the tax consequences of investing in the ordinary shares in their particular circumstances. The discussion below is included for general information purposes only.

Please note that this summary does not describe the tax considerations for:

(i) holders of ordinary shares if such holders, and in the case of individuals, his/her partner or certain of their relatives by blood or marriage in the direct line (including foster children), have a substantial interest or deemed substantial interest in us under the Netherlands Income Tax Act 2001 (in Dutch: "*Wet inkomstenbelasting 2001*"). Generally speaking, a holder of securities in a company is considered to hold a substantial interest in such company, if such holder alone or, in the case of individuals, together with his/her partner (statutorily defined term), directly or indirectly, holds (i) an interest of 5% or more of the total issued and outstanding capital of that company or of 5% or more of the issued and outstanding capital of a certain class of shares of that company; or (ii) rights to acquire, directly or indirectly, such interest; or (iii) certain profit sharing rights in that company that relate to 5% or more of the company's annual profits and/or to 5% or more of the company's liquidation proceeds. A deemed substantial interest may arise if a substantial interest (or part thereof) in a company has been disposed of, or is deemed to have been disposed of, on a non-recognition basis;

(ii) holders of ordinary shares in us that qualify or qualified as a participation for purposes of the Netherlands Corporate Income Tax Act 1969 (in Dutch: "*Wet op de vennootschapsbelasting 1969*"). Generally, a taxpayer's shareholding of 5% or more in a company's nominal paid-up share capital qualifies as a participation. A holder may also have a participation if such holder does not have a 5% shareholding but a related entity (statutorily defined term) has a participation or if the company in which the shares are held is a related entity (statutorily defined term);

(iii) holders of ordinary shares who are individuals for whom the ordinary shares or any benefit derived from the ordinary shares are compensation or deemed to be compensation for employment activities, including deemed employment activities performed by such holders or certain individuals related to such holders (as defined in the Netherlands Income Tax Act 2001); and

(iv) pension funds, investment institutions (in Dutch: "*fiscale beleggingsinstellingen*"), exempt investment institutions (in Dutch: "*vrijgestelde beleggingsinstellingen*") and other entities that are, in whole or in part, not subject to or 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.

Except as otherwise indicated, this summary only addresses Netherlands national tax legislation and published regulations, whereby the Netherlands means the part of the Kingdom of the Netherlands located in Europe, as in effect on the date hereof and as interpreted in published case law until this date, without prejudice to any amendment introduced at a later date and implemented with or without retroactive effect.

Withholding Tax

Dividends distributed by us generally are subject to Netherlands dividend withholding tax at a rate of 15%. The expression "dividends distributed" includes, among other things:

- distributions in cash or in kind, deemed and constructive distributions and repayments of paid-in capital not recognized for Netherlands dividend withholding tax purposes;
- liquidation proceeds, proceeds of redemption of ordinary shares, or proceeds of the repurchase of ordinary shares by us or one of our subsidiaries or other affiliated entities to the extent such proceeds exceed the average paid-in capital of those shares as recognized for purposes of Netherlands dividend withholding tax;
- an amount equal to the par value of ordinary shares issued or an increase of the par value of ordinary shares, to the extent that it does not appear that a contribution, recognized for purposes of Netherlands dividend withholding tax, has been made or will be made; and
- partial repayment of the paid-in capital, recognized for purposes of Netherlands dividend withholding tax, if and to the extent that we have net profits (in Dutch: "*zuivere winst*"), unless the holders of ordinary shares have resolved in advance at a general meeting to make such repayment and the par value of the ordinary shares concerned has been reduced by an equal amount by way of an amendment of our articles of association.

If a holder of ordinary shares is resident in a country other than the Netherlands and if a double taxation convention is in effect between the Netherlands and such other country, such holder of ordinary shares may, depending on the terms of that double taxation convention, be eligible for a full or partial exemption from, or refund of, Netherlands dividend withholding tax.

Individuals and corporate legal entities who are resident or deemed to be resident in the Netherlands for Netherlands tax purposes ("Netherlands Resident Individuals" and "Netherlands Resident Entities" as the case may be), other than individuals who have made an election for the application of the rules of the Netherlands Income Tax Act 2001 as they apply to residents of the Netherlands, can generally credit the Netherlands dividend withholding tax against their income tax or corporate income tax liability. The same generally applies to holders of ordinary shares that are neither resident nor deemed to be resident of the Netherlands and holders of ordinary shares that are individuals who have made an election for the application of the rules of the Netherlands Income Tax Act 2001 as they apply to residents of the Netherlands if the ordinary shares are attributable to a Netherlands permanent establishment of such non-resident holder.

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

- 3% of the portion of the distribution paid by us that is subject to Netherlands 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 Netherlands dividend withholding tax that we are required to remit to the Netherlands tax authorities, it does not reduce the amount of tax that we are required to withhold on dividends distributed.

Pursuant to legislation to counteract "dividend stripping", a reduction, exemption, credit or refund of Netherlands dividend withholding tax is denied if the recipient of the dividend is not the beneficial owner as

described in the Netherlands Dividend Withholding Tax Act 1965. This legislation generally targets situations in which a shareholder retains its economic interest in shares but reduces the withholding tax costs on dividends by a transaction with another party. It is not required for these rules to apply that the recipient of the dividends is aware that a dividend stripping transaction took place. The Netherlands State Secretary of Finance takes the position that the definition of beneficial ownership introduced by this legislation will also be applied in the context of a double taxation convention.

Certain entities (i) that are resident in another E.U. member state, (ii) that are resident in a designated state that is a party to the Agreement on the European Economic Area (currently Liechtenstein, Iceland and Norway) or (iii) that are resident in a designated jurisdiction which has an arrangement for the exchange of tax information with the Netherlands and that hold our ordinary shares as portfolio investment (i.e. such ordinary shares are not held with a view to the establishment or maintenance of lasting and direct economic links between such holder of ordinary shares and us and such ordinary shares do not allow such holder of ordinary shares to participate effectively in the management or control of us) and that are not subject to taxation levied by reference to profits in their state of residence, may be entitled to a refund of Dutch dividend withholding tax, provided:

(i) such entity, had it been a resident in the Netherlands, would not be subject to corporate income tax in the Netherlands;

(ii) such entity can be considered to be the beneficial owner of the dividends;

(iii) such entity does not perform a similar function to that of a fiscal investment institution (*fiscale beleggingsinstelling*) or an exempt investment Institution (*vrijgestelde beleggingsinstelling*) as defined in the Dutch Corporate Income Tax Act 1969; and

(iv) certain administrative conditions are met.

Dividend distributions to a U.S. holder of ordinary shares (with an interest of less than 10% of the voting rights in us) are generally subject to 15% dividend withholding tax, which is equal to the rate such U.S. holder may be entitled to under the Convention Between the Kingdom of the Netherlands and the U.S. for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income, executed in Washington on December 18, 1992, as amended from time to time, or the U.S.-Dutch Treaty, or the Netherlands-U.S. Convention. As such, there is no need to claim a refund of the excess of the amount withheld over the tax treaty rate.

On the basis of article 35 of the Netherlands-U.S. Convention, qualifying U.S. pension trusts are under certain conditions entitled to a full exemption from Dutch dividend withholding tax. Such qualifying exempt U.S. pension trusts must provide us form IB 96 USA, along with a valid certificate, for the application of relief at source from dividend withholding tax. If we receive the required documentation prior to the relevant dividend payment date, then we may apply such relief at source. If a qualifying exempt U.S. pension trust fails to satisfy these requirements prior to the payment of a dividend, then such qualifying exempt pension trust may claim a refund of Dutch withholding tax by filing form IB 96 USA with the Dutch tax authorities. On the basis of article 36 of the Netherlands-U.S. Convention, qualifying exempt U.S. organizations are under certain conditions entitled to a full exemption from Dutch dividend withholding tax. Such qualifying exempt U.S. organizations are not entitled to claim relief at source, and instead must claim a refund of Dutch withholding tax by filing form IB 95 USA with the Dutch tax authorities.

Taxes on Income and Capital Gains

Netherlands Resident Individuals

If a holder of ordinary shares is a Netherlands Resident Individual (including the non-resident individual holder who has made an election for the application of the rules of The Netherlands Income Tax Act 2001 as they

apply to residents of the Netherlands), any benefit derived or deemed to be derived from the ordinary shares is taxable at the progressive income tax rates (with a maximum of 52%), if:

(a) the ordinary shares are attributable to an enterprise from which the Netherlands Resident Individual derives a share of the profit, whether as an entrepreneur or as a person who has a co-entitlement to the net worth (in Dutch: *"medegerechtigd tot het vermogen"*) of such enterprise, without being an entrepreneur or a shareholder, as defined in the Netherlands Income Tax Act 2001; or

(b) the holder of the ordinary shares is considered to perform activities with respect to the ordinary shares that go beyond ordinary asset management (in Dutch: "*normaal, actief vermogensbeheer*") or derives benefits from the ordinary shares that are taxable as benefits from other activities (in Dutch "*resultaat uit overige werkzaamheden*").

If the above-mentioned conditions (a) and (b) do not apply to the individual holder of ordinary shares, the ordinary shares are recognized as investment assets and included as such in such holder's net investment asset base (in Dutch: "*rendementsgrondslag*"). Such holder will be taxed annually on a deemed income of 4% of his or her net investment assets for the year at an income tax rate of 30%. The net investment assets for the year are the fair market value of the investment assets less the allowable liabilities on January 1 of the relevant calendar year. A tax free allowance may be available. Actual benefits derived from the ordinary shares are as such not subject to Netherlands income tax.

Netherlands Resident Entities

Any benefit derived or deemed to be derived from the ordinary shares held by Netherlands Resident Entities, including any capital gains realised on the disposal thereof, will generally be subject to Netherlands corporate income tax at a rate of 25% (a corporate income tax rate of 20% applies with respect to taxable profits up to €200,000).

Non-Residents of the Netherlands

A holder of ordinary shares will not be subject to Netherlands taxes on income or on capital gains in respect of any payment under the ordinary shares or any gain realised on the disposal or deemed disposal of the ordinary shares, provided that:

(i) such holder is neither a resident nor deemed to be resident in the Netherlands for Netherlands tax purposes and, if such holder is an individual, such holder has not made an election for the application of the rules of the Netherlands Income Tax Act 2001 as they apply to residents of The Netherlands;

(ii) such holder does not have an interest in an enterprise or a deemed enterprise (statutorily defined term) which, in whole or in part, is either effectively managed in the Netherlands or is carried out through a permanent establishment, a deemed permanent establishment or a permanent representative in the Netherlands and to which enterprise or part of an enterprise the ordinary shares are attributable or deemed attributable; and

(iii) in the event such holder is an individual, such holder does not carry out any activities in the Netherlands with respect to the ordinary shares that go beyond ordinary asset management and does not derive benefits from the ordinary shares that are taxable as benefits from other activities in the Netherlands.

Gift and Inheritance Taxes

Residents of the Netherlands

Gift and inheritance taxes will arise in the Netherlands with respect to a transfer of the ordinary shares by way of a gift by, or on the death of, a holder of ordinary shares who is resident or deemed to be resident in the Netherlands at the time of the gift or his/her death.

Non-residents of the Netherlands

No Netherlands gift or inheritance taxes will arise on the transfer of the ordinary shares by way of gift by, or on the death of, a holder of ordinary shares who is neither resident nor deemed to be resident in the Netherlands, unless:

(i) 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, 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 transfer is otherwise construed as a gift or inheritance made by, or on behalf of, a person who, at the time of the gift or death, is or is deemed to be resident in the Netherlands.

For purposes of Netherlands gift and inheritance taxes, amongst others, a person that holds the Netherlands nationality will be deemed to be resident in the Netherlands if such person has been resident in the Netherlands at any time during the ten years preceding the date of the gift or his/her death. Additionally, for purposes of Netherlands gift tax, amongst others, a person not holding the Netherlands nationality will be deemed to be resident in the Netherlands if such person 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.

Other Taxes and Duties

No Netherlands VAT and no Netherlands registration tax, stamp duty or any other similar documentary tax or duty will be payable by a holder of ordinary shares on any payment in consideration for the holding or disposal of the ordinary shares.

Certain Material U.S. Federal Income Tax Considerations

The following is a summary of certain material U.S. federal income tax considerations relating to the acquisition, ownership and disposition of our ordinary shares by a U.S. holder (as defined below). This summary addresses only the U.S. federal income tax considerations for U.S. holders that are initial purchasers of our ordinary shares pursuant to the offering and that will hold such 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. 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:

- banks, financial institutions or insurance companies;
- brokers, dealers or traders in securities, currencies, commodities, or notional principal contracts;
- tax-exempt entities or organizations, including an “individual retirement account” or “Roth IRA” as defined in Section 408 or 408A of the Code (as defined below), respectively;
- real estate investment trusts, regulated investment companies or grantor trusts;
- persons that hold the ordinary shares as part of a “hedging,” “integrated” or “conversion” transaction or as a position in a “straddle” for U.S. federal income tax purposes;
- partnerships (including entities classified as partnerships for U.S. federal income tax purposes) or other pass-through entities, or persons that will hold our shares through such an entity;
- S corporations;
- certain former citizens or long term residents of the United States;
- persons that received our shares as compensation for the performance of services;
- persons that acquire ordinary shares as a result of holding or owning our preferred shares;

- holders that own directly, indirectly, or through attribution 10% or more of the voting power or value our shares; and
- holders that have a "functional currency" other than the U.S. dollar.

Further, this summary does not address the U.S. federal estate, gift, or alternative minimum tax considerations, or any U.S. state, local, or non-U.S. tax considerations of the acquisition, ownership and disposition of our ordinary shares.

This description is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, existing, proposed and temporary U.S. Treasury Regulations promulgated thereunder and administrative and judicial interpretations thereof, in each case as in effect and available on the date hereof. All the foregoing is subject to change, which change could apply retroactively, and to differing interpretations, all of which could affect the tax considerations described below. There can be no assurances that the U.S. Internal Revenue Service, or the IRS, will not take a position concerning the tax consequences of the acquisition, ownership and disposition of our ordinary shares or that such a position would not be sustained. Holders should consult their own tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning, and disposing of our ordinary shares in their particular circumstances.

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:

- 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, any state thereof, 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 United States person.

If a partnership (or any other entity treated as a partnership for U.S. federal income tax purposes) holds ordinary shares, the U.S. federal income tax consequences relating to an investment in our ordinary shares will depend in part upon the status of the partner and the activities of the partnership. Such a partner or partnership should consult its tax advisor regarding the U.S. federal income tax considerations of acquiring, owning and disposing of our ordinary shares in its particular circumstances.

As indicated below, this discussion is subject to U.S. federal income tax rules applicable to a "passive foreign investment company," or a PFIC.

Persons considering an investment in our ordinary shares should consult their own tax advisors as to the particular tax consequences applicable to them relating to the acquisition, ownership and disposition of our ordinary shares, including the applicability of U.S. federal, state and local tax laws and non-U.S. tax laws.

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 either long-term or short-term capital gain depending upon whether the U.S. holder has held our

ordinary shares for more than one year as of the time such distribution is received. 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. Non-corporate U.S. holders may qualify for the preferential rates of taxation with respect to dividends on ordinary shares applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year) applicable to qualified dividend income (as discussed below). The Company, which is incorporated under the laws of the Kingdom of the Netherlands, believes that it qualifies as a resident of the Netherlands for purposes of, and is eligible for the benefits of, the Convention between the United States of America and the Kingdom of the Netherlands for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with respect to Taxes on Income, signed on December 18, 1992, as amended and currently in force, or the U.S.-Netherlands Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-Netherlands Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Therefore, subject to the discussion under "Passive Foreign Investment Company Considerations," below, if the U.S.-Netherlands Tax Treaty is applicable, such dividends will generally be "qualified dividend income" in the hands of individual U.S. holders, provided that certain conditions are met, including holding period and the absence of certain risk reduction transaction requirements are met. The dividends will not be eligible for the dividends-received deduction generally allowed to corporate U.S. holders

U.S. holder generally may claim the amount of Dutch income withholding tax withheld as either a deduction from gross income or a credit against U.S. federal income tax liability. However, the foreign tax credit is subject to numerous complex limitations that must be determined and applied on an individual basis. Generally, the credit cannot exceed the proportionate share of a U.S. holder's U.S. federal income tax liability that such U.S. holder's taxable income bears to such U.S. holder's worldwide taxable income. In applying this limitation, a U.S. holder's various items of income and deduction must be classified, under complex rules, as either "foreign source" or "U.S. source." In addition, this limitation is calculated separately with respect to specific categories of income. The amount of a distribution with respect to the ordinary shares that is treated as a "dividend" may be lower for U.S. federal income tax purposes than it is for Dutch income tax purposes, potentially resulting in a reduced foreign tax credit for the U.S. holder. Each U.S. holder should consult its own tax advisors regarding the foreign tax credit rules.

In general, the amount of a distribution paid to a U.S. holder in a foreign currency will be the dollar value of the foreign currency calculated by reference to the spot exchange rate on the day the U.S. holder receives the distribution, regardless of whether the foreign currency is converted into U.S. dollars at that time. Any foreign currency gain or loss a U.S. holder realizes on a subsequent conversion of foreign currency into U.S. dollars will be U.S. source ordinary income or loss. If dividends received in a foreign currency are converted into U.S. dollars on the day they are received, a U.S. holder should not be required to recognize foreign currency gain or loss in respect of the dividend.

Sale, exchange or other taxable disposition of our ordinary shares. A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale, exchange or other taxable disposition 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. The adjusted tax basis in an ordinary share generally will be equal to the cost of such ordinary share. Capital gain from the sale, exchange or other taxable disposition of ordinary shares of a non-corporate U.S. holder is generally eligible for a preferential rate of taxation applicable to capital gains, if the non-corporate U.S. holder's holding period determined at the time of such sale, exchange or other taxable disposition for such ordinary shares exceeds one year (i.e., such gain is long-term taxable gain). The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations under the Code. Any such gain or loss that a U.S. holder recognizes generally will be treated as U.S. source income or loss for foreign tax credit limitation purposes.

For a cash basis taxpayer, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the settlement date of the purchase or sale. In that case, no foreign currency exchange gain or loss will result from currency fluctuations between the trade date and the settlement date of such a purchase or sale. An accrual basis taxpayer, however, may elect the same treatment required of cash basis taxpayers with respect to purchases and sales of our ordinary shares that are traded on an established securities market, provided the election is applied consistently from year to year. Such election may not be changed without the consent of the IRS. For an accrual basis taxpayer who does not make such election, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the trade date of the purchase or sale. Such an accrual basis taxpayer may recognize exchange gain or loss based on currency fluctuations between the trade date and the settlement date. Any foreign currency gain or loss a U.S. Holder realizes will be U.S. source ordinary income or loss.

Medicare Tax. Certain U.S. holders that are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their "net investment income," which may include all or a portion of their dividend income and net gains from the disposition of ordinary shares. Each U.S. holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in our ordinary shares.

Passive foreign investment company considerations. If we are classified as a passive foreign investment company, or PFIC, in any taxable year, a U.S. holder would be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

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, after applying certain look-through rules with respect to the income and assets of its subsidiaries, either: (i) at least 75% of its gross income is "passive income" or (ii) at least 50% of the average quarterly value of its total gross assets (which, assuming we are not a CFC for the year being test, would be measured by fair market value of the assets, and for which purpose the total value of our assets may be determined in part by the market value of our ordinary shares, which is subject to change) 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, gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income, and includes amounts derived by reason of the temporary investment of funds raised in offerings of our ordinary shares. If a non-U.S. corporation owns directly or indirectly at least 25% by value of the stock of another corporation, the non-U.S. corporation is treated for purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation and as receiving directly its proportionate share of the other corporation's income. If we are classified as a PFIC in any year with respect to which a U.S. holder owns our ordinary shares, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns our ordinary shares, regardless of whether we continue to meet the tests described above.

Although the matter is not free from doubt, we believe that we were not a PFIC during our 2013 taxable year and may not be a PFIC during our 2014 taxable year. 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 after the offering. In addition, the composition of our income and assets will be affected by how, and how quickly, we use the cash proceeds from this offering in our business.

If we are a PFIC, and you are a U.S. holder, then unless you make one of the elections described below, a special tax regime will apply to both (a) any "excess distribution" by us to you (generally, your ratable portion of distributions in any year which are greater than 125% of the average annual distribution received by you in the shorter of the three preceding years or your holding period for our ordinary shares) and (b) any gain realized on the sale or other disposition of the ordinary shares. Under this regime, any excess distribution and realized gain will be treated as ordinary income and will be subject to tax as if (a) the excess distribution or gain had been realized ratably over your holding period, (b) the amount deemed realized in each year had been subject to tax in each year of that holding period at the highest marginal rate for such year (other than income allocated to the current period or any taxable period before we became a PFIC, which would be subject to tax at the U.S. holder's regular ordinary income rate for the current year and would not be subject to the interest charge discussed below), and (c) the interest charge generally applicable to underpayments of tax had been imposed on the taxes deemed to have been payable in those years. In addition, dividend distributions made to you will not qualify for the lower rates of taxation applicable to long-term capital gains discussed above under "Distributions."

Certain elections exist that may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment (such as mark-to-market treatment) of our ordinary shares. If a U.S. holder makes the mark-to-market election, the U.S. holder generally will recognize as ordinary income any excess of the fair market value of the ordinary shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ordinary shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. holder makes the election, the U.S. holder's tax basis in the ordinary shares will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of ordinary shares in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). The mark-to-market election is available only if we are a PFIC and our ordinary shares are "regularly traded" on a "qualified exchange." Our ordinary shares will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the ordinary shares are traded on a qualified exchange on at least 15 days during each calendar quarter (subject to the rule that trades that have as one of their principle purposes the meeting of the trading requirement as disregarded). The NASDAQ Global Market is a qualified exchange for this purpose and, consequently, if the ordinary shares are regularly traded, the mark-to-market election will be available to a U.S. holder.

We do not currently intend to provide the information necessary for U.S. holders to make qualified electing fund elections if we were treated as a PFIC for any taxable year. U.S. Holders should consult their tax advisors to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

If we are determined to be a PFIC, the general tax treatment for U.S. Holders described in this section would apply to indirect distributions and gains deemed to be realized by U.S. Holders in respect of any of our subsidiaries that also may be determined to be PFICs.

If a U.S. holder owns ordinary shares during any taxable year in which we are a PFIC and the U.S. holder recognizes gain on a disposition of our ordinary shares or receives distributions with respect to our ordinary shares, the U.S. holder generally will be required to file an IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund) with respect to the company, generally with the U.S. holder's federal income tax return for that year. If our company were a PFIC for a given taxable year, then you should consult your tax advisor concerning your annual filing requirements.

The U.S. federal income tax rules relating to PFICs are complex. Prospective U.S. investors are urged to consult their own tax advisers with respect to the acquisition, ownership and disposition of our ordinary shares, the consequences to them of an investment in a PFIC, any elections available with respect to our ordinary shares and the IRS information reporting obligations with respect to the acquisition, ownership and disposition of our ordinary share.

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 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.

Certain Reporting Requirements With Respect to Payments of Offer Price. U.S. holders paying more than U.S. $100,000 for our ordinary shares generally may be required to file IRS Form 926 reporting the payment of the Offer Price for our ordinary shares to us. Substantial penalties may be imposed upon a U.S. holder that fails to comply. Each U.S. holder should consult its own tax advisor as to the possible obligation to file IRS Form 926.

Foreign Asset Reporting. Certain U.S. holders who are individuals are required to report information relating to an interest in our ordinary shares, subject to certain exceptions (including an exception for shares held in accounts maintained by U.S. financial institutions) by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. U.S. holders are urged to consult their tax advisors regarding their information reporting obligations, if any, with respect to their ownership and disposition of our ordinary shares.

THE DISCUSSION ABOVE IS A GENERAL SUMMARY. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PROSPECTIVE INVESTOR. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN ORDINARY SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

UNDERWRITING

Leerink Partners LLC and Deutsche Bank Securities Inc. are acting as representatives of the underwriters. 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	
Deutsche Bank Securities Inc.	
JMP Securities	
HC Wainwright & Co., LLC	
Total	

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 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	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at $ million and are payable by us.

Option to Purchase Additional Ordinary Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to 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 officers and all of our other existing security holders have agreed not to sell or transfer any ordinary shares or securities convertible into or exchangeable or exercisable for ordinary shares, for 180 days after the date of this prospectus without first obtaining the written consent of the representatives. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell (including any short sale) any share capital;
- sell any option or contract to purchase any share capital;
- purchase any option or contract to sell any share capital;
- grant any option, right or warrant for the sale of any share capital;
- otherwise dispose of or transfer any share capital;
- request or demand that we file a registration statement related to the share capital; and
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any share capital, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to ordinary shares and to securities convertible into or exchangeable or exercisable for ordinary shares. It also applies to ordinary shares owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

NASDAQ Global Market Listing

We intend to apply to have our ordinary shares listed on The NASDAQ Global Market under the symbol " ."

Determination of Offering Price

Before this offering, there has been no public market for our ordinary shares. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us;
- our financial information;
- the history of, and the prospects for, our company and the industry in which we compete;
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our potential future revenues;
- the present state of our development; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Stamp Taxes

If you purchase ordinary shares offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

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 the 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 of ordinary 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 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

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory,

investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses. In addition, affiliates of Leerink Partners, one of the underwriters, are beneficial owners of less than 1% of our outstanding share capital prior to giving effect to the offering.

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 INVESTORS

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, each referred to herein as a Relevant Member State, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, referred to herein as the Relevant Implementation Date, no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

- to any person, legal entity or other party which is a "qualified investor" as defined in the Prospectus Directive;
- 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 per Relevant Member State (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 of the underwriters for any such offer; or
- in any other circumstances falling within the scope of Articles 1(2), Article 3(2) or 4 of the Prospectus Directive,

provided that no such offer of securities shall require the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this statement, the expression an "offer to the public" in relation to any securities in any Relevant Member State means a communication in any form and by any means of sufficient information on the

terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, 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 and includes any relevant implementing measure in the Relevant Member State.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

- to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA; or
- where no consideration is given for the transfer; or where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, referred to herein as the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated. Each such person is referred to herein as a Relevant Person.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant Person should not act or rely on this document or any of its contents.

EXPENSES OF THE OFFERING

We estimate that our expenses in connection with this offering, other than underwriting discounts and commissions, will be as follows:

Expenses	Amount
U.S. Securities and Exchange Commission registration fee	$
FINRA filing fee	$13,500
NASDAQ listing fee	$
Printing and engraving expenses	$
Legal fees and expenses	$
Accounting fees and expenses	$
Miscellaneous costs	$
Total	$

All amounts in the table are estimates except the U.S. Securities and Exchange Commission registration fee and the FINRA filing fee. We will pay all of the expenses of this offering.

LEGAL MATTERS

Certain legal matters with respect to U.S. federal law and New York law in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. 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 NautaDutilh N.V., Amsterdam, the Netherlands. Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York, is counsel to the underwriters with respect to U.S. federal law and New York law. Stibbe N.V., Amsterdam, the Netherlands, is counsel to the underwriters with respect to Dutch law.

EXPERTS

The financial statements of ProQR Therapeutics B.V. as of December 31, 2013 and 2012 and for the year ended December 31, 2013 and for the period from February 21, 2012 (inception) through December 31, 2012 included in this prospectus have been audited by Deloitte Accountants B.V., an independent registered public accounting firm as stated in their report appearing herein. Such financial statements are included in reliance upon the report of such firm, given upon their authority as experts in auditing and accounting.

ENFORCEABILITY OF CIVIL LIABILITIES

We are incorporated under the laws of the Netherlands. Substantially all of our business is conducted, and substantially all of our assets are located, in the Netherlands. Most of our directors 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 board, supervisory board 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 obtain from a Dutch court leave to enforce the judgment rendered by a U.S. court. Under current practice, however, a Dutch court will grant leave to enforce, without a review on the merits of the underlying claim, if it 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.

If no leave to enforce is granted, claimants must litigate the claim again before a Dutch competent court.

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 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*). To obtain compensation for damages, individual claimants can base their claim on the declaratory judgment obtained by the foundation or association but they still need to individually sue the defendant for damages. Alternatively, 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

We have filed with the SEC a registration statement on Form F-1 under the Securities Act, including relevant exhibits and schedules, with respect to the ordinary shares to be sold in this offering. This prospectus, which constitutes a part of the registration statement, does not contain all of the information contained in the registration statement. You should read the registration statement and its exhibits for further information with respect to us and our shares. Some of these exhibits consist of documents or contracts that are described in this prospectus in summary form. You should read the entire document or contract for the complete terms. 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.

After this offering, we will be subject to the reporting requirements of the Securities Exchange Act of 1934, or 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. However, we plan to produce quarterly financial reports and furnish them to the SEC approximately 45 days after the end of each of the first three quarters of our fiscal year and to file our annual report on Form 20-F approximately 90 days after the end of our fiscal year. In addition, our "insiders" are not subject to the SEC's rules that prohibit short-swing trading. Our annual financial statements will be prepared in accordance with IFRS as issued by the IASB and audited by an independent registered public accounting firm.

We also maintain an internet website at www.proqr-tx.com. Information contained in or connected to our website is not a part of this prospectus.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Supervisory Board and Shareholders of
ProQR Therapeutics B.V.
Leiden, The Netherlands

We have audited the accompanying statements of financial position of ProQR Therapeutics B.V. (the "Company") as of December 31, 2013 and 2012, and the related statements of comprehensive loss, equity and cash flows for the year ended December 31, 2013 and the period from February 21, 2012 (date of inception of the Company) through December 31, 2012 (the "Financial Statements"). These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States) and International Standards on Auditing. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal controls over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we do not express such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the accompanying Financial Statements present fairly, in all material respects, the financial position of the Company as of December 31, 2013 and December 31, 2012, the results of their operations and their cash flows for the year ending December 31, 2013 and the period from February 21, 2012 (date of inception of the Company) through December 31, 2012 in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

/s/ Deloitte Accountants B.V.

Amsterdam, The Netherlands
July 10, 2014

PROQR THERAPEUTICS B.V.

Statement of Financial Position

(€ in thousands)

	At December 31,	
	2012	2013
Assets		
Current assets:		
Cash and cash equivalents	€ 249	€ 4,129
Other receivables	27	59
Social securities and other taxes	23	73
Total current assets	299	4,261
Property, plant and equipment	—	204
Intangible assets	39	39
Total assets	338	4,504
Liabilities and stockholders' equity		
Current liabilities:		
Convertible loan	—	2,514
Finance lease liabilities	—	35
Trade payables	95	745
Social security and other taxes	3	29
Pension premiums	7	17
Other current liabilities	38	262
Total current liabilities	143	3,602
Finance lease liabilities	—	48
Borrowings	96	943
Total liabilities	239	4,593
Stockholders' equity	99	(89)
Total liabilities and stockholders' equity	€ 338	€ 4,504

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

PROQR THERAPEUTICS B.V.

Statement of Comprehensive Loss

(€ in thousands, except share data and per share data)

	Period From February 21, 2012 (Inception) Through December 31, 2012	Year Ended December 31, 2013
Other income	**€ 23**	**€ 116**
Research and development costs	(285)	(2,550)
General and administrative costs	(157)	(764)
Share-based compensation	—	(41)
Total operating costs	**(442)**	**(3,355)**
Operating result	**(419)**	**(3,239)**
Finance income and expense	1	(14)
Result before corporate income taxes	**(418)**	**(3,253)**
Income taxes	—	—
Net loss (attributable to equity holders of the Company)	**(418)**	**(3,253)**
Other comprehensive income	—	—
Total comprehensive loss (attributable to equity holders of the Company)	**€ (418)**	**€ (3,253)**
Share information		
Weighted average number of shares outstanding	24,556	54,199
Earnings per share for result attributable to the equity holders of the Company during per period (expressed in Euro per share)		
Basic and diluted loss per share	**€ (17.04)**	**€ (60.01)**

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

PROQR THERAPEUTICS B.V.

Statement of Changes in Equity

(€ in thousands, except for share data)

	Attributable to Equity Holders of the Company					
	Number of Shares	Share Capital	Share Premium Reserve	Equity Settled Employee Benefit Reserve	Accumulated Deficit	Total Equity
Balance at February 21, 2012	18,000	€ 18	€ —	€ —	€ —	€ 18
Net loss	—	—	—	—	(418)	(418)
Shares issued in the period	17,293	17	484	—	—	501
Treasury shares issued to Stichting ProQR Therapeutics Participation	(1,765)	(2)	—	—	—	(2)
Balance at December 31, 2012	**33,528**	**33**	**484**	**—**	**(418)**	**99**
Net loss	—	—	—	—	(3,253)	(3,253)
Recognition of share-based payments	—	—	—	41	—	41
Shares issued in the period	35,291	35	3,394	—	—	3,429
Treasury shares issued to Stichting ProQR Therapeutics Participation	(8,820)	(9)	(396)	—	—	(405)
Balance at December 31, 2013	**59,999**	**€ 59**	**€ 3,482**	**€ 41**	**€ (3,671)**	**€ (89)**

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

PROQR THERAPEUTICS B.V.

Statement of Cash Flows

(€ in thousands)

	Period From February 21, 2012 (Inception) Through December 31, 2012	Year Ended December 31, 2013
Cash flow from operating activities		
Net loss	€ (418)	€ (3,253)
Adjustments for:		
Depreciation	—	24
Share-based payment expenses	—	41
Interest expense/(income)	(1)	14
Changes in other receivables	(50)	(81)
Changes in trade and other payables	142	910
Corporate income tax paid	—	—
Interest received	2	13
Net cash used in operating activities	(325)	(2,332)
Cash flow from investing activities		
Purchases of property, plant and equipment	—	(137)
Purchases of intangible assets	(39)	—
Net cash used in investing activities	(39)	(137)
Cash flow from financing activities		
Proceeds from issuance of shares	518	3,023
Proceeds from borrowings	95	3,326
Net cash generated by financing activities	613	6,349
Net increase in cash and cash equivalents	**249**	**3,880**
Cash and cash equivalents at the beginning of the year	—	249
Cash and cash equivalents at the end of the year	**€ 249**	**€ 4,129**

The accompanying notes form an integral part of the consolidated financial statements.

PROQR THERAPEUTICS B.V.

Notes to the Financial Statements

1. General Information

ProQR Therapeutics B.V., or ProQR or the Company, is a development stage company that primarily focuses on the development and commercialization of novel therapeutic medicines.

The Company is a limited liability company incorporated in the Netherlands, on February 21, 2012 with its statutory seat in Leiden, the Netherlands. The address of its headquarters and registered office is Darwinweg 24, 2333 CR Leiden, the Netherlands.

Going concern

The management board of ProQR has, upon preparing and finalizing the 2013 financial statements, assessed the Company's ability to fund its operations for a period of at least one year after the date of signing these financial statements.

The management board of the Company is confident about the continuity of the Company based on its existing funding, taking into account the funding provided by the financing transaction described under the 'Events after the balance sheet date' as described in Note 21, and the projected cash flows based on the activities under execution on the basis of ProQR's business plan, which includes, amongst other activities, the conduct of toxicology studies with QR-010 and a Phase 1b clinical study of QR-010 in patients suffering from Cystic Fibrosis.

2. Adoption of new and revised International Financial Reporting Standards

The financial statements have been prepared on the basis of International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB"). New Standards and Interpretations, which became effective as of January 1, 2013, did not have a material impact on our consolidated financial statements.

The Company has not applied the following new and revised IFRSs that have been issued but are not yet effective:

IFRS 9	*Financial Instruments*[1]
IFRS 14	*Regulatory Deferral Accounts*[4]
Amendments to IFRS 1	*First Time Adoption*[3]
Amendments to IFRS 2	*Share-based Payment*[3]
Amendments to IFRS 3	*Business Combination*[3]
Amendments to IFRS 8	*Operating Segment*[3]
Amendments to IFRS 10/IFRS 12/IAS 27	*Investment Entities*[2]
Amendments to IFRS 13	*Fair Value Measurement*[3]
Amendments to IAS 16	*Clarification of Acceptable Methods of Depreciation*[3]
Amendments to IAS 19	*Defined Benefits Plans: Employee Contributions*[3]
Amendments to IAS 24	*Related Party Disclosure*[3]
Amendments to IAS 32	*Offsetting Financial Assets and Financial Liabilities*[2]
Amendments to IAS 36	*Recoverable Amount Disclosures for Non-Financial Assets*[2]
Amendments to IAS 38	*Intangible Assets*[3]
Amendments to IAS 39	*Novation of Derivatives and Continuation of Hedge Accounting*[2]
Amendments to IAS 40	*Intangible Assets*[3]
IFRIC 21	*Levies*[2]

1 Effective date not yet determined
2 Effective for annual periods beginning on or after January 1, 2014, with earlier adoption allowed.
3 Effective for annual periods beginning on or after July 1, 2014, with earlier adoption allowed.
4 Effective for annual periods beginning on or after January 1, 2016.

The adoption of these Standards and Interpretations are not expected to have a material effect on the financial statements.

3. Significant accounting policies

(a) Statement of compliance

The financial statements of ProQR Therapeutics B.V., or the Company, have been prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the IASB.

(b) Basis of preparation

The financial statements have been prepared on the historical cost basis except for financial instruments and share-based payment obligations which have been based on fair value. Historical cost is generally based on the fair value of the consideration given in exchange for assets. Furthermore, the financial statements are presented in euros and all values are rounded to the nearest euro except where otherwise indicated.

The preparation of financial statements in conformity with IFRS requires the use of certain critical accounting estimates. It also requires management to exercise its judgment in the process of applying the Company's accounting policies. The areas involving a higher degree of judgment or complexity or areas where assumptions and estimates are significant to the financial statements are disclosed in Note 5.

(c) Basis of consolidation

The financial statements incorporate the financial statements of the Company and its special purpose entity called 'Stichting ProQR Therapeutics Participation', a Dutch foundation (the "Foundation"). The Foundation was founded with the sole purpose of holding company shares while issuing depositary receipts to employees of the Company upon exercise of equity awards. The Foundation retains the voting rights over the shares in respect of which depository shares are issued. The Foundation is controlled by the management of the Company. Control is achieved where the Company has the power to govern the financial and operating policies of an entity so as to obtain benefits from its activities. As the Foundation's only director is Mr. de Boer, and given the fact that the voting rights held by the Foundation can be used for the benefit of enforcing the interests of the Company's management, the Company concluded that the Foundation is controlled by the management of the Company. The Foundation applies the same accounting principles as those used by the Company.

(d) Recognition of other income

Other income includes amounts earned from third parties and are recognized when earned in accordance with the substance and under the terms of the related agreements and when it is probable that the economic benefits associated with the transaction will flow to the entity and the amount of the income can be measured reliably. Other income relates to a grant received from patient organization the Cystic Fibrosis Foundation for a specific research project that ran in 2012 and 2013. The grant is recognized in other income in the same period in which the related R&D costs are recognized.

(e) Government grants—WBSO

The WBSO ("afdrachtvermindering speur- en ontwikkelingswerk") is a Dutch fiscal facility that provides subsidies to companies, knowledge centres and self-employed people who perform research and development activities (as defined in the WBSO Act). Under this Act, a contribution is paid towards the labor costs of

employees directly involved in research and development. The contribution is in the form of a reduction of payroll taxes and social security contributions. Subsidies relating to labor costs are deferred and recognized in the income statement as negative labor costs over the period necessary to match them with the labor costs that they are intended to compensate.

(f) Foreign currencies

Items included in the Company's financial statements are measured using the currency of the primary economic environment it operates in ("the functional currency"). The financial statements are presented in Euros, which is the Company's functional and presentation currency.

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in the income statement.

(g) Classes of financial instruments

Financial instruments are both primary financial instruments, such as receivables and payables, and financial derivatives. For primary financial instruments, reference is made to the treatment per the corresponding balance sheet item.

Financial derivatives are valued at fair value. Upon first recognition, financial derivatives are recognized at fair value and then revalued as at balance sheet date.

(h) Pension obligations

The Company operates a defined contribution pension plan for all employees funded through payments to an insurance company. The Company has no legal or constructive obligation to pay further contributions once the contributions have been paid. The contributions are recognized as employee benefit expense when they are due. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in the future payments is available.

(i) Share-based payments

The Company operates an equity-settled, share-based compensation plan. The costs of employee share option plans are measured at the fair value of the equity instruments at the grant date.

The fair value determined at the grant date of the equity-settled share-based payments is expensed, based on the Company's estimate of equity instruments that will eventually vest. At the end of each reporting period, the Company revises its estimate of the number of equity instruments expected to vest. The impact of the revision of the original estimates, if any, is recognized in profit or loss such that the cumulative expense reflects the revised estimate, with a corresponding adjustment to the equity-settled employee benefits reserve.

(j) Taxation

Income tax expense represents the sum of the tax currently payable and deferred tax.

Current tax

The tax currently payable is based on taxable profit for the year. Taxable profit differs from profit as reported in the income statement because of items of income or expense that are taxable or deductible in other years and items that are never taxable or deductible. The Company's liability for current tax is calculated using tax rates that have been enacted or substantively enacted by the end of the reporting period.

Deferred tax

Deferred tax is recognized on differences between the carrying amounts of assets and liabilities in the financial statements and the corresponding tax bases used in the computation of taxable profit.

The carrying amount of deferred tax assets is reviewed at the end of each reporting period and reduced to the extent that it is no longer probable that sufficient taxable profits will be available to allow all or part of the asset to be recovered. Since the Company does not expect to be profitable in the foreseeable future, its deferred tax assets are valued at €nil.

Deferred tax assets and liabilities are measured at the tax rates that are expected to apply in the period in which the liability is settled or the asset realised, based on tax rates (and tax laws) that have been enacted or substantively enacted by the end of the reporting period. The measurement of deferred tax liabilities and assets reflects the tax consequences that would follow from the manner in which the Company expects, at the end of the reporting period, to recover or settle the carrying amount of its assets and liabilities.

(k) Intangible assets

Licenses

Acquired patents have a finite useful life and are carried at cost less accumulated amortisation and impairment losses. Amortisation is calculated using the straight-line method to allocate the cost of patents over their estimated useful lives (generally 10 years unless a patent expires prior to that date). Amortisation begins when an asset is available for its intended use.

Research and development

Research expenditures are recognized as expenses as incurred. Costs incurred on development projects are recognized as intangible assets of the date that it can be established that it is probable that future economic benefits that are attributable to the asset will flow to the Company considering its commercial and technological feasibility, generally when filed for regulatory approval for commercial production, and when costs can be measured reliably. Given the current stage of the development of the Company’s products no development expenditures have yet been capitalized.

Registration costs for patents are part of the expenditures for the research and development project. Therefore, registration costs for patents are expensed as incurred as long as the research and development project concerned does not yet meet the criteria for capitalization.

(l) Impairment of tangible and intangible assets

At the end of each reporting period, the Company reviews the carrying amounts of its tangible and intangible assets to determine whether there is any indication that those assets have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of the impairment loss (if any). Where it is not possible to estimate the recoverable amount of an individual asset, the Company estimates the recoverable amount of the cash-generating unit to which the asset belongs. Where a reasonable and consistent basis of allocation can be identified, corporate assets are also allocated to individual cash-generating units, or otherwise they are allocated to the smallest group of cash-generating units for which a reasonable and consistent allocation basis can be identified.

Intangible assets with indefinite useful lives and intangible assets not yet available for use are tested for impairment at least annually, and whenever there is an indication that the asset may be impaired.

The recoverable amount is the higher of fair value less costs to sell and value in use. In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset for which the estimates of future cash flows have not been adjusted.

If the recoverable amount of an asset (or cash-generating unit) is estimated to be less than its carrying amount, the carrying amount of the asset (or cash-generating unit) is reduced to its recoverable amount. An impairment loss is recognized immediately in profit or loss, unless the relevant asset is carried at a revalued amount, in which case the impairment loss is treated as a revaluation decrease.

Where an impairment loss subsequently reverses, the carrying amount of the asset (or cash-generating unit) is increased to the revised estimate of its recoverable amount, but so that the increased carrying amount does not exceed the carrying amount that would have been determined had no impairment loss been recognized for the asset (or cash-generating unit) in prior years. A reversal of an impairment loss is recognized immediately in profit or loss, unless the relevant asset is carried at a revalued amount, in which case the reversal of the impairment loss is treated as a revaluation increase.

(m) Financial assets

All financial assets are recognized and derecognized on the trade date where the purchase or sale of a financial asset is under a contract whose terms require delivery of the financial asset within the timeframe established by the market concerned, and are initially measured at fair value, plus transaction costs, except for those financial assets classified as at fair value through profit or loss, which are initially measured at fair value.

Loans and receivables

Trade receivables, loans and other receivables that have fixed or determinable payments that are not quoted in an active market are classified as “loans and receivables”. Loans and receivables are measured at amortized cost using the effective interest method, less any impairment.

An allowance for doubtful accounts is established when there is objective evidence that the Company will not be able to collect all amounts due according to the original terms of receivables. Significant financial difficulties of the debtor, probability that the debtor will enter into bankruptcy or financial reorganization, and default or delinquency in payments are considered indicators that the trade receivable is impaired. Loans and receivables are included in ‘current assets’, except for maturities greater than 12 months after the balance sheet date, which are classified as ‘non-current assets’.

For all financial assets, the fair value approximates its carrying value.

(n) Cash and cash equivalents

Cash and cash equivalents include cash on hand and all highly liquid investments with original maturities of three months or less that are convertible to a known amount of cash and bear an insignificant risk of change in value.

(o) Financial liabilities and equity instruments

Debt and equity instruments are classified as either financial liabilities or as equity in accordance with the substance of the contractual arrangement.

Equity instruments

An equity instrument is any contract that evidences a residual interest in the assets of an entity after deducting all of its liabilities. Equity instruments issued by the Company are recognized at the proceeds received, net of direct issue costs.

Compound instruments

The component parts of compound instruments (convertible bonds) issued by the Company are classified separately as financial liabilities and equity in accordance with the substance of the contractual arrangement. At the date of issue, the fair value of the liability component is estimated using the prevailing market interest rate for a similar non-convertible instrument. This amount is recorded as a liability on an amortised cost basis using the effective interest method until extinguished upon conversion or at the instrument's maturity date. The equity component is determined by deducting the amount of the liability component from the fair value of the compound instrument as a whole. This is recognized and included in equity, net of income tax effects, and is not subsequently remeasured.

Other financial liabilities

Other financial liabilities, including borrowings, are initially measured at fair value, net of transaction costs incurred, and are subsequently measured at amortised cost using the effective interest method, with interest expense recognized on an effective yield basis.

The effective interest method is a method of calculating the amortised cost of a financial liability and of allocating interest expense over the relevant period. The effective interest rate is the rate that exactly discounts estimated future cash payments through the expected life of the financial liability, or, where appropriate, a shorter period.

Borrowings and other financial liabilities are classified as 'non-current liabilities,' other than liabilities with maturities up to one year, which are classified as "current liabilities".

The Company derecognizes financial liabilities when the liability is discharged, cancelled or expired. For all financial liabilities, the fair value approximates its carrying amount.

4. Financial risk management

The Company's activities expose it to a variety of financial risks: market risk (including currency risk, interest rate risk and price risk), credit risk and liquidity risk. The Company's overall financial risk management seeks to minimize potential adverse effects resulting from unpredictability of financial markets on the Company's financial performance.

Risk management is carried out by the finance department. The finance department identifies and evaluates financial risks and proposes mitigating actions if deemed appropriate.

(a) Market risk

Foreign exchange risk arises from future commercial transactions and recognized assets and liabilities in foreign currencies. In the periods presented, the Company had no significant outstanding receivables, but had expenditures in various currencies, predominately (€1,258,000) in US Dollars. The Company has an exposure associated with the time delay between entering into a contract, budget or forecast and the realization thereof. The impact of fair value measurements on the financial statements is limited.

(b) Interest rate risk

The Company's exposure to interest rate risks is limited due to the use of loans with fixed rates. The Company has two loans and a financial lease with a fixed interest, totalling €3,575,000 at December 31, 2013. Details on the interest rates and maturities of these loans are provided in Notes 11 and 12.

(c) Credit risk

Credit risk represents the risk of financial loss caused by default of the counterparty. The Company has no large receivables balances with external parties. The Company's principal financial assets are cash and cash equivalents which are placed at ABN Amro and Rabobank.

(d) Liquidity risk

Liquidity risk represents the risk that an entity will encounter difficulty in meeting obligations associated with its financial liabilities. Prudent liquidity risk management implies ensuring sufficient availability of cash resources for funding of operations and planning to raise cash as if and when needed, either through issue of shares or through credit facilities. Management monitors rolling forecasts of the Company's liquidity reserve on the basis of expected cash flow.

The table below summarizes ProQR's undiscounted liabilities at year-end 2013:

	2014	2015	2016	2017	2018 and beyond
			(€ in thousands)		
Other non-current liabilities	€ —	€—	€—	€ 314	€ 629
Convertible loan	2,514	—	—	—	—
Finance lease liabilities	35	33	15	—	—
Trade payables	745	—	—	—	—
Social security and other taxes	29	—	—	—	—
Pension premiums	17	—	—	—	—
Other current liabilities	262	—	—	—	—
Total	€3,602	€ 33	€ 15	€ 314	€ 629

5. Critical accounting estimates and judgments

In the application of the Company's accounting policies, which are described in Note 3, management is required to make judgments, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates.

The estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised if the revision affects only that period or in the period of the revision and future periods if the revision affects both current and future periods.

(a) Share-based payments

Share options granted to employees and consultants are measured at the fair value of the equity instruments granted. Fair value is determined through the use of an option-pricing model considering, among others, the following variables:

a) The exercise price of the option;

b) The expected life of the option;

c) The current value of the underlying shares;

d) The expected volatility of the share price;

e) The dividends expected on the shares; and

f) The risk-free interest rate for the life of the option.

For the Company's share option plans, management's judgment is that the Black-Scholes valuation method is the most appropriate for determining the fair value of the Company's share options.

Since the Company's ordinary shares are not publicly traded, there is no published share price information. Consequently the Company needs to estimate the fair value of its shares and the expected volatility of that value. The expected volatility of all options granted is therefore based on the average historical volatility of the Company's peers over a period that agrees with the period of maturity. All assumptions and estimates are further discussed in Note 13(d) to the financial statements. The value of the underlying shares was determined on the basis of the prior sale of company stock method. As such, the Company has benchmarked the value per share to external transactions of Company shares and external financing rounds.

The result of the share option valuations and the related compensation expense is dependent on the model and input parameters used. Even though management considers the fair values reasonable and defensible based on the methodologies applied and the information available, others might derive a different fair value for the Company's share options.

(b) Corporate income taxes

The Company recognizes deferred tax assets arising from unused tax losses or tax credits only to the extent that the Company has sufficient taxable temporary differences or there is convincing evidence that sufficient taxable profit will be available against which the unused tax losses or unused tax credits can be utilized. Management's judgment is that such convincing evidence is currently not sufficiently available and a deferred tax asset is therefore only recognized to the extent that the Company has sufficient taxable temporary differences.

6. Cash and cash equivalents

	December 31, 2012	December 31, 2013
	(€ in thousands)	
Cash at banks	€ 249	€ 4,129
	€ 249	€ 4,129

The cash at banks is at full disposal of the Company.

7. Other receivables

	December 31, 2012	December 31, 2013
	(€ in thousands)	
Prepayments	€ 3	€ 3
Other receivables	24	57
	€ 27	€ 59

All receivables are considered short-term and due within one year.

8. Social securities and other taxes

	December 31, 2012	December 31, 2013
	(€ in thousands)	
Value added tax	€ 23	€ 73
	€ 23	€ 73

9. Property, plant and equipment ('PP&E')

	Period February 21, – December 31, 2012	Year ended December 31, 2013
	(€ in thousands)	
PP&E at cost:		
Leasehold improvements	€ —	€ 5
Laboratory equipment	—	190
Other	—	33
PP&E at cost	—	228
Depreciation for the period:		
Leasehold improvements	—	1
Laboratory equipment	—	19
Other	—	4
Accumulated depreciation	—	24
Carrying value at the end of the period	—	204
Carrying value per category at the end of the period		
Leasehold improvements	—	4
Laboratory equipment	—	171
Other	—	29
Total carrying value at the end of the period	—	€ 204

The depreciation charge is included in the research and development costs (€24,000) and the general and administrative costs (€nil).

10. Intangible assets

	Period February 21, – December 31, 2012	Year ended December 31, 2013
	(€ in thousands)	
Intangible Assets, at cost		
Licenses	€ 39	€ 39
Intangible assets at cost	39	39
Additions, at cost		
Licenses	—	—
Movement for the period	—	—
Amortization for the period		
Licenses	—	—
Accumulated amortization	—	—
Carrying value at the end of the period	€ 39	€ 39

In 2012, the Company acquired an exclusive license from the Massachusetts General Hospital. The initial payment in respect of the license, in the amount of €39,000, will be amortized over the commercial life of products based on the license during the patent-life.

11. Current liabilities

	December 31, 2012	December 31, 2013
	(€ in thousands)	
Convertible loan[a]	€ —	€ 2,514
Current portion finance lease liabilities	—	35
Trade payables	95	745
Social securities and other taxes	3	29
Pension premiums	7	17
Accrued expenses and other liabilities	38	262
	143	3,602

(a) Convertible loan

	Period February 21 – December 31 2012	Year ended December 31, 2013
	(€ in thousands)	
Balance at the beginning of the period	€ —	€ —
Initial recognition new convertible loan	—	2,500
Accrued interest	—	14
Balance at the end of the period	—	2,514

On November 15, 2013, the Company concluded a convertible loan amounting to €2,500,000 with a number of shareholders. The loan carries interest of 6% per annum and was convertible into shares in a new financing round. The participants to the convertible loan had the right to receive an agreed-upon discount on the issue price of new shares if they elected to convert their loan in any new financing round.

The majority of the Company's current liabilities are denominated in euros.

12. Liabilities

(a) Finance lease liabilities

	Period February 21 – December 31 2012	Year ended December 31, 2013
	(€ in thousands)	
Balance at the beginning of the period	€ —	€ —
Initial recognition new finance leases	—	91
Interest expense accrued	—	11
Payment of finance lease liabilities	—	(19)
Balance at the end of the period	—	83
Current portion at the end of the period	—	(35)
	—	48

Certain of the Company's property, plant and equipment items are subject to finance leases. These leases relate to laboratory equipment.

Future minimum lease payments under finance leases as at December 31, 2013 are as follows:

	2012		2013	
	Minimum payments	Present value of payments	Minimum payments	Present value of payments
	(€ in thousands)			
Within one year	€ —	€ —	€ 35	€ 34
After one year but not more than five years	—	—	48	46
More than five years	—	—	—	—

As of December 31, 2013, the carrying value of leased assets was €83,000, all of which related to laboratory equipment. The interest used for the present value of payments is 2%.

(b) Borrowings

	December 31, 2012	December 31, 2013
	(€ in thousands)	
Innovation credit	€ 95	€ 922
Accrued interest on innovation credit	1	21
	96	943

Innovation credit ("Innovatiekrediet")

On June 1, 2012, ProQR was awarded an Innovation credit by the Dutch government, through its agency AgentschapNL of the Ministry of Economic Affairs, for the Company's Cystic Fibrosis program. The credit was increased in the course of 2013. The credit covers 35% of the costs incurred in respect of the program up to an initial maximum of €5.0 million through November 30, 2015.

The credit is interest-bearing at a rate of 10% per annum. The credit, including accrued interest, is repayable in three instalments on January 31, 2017, January 31, 2018 and January 31, 2019, depending on the technical success of the program.

The assets which are co-financed with the granted innovation credit are subject to a right of pledge of the benefit of AgentschapNL.

13. Shareholders' equity

(a) Issued capital

	December 31, 2012	December 31, 2013
	(€ in thousands)	
Share capital	€ 33	€ 59
Share premium	484	3,482
	€ 517	€ 3,541

The authorized share capital of the Company amounting to €90,000 consists of 90,000 ordinary shares with a par value of €1.00 per share. All issued shares have been fully paid in cash.

(b) Treasury shares

All treasury shares presented in the statement of changes in equity relate to shares that have been issued during the period to the Foundation. As these share have legally been issued, but the Foundation is within control of the Company, these shares are presented as treasury shares.

(c) Equity settled employee benefit reserve

The costs of share options for employees, members of the supervisory board, members of the management board and consultants are recognized in the income statement, together with a corresponding increase in equity during the vesting period, taking into account (deferral of) corporate income taxes. The accumulated expense of share options recognized in the income statement is shown separately in the equity category ‘equity settled employee benefit reserve’ in the ‘statement of changes in equity’.

(d) Share options

The Company operates an equity-settled share-based compensation plan which was introduced in 2013. The supervisory board may grant options to employees, members of the supervisory board, members of the management board and consultants. The compensation expenses included in operating costs for this plan were €41,000 in 2013.

Options granted under this stock option plan are exercisable once vested. Any vesting schedule may be attached to the granted options, however the typical vesting period is four years (25% after every year). The options expire ten years after date of grant. Options granted under the stock option plan are granted at exercise prices which equal the fair value of the ordinary shares of the Company at the date of the grant.

The Company accounts for its employee stock options under the fair value method. The fair value of the options is estimated at the date of grant using the Black-Scholes option-pricing model, with the following assumptions:

	Options granted in 2013
Risk-free interest rate	0.942%
Expected dividend yield	0%
Expected volatility	93.8%
Expected life in years	5 years

The resulting weighted average grant date fair value of the options amounted to €80.78 as of December 31, 2013.

Movements in the number of options outstanding and their related weighted average exercise prices are as follows:

	Number of options	Average exercise price
Balance at January 1, 2013	—	€ —
Granted	3,736	113.34
Forfeited	(10)	113.34
Exercised	—	—
Lapsed	—	—
Balance at December 31, 2013	3,726	113.34

Please refer to Note 20 for options of key management personnel.

14. Research and development costs

Research and development costs amounted to €2,550,000 in 2013 (2012: €285,000) and comprise allocated employee costs, the costs of materials and laboratory consumables, license- and IP-costs and allocated other costs.

15. Employee benefits

	Period February 21 – December 31 2012	January 1 – December 31 2013
	(€ in thousands)	
Wages and salaries	€ 138	€ 677
Social security costs	15	112
Pension costs—defined contribution plans	7	49
Other personnel costs	19	71
	179	909
Average number of employees for the period	3.0	13.4

Included in the wages and salaries for 2013 is a credit of €150,000 (2012: €37,000) with respect to WBSO subsidies; see Note 3(e).

16. Financial income and expense

	Period February 21 – December 31 2012	January 1 – December 31 2013
	(€ in thousands)	
Interest income:		
Current accounts and deposits	€ 2	€ 24
Interest costs:		
Interest on loans	1	38
Finance (costs)/income—net	1	(14)

17. Income taxes

The calculation of the tax charge is as follows:

	January 1 – December 31, 2013
	(€ in thousands)
Income tax provision based on domestic rate (25%)	€ 813
Less: Valuation allowance	(813)
Income tax charge	—
Effective tax rate	0%

Due to the operating losses incurred since inception the Company has no tax provisions as of the balance sheet date. Furthermore, no significant temporary differences exist between accounting and tax results.

Realization of deferred tax assets is dependent on future earnings, if any, the timing and amount of which are uncertain. Accordingly, the Company has not yet recognized any deferred tax asset related to operating losses. As per December 31, 2013, the Company has a total amount of €3.7 million tax loss carry-forwards available for offset against future taxable profits. According to current tax regulations the first amount of the tax loss carry-forwards will expire in 2021.

18. Earnings per share

(a) Basic and diluted earnings per share

Basic earnings per share are calculated by dividing the result attributable to equity holders of the Company by the weighted average number of shares outstanding during the year.

	Period February 21 – December 31 2012	January 1 – December 31 2013
	(€ in thousands)	
Result attributable to equity holders of the Company	€ (418)	€ (3,253)
Weighted average number of shares	24,556	54,199
Basic (and diluted) earnings per share (€ per share)	(17.04)	(60.01)

(b) Diluted earnings per share

For the periods included in these financial statements, the share options are not included in the diluted earnings per share calculation as the Company was loss-making in all periods. Due to the anti-dilutive nature of the outstanding options, basic and diluted earnings per share are equal.

(c) Dividends per share

The Company did not declare dividends for any of the years presented in these financial statements.

19. Commitments and contingencies

(a) Claims

There are no claims known to management related to the activities of the Company.

(b) Rent

Since 2012, the Company is domiciled in Leiden. It has concluded rental agreements for laboratory space and offices with MicroSafe Laboratories and Pharming Technologies B.V. The first of these agreements runs until December 31, 2014; the second automatically renews annually.

The annual obligation currently amounts to €194,000, while the 2013 rent expense amounted to €113,000 (2012:€13,000).

(c) Patent license agreement

The Company and The General Hospital Corporation have concluded a Patent License Agreement under which the Company may have certain royalty obligations. ProQR has concluded license agreements with third parties that may require the Company to pay royalties or milestone fees if certain defined development milestones are achieved.

(d) Research and development commitments

The Company has committed itself to a number of obligations amounting to €953,000, all of which are due in 2014.

20. Related-party transactions

Details of transactions between the Company and related parties are disclosed below.

(a) Compensation of the Supervisory Board

The sole member of the supervisory board during 2013, Gerard Platenburg, was appointed on August 21, 2012. His remuneration for 2013 amounted to €34,000 (2012: €8,000), of which €22,000 was attributable to advisory fees paid to Progress Therapeutics B.V., a company owned and controlled by Mr. Platenburg, and €12,000 was attributable to share-based payments to Mr. Platenburg. The remuneration comprised only short-term employee benefits as set out in the table below:

		2013		
	Period February 21 – December 31 2012	Advisory fees	Share-based payments	Total
		(€ in thousands)		
G.J. Platenburg	€ 8	€ 22	€ 12	€ 34
	€ 8	€ 22	€ 12	€ 34

As of December 31, 2013, Progress Therapeutics B.V., a company owned and controlled by Mr. Platenburg, holds 9,177 ordinary shares in the Company and Mr. Platenburg holds 1,059 options.

(b) Compensation of key management personnel

The total remuneration of the chief executive officer and senior management in 2013 amounted to €355,000 with the details set out in the table below:

		2013			
	Period February 21 – December 31, 2012	Short term employee benefits	Post employment benefits	Share-based payments	Total
		(€ in thousands)			
Mr. D.A. de Boer	€ 88	€ 180	€ 8	€ 7	€195
Senior Management	53	134	11	15	160
	€ 141	€ 314	€ 19	€ 22	€355

As of December 31, 2013, Daniel de Boer, founder of the Company, holds 12,709 ordinary shares in the Company. 3,529 of these shares were paid-in through a loan that Mr. de Boer received from the Company for a total value of €402,000. As part of the agreement, Mr. de Boer has a put option to return the shares to the Company under certain conditions. This put option is accounted for as a fully vested option for which share-based payment expenses are recognized.

In addition, as Mr. de Boer has the right to return the shares to the Company in order to repay his loan, the full loan amount of €402,000 is netted in equity, and the related shares are treated as treasury shares.

(c) Other related party transactions

The Company has loan agreements with the Foundation which is a related party, since a member of the Company's management board and shareholder is also chairman of the Foundation. These loans carry interest of 4% per annum. On December 31, 2013, a total amount of €7,000 (2012: €2,000) was outstanding. At December 31, 2013 the Company had issued 10,585 shares (December 31, 2012: 1,765 shares) to the Foundation, which are considered treasury shares.

21. Events after balance sheet date

(a) Financing round

On April 17, 2014, the Company completed a financing round of €41,998,000, which includes conversion of the existing convertible loan, with existing and new shareholders, against issuance of 81,187 preferred shares to investors.

(b) Repayment of loan Mr. D. de Boer

On June 20, 2014, Mr. D. de Boer repaid to ProQR the loan described in Note 20 through the sale of ordinary shares to the Foundation.

22. Segment Information

The Company operates in one reportable segment, which comprises the discovery and development of innovative, RNA based therapeutics. The management board is identified as the chief operating decision maker. The management board reviews the operating results regularly to make decisions about resources and to assess overall performance.

The Company has not generated any revenues since inception.

The amounts provided to the management board with respect to total assets and liabilities are measured in a manner consistent with that of the financial statements.

Shares

ORDINARY SHARES

Prospectus

Leerink Partners
Deutsche Bank Securities
JMP Securities
H.C. Wainwright & Co., LLC

, 2014

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 6. ***Indemnification of directors.***

Although Dutch law does not expressly provide for the indemnification of directors, the concept of indemnification of directors of a company for liabilities arising from their actions as members of the management board and supervisory board is, in principle, accepted in the Netherlands. Our articles of association provide that we will indemnify our management board members, supervisory board members, former management board members and former supervisory board members against (i) any financial losses or damages incurred by such indemnified person and (ii) any expense reasonably paid or incurred by such indemnified person in connection with any threatened, pending or completed suit, claim, action or legal proceedings, whether civil, criminal, administrative or investigative and whether formal or informal, in which he becomes involved, to the extent this relates to his position with the company, in each case to the fullest extent permitted by applicable law. No indemnification shall be given to an indemnified person (a) if a Dutch court has established, without possibility for appeal, that the acts or omissions of such indemnified person that led to the financial losses, damages, suit, claim, action or legal proceedings result from either an improper performance of his duties as an officer of the company or an unlawful or illegal act and (b) to the extent that his financial losses, damages and expenses are covered by an insurance and the insurer has settled these financial losses, damages and expenses (or has indicated that it would do so). Our supervisory board may stipulate additional terms, conditions and restrictions in relation to such indemnification.

Reference is made to Sections 6 and 7 of the form of Underwriting Agreement filed as Exhibit 1.1 to the registration statement, which sets forth the registrant's and the underwriters' respective agreement to indemnify each other and to provide contribution in circumstances where indemnification is unavailable.

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

Item 7. ***Recent sales of unregistered securities***

Set forth below is information regarding option awards and unrestricted and restricted share issuances made by us since our incorporation in February 2012. Also included is the consideration, if any, received by us for such option awards and shares and information relating to the section of the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

Option awards

The table below summarizes all the option awards we have made since our inception pursuant to our Stock Option Plan. The grant of the option awards and the issuance of ordinary shares upon the exercise of options described in the table below were or will be made pursuant to Regulation S under the Securities Act, written compensatory plans or arrangements with our employees and directors in reliance on the exemption provided by Rule 701 promulgated under Section 3(b) of the Securities Act, or Rule 701. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Date Of Grant	Number Of Shares Underlying Share Options	Current Exercise Price Per Share
September 26, 2013	2,677	€113.34
December 1, 2013	1,059	€113.34
January 1, 2014	100	€113.34
January 14, 2014	1,200	€113.34
February 1, 2014	700	€113.34
May 1, 2014	1,059	€309.50
May 31, 2014	235	€309.50
June 30, 2014	2,490	€309.50

Share issuances

On April 21, 2012, we entered into a seed loan agreement with certain investors and the chairman of our supervisory board, Dinko Valerio, in the principal amount of €300,000. On August 21, 2012, we issued an aggregate of 17,293 ordinary shares pursuant to the conversion of the seed loan agreement and for additional consideration of €201,765 in cash.

On February 6, 2013, we issued an aggregate of 19,371 ordinary shares to certain investors for aggregate consideration of €1,472,601 in cash.

On May 3, 2013, we issued an aggregate of 15,920 ordinary shares to certain investors for aggregate consideration of €1,559,770 in cash.

On November 22, 2013, we issued convertible notes to certain investors in the principal amount of €2,500,000.

On April 17, 2014, we issued an aggregate of 81,187 preferred shares pursuant to the conversion of the convertible notes and for additional consideration of €39,498,410 in cash.

On June 30, 2014, we issued 601 depository receipts to two existing shareholders upon the exercise of options to purchase depository receipts for aggregate consideration of €68,117 in cash.

All of the foregoing issuances were made outside the United States pursuant to Regulation S or to U.S. persons pursuant to Section 4 (2) of the Securities Act.

Item 8. ***Exhibits and financial statement schedules***

(a) The Exhibit Index is incorporated herein by reference.

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or the notes thereto.

Item 9. ***Undertakings***

(a) The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

(b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the

Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

(c) The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-1 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, on , 2014.

PROQR THERAPEUTICS B.V.

By: _____
Name: Daniel de Boer
Title: Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints Daniel de Boer and René Beukema, and each of them, as attorney-in-fact with full power of substitution, for him or her in any and all capacities, to do any and all acts and all things and to execute any and all instruments which said attorney and agent may deem necessary or desirable to enable the registrant to comply with the Securities Act, and any rules, regulations and requirements of the Securities and Exchange Commission thereunder, in connection with the registration under the Securities Act of ordinary shares of the registrant (the "Shares"), including, without limitation, the power and authority to sign the name of each of the undersigned in the capacities indicated below to the Registration Statement on Form F-1 (the "Registration Statement") to be filed with the Securities and Exchange Commission with respect to such Shares, to any and all amendments or supplements to such Registration Statement, whether such amendments or supplements are filed before or after the effective date of such Registration Statement, to any related Registration Statement filed pursuant to Rule 462(b) under the Securities Act, and to any and all instruments or documents filed as part of or in connection with such Registration Statement or any and all amendments thereto, whether such amendments are filed before or after the effective date of such Registration Statement; and each of the undersigned hereby ratifies and confirms all that such attorney and agent shall do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

SIGNATURES	TITLE	DATE
_____ Daniel de Boer	Chief Executive Officer *(Principal Executive Officer)*	, 2014
_____ André Verwei	Head of Finance *(Principal Financial and Accounting Officer)*	, 2014
_____ Dinko Valerio	Chairman, Supervisory Board	, 2014
_____ Antoine Benjamin Papiernik	Director, Supervisory Board	, 2014
_____ Henri Termeer	Director, Supervisory Board	, 2014

PROQR THERAPEUTICS B.V.
Authorized Representative in the United States

By: _____ , 2014
Name:
Title:

Table of Contents

EXHIBIT INDEX

Exhibit No.	Description
1.1*	Form of Underwriting Agreement
3.1*	Articles of Association of the Registrant as in effect prior to this offering
3.2*	Amended Articles of Association of the Registrant to be effective upon the closing of this offering
4.1*	Registration Rights Agreement by and between the Registrant and the shareholders party thereto
5.1*	Form of Opinion of NautaDutilh N.V., Dutch legal counsel of the Registrant
8.1*	Form of Tax Opinion of Goodwin Procter LLP
8.2*	Form of Tax Opinion of NautaDutilh N.V. (included in Exhibit 5.1)
10.1*	Exclusive Patent License Agreement dated as of May 29, 2012 by and between the Registrant and The General Hospital Corporation d/b/a Massachusetts General Hospital
10.2*+	Employment Agreement dated as of October 2, 2013 by and between the Registrant and Daniel Anton de Boer
10.3*+	Employment Agreement dated as of October 2, 2013 by and between the Registrant and René Beukema
21.1	Subsidiaries of the Registrant
23.1*	Consent of Deloitte Accountants B.V., Independent Registered Public Accounting Firm
23.2*	Form of Consent of NautaDutilh N.V. (included in Exhibit 5.1)
23.3*	Form of Consent of Goodwin Procter LLP (included in Exhibit 8.1)
23.4*	Form of Consent of NautaDutilh N.V. (included in Exhibit 8.2)
24.1	Powers of Attorney (included on signature page)

* To be filed by amendment

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

\+ Management contract or compensatory plan or arrangement

Exhibit 21.1

Subsidiaries of the Registrant

None