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

FORM 20-F

(Mark One)

REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

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

For the fiscal year ended December 31, 2019

OR

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

OR

SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of event requiring this shell company report: Not applicable
For the transition period from ____ to ____

Commission file number 001-36622

PROQR THERAPEUTICS N.V.

(Exact name of Registrant as specified in its charter)

The Netherlands

(Jurisdiction of incorporation or organization)

**Zernikedreef 9
2333 CK Leiden
The Netherlands**

(Address of principal executive offices)

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(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, nominal value € 0.04 per share	PRQR	NASDAQ Stock Market

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None
(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None
(Title of Class)

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

Ordinary shares, nominal value € 0.04 per share: 49,745,687

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

Yes No

Note – Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

Yes No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or an emerging growth company. See definition of "large accelerated filer", "accelerated filer", and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer

Accelerated filer

Non-accelerated filer

Emerging growth company

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards[†] provided pursuant to section 13(a) of the Exchange Act.

[†]The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP

International Financial Reporting Standards Other
as issued by the International Accounting Standards Board

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

Item 17 Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes No

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court.

Yes No

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Introduction

This document contains information required for the annual report on Form 20-F for the year ended December 31, 2019 of ProQR Therapeutics N.V. (the “2019 Form 20-F”). Unless the context specifically indicates otherwise, references in this 2019 Form 20-F to “ProQR Therapeutics N.V.,” “ProQR Therapeutics,” “ProQR,” “we,” “our,” “ours,” “us,” the “Company” or similar terms refer to ProQR Therapeutics N.V.

IFRS based information

The audited financial statements as at December 31, 2019 and 2018, and for the years ended December 31, 2019, December 31, 2018 and December 31, 2017, included in the 2019 Form 20-F have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB).

Non-GAAP information

In presenting and discussing our financial position, operating results and cash flows, management uses certain non-GAAP financial measures. These non-GAAP financial measures should not be viewed in isolation as alternatives to the equivalent IFRS measure and should be used in conjunction with the most directly comparable IFRS measure(s).

Exchange rates

All references in this annual report 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 maintain our books and records in euro. We present our financial statements in euro, which is the Company’s functional currency.

Fair value information

In presenting our financial position, fair values are used for the measurement of various items in accordance with the applicable accounting standards. These fair values are based on market prices, where available, and are obtained from sources that are deemed to be reliable. Readers are cautioned that these values are subject to changes over time and are only valid at the balance sheet date. When quoted prices or observable market values do not exist, fair values are estimated using valuation models, which we believe are appropriate for their purpose. They require management to make significant assumptions with respect to future developments which are inherently uncertain and may therefore deviate from actual developments. Critical assumptions used are disclosed in the financial statements. In certain cases, independent valuations are obtained to support management’s determination of fair values.

Trademarks

“ProQR” and “Axiomer” are our main trademarks. Other trademarks or trade names referred to in this annual report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this annual report 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.

Forward-looking statements

Pursuant to provisions of the United States Private Securities Litigation Reform Act of 1995, ProQR is providing the following cautionary statement.

This document contains certain forward looking statements with respect to the financial condition, results of operations and business of ProQR and certain of the plans and objectives of ProQR with respect to these items. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events, including our clinical development plans or our future financial performance, our development programs, including timing, plans, results and therapeutic potential with respect to our product candidates, our business operations, including timing of commencing clinical trials and enrollment of patients therein, the expected impact of the COVID-19 on our business operations, including our research and development plans and timelines and the supply chain for our clinical and development programs, and our financial position and cash runway, expressed or implied by these forward-looking statements. Forward-looking statements can be identified generally as those containing words as “aim,” “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions, although not all forward-looking statements contain these identifying words.

Known and unknown risks, uncertainties and other factors may cause our actual results, performance or achievements, including in relation to the clinical development of sepfarsen (formerly known as QR-110), QR-421a, QR-1123, QR-504a, eluforsen (formerly known as QR-010) or any other pipeline program, to be materially different from our expectations. These risks include, but are not limited to, the cost, timing and results of preclinical studies and clinical trials and other development activities by us and our collaborative partners, the impact on our operations and activities that may be slowed or halted by the COVID-19 pandemic; the likelihood of our clinical programs being executed on timelines provided and reliance on our contract research organizations and predictability of timely enrollment of subjects and patients to advance our clinical trials and maintain their own operations; our reliance on contract manufacturers to supply materials for research and development and the risk of supply interruption from a contract manufacturer; the potential for future data to alter initial and preliminary results of early-stage clinical trials; the unpredictability of the duration and results of the regulatory review of applications or clearances that are necessary to initiate and continue to advance and progress our clinical programs; the ability to secure, maintain and realize the intended benefits of collaborations with partners; the possible impairment of, inability to obtain, and costs to obtain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in research and development; and general business, financial and accounting risks and litigation, and the other risks discussed in further detail in Item 3.D: “Risk Factors”.

Forward-looking statements appear in a number of places in this Annual Report and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to management. By their nature, forward-looking statements involve risk and uncertainty, because they relate to events that depend on circumstances that will occur in the future. As a result, ProQR’s actual future results may differ materially from the plans, goals and expectations set forth in such forward-looking statements. For a discussion of factors that could cause future results to differ from such forward-looking statements, reference is made to the information in Item 3.D: “Risk Factors”.

Forward-looking statements speak only as of the date they are made, and we do not undertake any obligation to update them in light of new information or future developments or to release publicly any revisions to these statements in order to reflect later events or circumstances or to reflect the occurrence of unanticipated events.

Part I

Item 1: Identity of Directors, Senior Management and Advisers

Not applicable.

Item 2: Offer Statistics and Expected Timetable

Not applicable.

Item 3: Key Information

A. Selected financial data

The following table sets forth selected financial data for ProQR Therapeutics N.V. for the periods indicated. We derived the selected financial data from our consolidated audited financial statements 2015 through 2019.

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 the information in Item 5: “Operating and Financial Review and Prospects” and with our audited consolidated financial statements and notes thereto included elsewhere in this annual report. Our financial statements are prepared in accordance with IFRS as issued by the IASB.

	Year Ended December 31, 2019	Year Ended December 31, 2018	Year Ended December 31, 2017	Year Ended December 31, 2016	Year Ended December 31, 2015
(€ in thousands, except for per share data)					
Statement of comprehensive loss data:					
Other income	1,933	5,761	1,495	1,828	3,235
Research and development costs	(46,491)	(29,514)	(31,153)	(31,923)	(23,401)
General and administrative costs	(12,887)	(12,540)	(10,840)	(9,478)	(6,837)
Operating result	(57,445)	(36,293)	(40,498)	(39,573)	(27,003)
Finance income and expense	402	(792)	(3,175)	470	6,171
Results related to associates	429	—	—	—	—
Corporate income taxes	(132)	(1)	(2)	—	—
Result for the year	(56,746)	(37,086)	(43,675)	(39,103)	(20,832)
Other comprehensive income	43	(28)	151	(16)	1
Total comprehensive loss (attributable to equity holders of the Company)	(56,703)	(37,114)	(43,524)	(39,119)	(20,831)
Share information					
Weighted average number of shares outstanding	41,037,244	34,052,520	25,374,807	23,346,507	23,343,262
Basic and diluted loss per share attributable to the equity holders of the Company (expressed in Euro per share)	€ (1.38) €	(1.08) €	(1.72) €	(1.67) €	(0.89)

	As at December 31,				
	2019	2018	2017	2016	2015
(€ in thousands)					
Statement of financial position data:					
Cash and cash equivalents	111,950	105,580	48,099	94,865	112,736
Total assets	117,535	110,231	53,103	100,109	115,247
Total liabilities	23,702	17,546	13,778	10,310	5,843
Total shareholders' equity	94,329	92,915	39,363	89,799	109,404

B. Capitalization and indebtedness

Not applicable.

C. Reasons for the offer and use of proceeds

Not applicable.

D. Risk factors

Our business is subject to numerous risks and uncertainties. If any of these risks actually occurs, our business, prospects, operating results and financial condition could suffer materially. These risks include, but are not limited to, the following:

Risks Related to Our Capital Needs and Financial Position

We are a 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 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 a significant portion of our resources to the development of our product candidates in cystic fibrosis (CF), eluforsen; Leber's congenital amaurosis (LCA), sepfarsen; epidermolysis bullosa (EB), QR-313; Usher syndrome, QR-421a; and autosomal dominant retinitis pigmentosa (adRP), QR-1123. We have had significant operating losses since our inception. Our net losses for the years ended December 31, 2017, December 31, 2018 and December 31, 2019 were, € 43,675,000, € 37,086,000 and € 56,746,000 respectively. At December 31, 2019, we had an accumulated deficit of € 211,746,000. 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. Most of our technologies and product candidates are in early stages of development – except for sepfarsen, which is in a late stage 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 material income we have generated has been from the receipt of (government) research grants. Our ability to generate revenue and become profitable depends upon our ability to obtain marketing approval and successfully commercialize sepfarsen, QR-421a, QR-1123 or any 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 product candidates 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, preclinical 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 our product candidates also depends on a number of additional factors, including our ability to:

- successfully complete development activities, including the ongoing and planned preclinical and clinical studies for our product candidates;
- complete and submit New Drug Applications (NDAs) to the U.S. Food and Drug Administration (FDA) and Marketing Authorization Applications (MAAs) to the European Medicines Agency (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;
- continue to 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 that we do not intend to sell ourselves in one or more markets;
- achieve acceptance among patients, clinicians and advocacy groups for any product we develop; and
- obtain coverage and adequate reimbursement for our products from third-parties, 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 preclinical 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. Moreover, commercialization of QR-421a will trigger payments of up to \$ 37.5 million pursuant to our agreement with Foundation Fighting Blindness (FFB). Under our collaboration with Ionis related to our QR-1123 product candidate, we will be required to make payments to Ionis upon achievement of development and sales milestones, and royalty payments as a percentage of annual net sales. See “Item 5. Operating and Financial Review and Prospects” and the notes to the financial statements included elsewhere in this annual report for more details on these transactions.

Even if we are able to generate revenues from the sale of any of our product candidates, 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 our product candidates.

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 preclinical 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 serve the United States, the European Union and certain other markets. As at December 31, 2019, we had € 111,950,000 in cash and cash equivalents. Based on our current operating plan, we believe that the existing cash and cash equivalents will be

sufficient to fund our anticipated level of operations into the second half of 2022. 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 preclinical studies and clinical trials for our product candidates, and the resumption of, and expenses associated with, our development activities that have been disrupted due to the COVID-19 outbreak;
- the clinical development plans we establish for these product candidates;
- the number and characteristics of product candidates that we develop or may in-license, or programs that we may pursue in our innovation unit;
- the terms of any collaboration arrangements we may choose to enter into;
- 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 may 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 to evaluate the success of our business to date and to assess our future viability.

We were founded 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. 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.

COVID-19 may materially and adversely affect our business and our financial results.

The recent outbreak of COVID-19 originated in Wuhan, China in December 2019 and has since spread globally, including to the United States and European countries. The continued spread of COVID-19 could adversely impact our clinical trials or preclinical studies, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. For instance, the COVID-19 outbreak has resulted in the delay of all of our ongoing and scheduled trials, including our ongoing pivotal trial of sepoparsen for LCA10. While we are implementing mitigation procedures designed to enable us to resume our development activities when the disruption resolves, there can be no assurance that these procedures will be successful or that we can avoid a material and adverse disruption to our business. As the outbreak continues, we have experienced the prioritization of hospital resources toward the outbreak and restrictions in travel. Furthermore, some patients may be unwilling to enroll in our trials or be unable to comply with clinical trial protocols if quarantines or travel restrictions impede patient movement or interrupt healthcare services. COVID-19 may also negatively affect the operations of third-party contract research organizations that we rely upon to carry out our clinical trials or the operations of our third-party manufacturers, which could result in delays or disruptions in the supply of our product candidates. While we do not currently believe our supply chain has been affected, there can be no assurances that we will not experience supply disruptions in the future. The negative impact COVID-19 has had and may continue to have to patient enrollment or treatment or the timing and execution of our clinical trials could cause costly delays to our clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our business and financial results.

In addition, COVID-19 has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions and business shutdowns. We have taken and may continue to take temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring some or all of our employees to work remotely, suspending all non-essential travel worldwide for our employees and discouraging employee attendance at industry events and in-person work-related meetings. These measures could negatively affect our business. For instance, temporarily requiring employees to work remotely may disrupt our operations or increase the risk of a cybersecurity incident. COVID-19 has also caused volatility in the global financial markets and threatened a slowdown in the global economy, which may negatively affect our ability to raise additional capital on attractive terms or at all.

The extent to which COVID-19 may impact our business will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, the severity of COVID-19 or the effectiveness of actions to contain and treat for COVID-19. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage, however, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business and our results of operation and financial condition.

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

We depend on the success of our product candidates, most of which are in early phases of development. We cannot be certain that we will be able to successfully complete the clinical development of, obtain regulatory approval for, or successfully commercialize our product candidates.

We currently have no products on the market, and only one of our product candidates, sepfarsen, is currently in a Phase 2/3 pivotal trial. In October 2019, we reported final results from our Phase 1/2 clinical trial of this lead product candidate, and in April 2019 we dosed the first patient in the pivotal trial for sepfarsen. There can be no assurance that we will complete the trial in the desired timeframe or at all, particularly since as of the date of this report, all of our ongoing and scheduled trials have experienced delay due to the COVID-19 outbreak.

Our business also depends on the successful clinical development, regulatory approval and commercialization of our other product candidates, and will require additional preclinical testing and substantial additional clinical development and regulatory approval efforts before we are permitted to commence their commercialization, if ever. It will be several years before we can complete a pivotal study for any of our other product candidates, if ever.

The clinical trials and manufacturing and marketing of our 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 preclinical 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 our existing funds. 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 be certain that any 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 our product candidates, our business will be substantially harmed.

We are not permitted to market our product candidates in the United States or the European Union until we receive an NDA approval from the FDA or an MAA approval from the European Commission, 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 MAA to the EMA for approval of our product candidates, we will need to complete the ongoing preclinical and toxicology studies, as well as proof-of-concept studies and Phase 1, Phase 2 and Phase 3 clinical trials. While we intend to submit marketing applications for our product candidates that successfully complete clinical development, there can be no assurance that we will be able to do so in a timely manner or at all. Successfully initiating and completing clinical programs 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 our product candidates for many reasons, including, among others:

- we may not be able to demonstrate that our product candidates are safe and effective in treating patients 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 our product candidates;
- the contract research organizations (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 preclinical studies and clinical trials insufficient to demonstrate that the clinical and other benefits of our products outweigh their safety risks;
- the FDA or the EMA may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA or the EMA may not accept data generated at our clinical trial sites;
- if our NDAs or MAAs, if and when submitted, are reviewed by the FDA or the EMA, as applicable, these regulatory agencies may have difficulties scheduling the necessary review meetings in a timely manner, may recommend against approval of our application or may require, as a condition of approval, additional preclinical 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 our product candidates. Any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

Changes in regulatory requirements, FDA guidance or unanticipated events during our clinical studies may occur, which may result in changes to clinical study protocols or additional clinical study requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance or unanticipated events during our clinical studies may force us to amend clinical study protocols or the FDA may impose additional clinical study requirements, or involve delays to the clinical trials. Amendments to our clinical study protocols would require resubmission to the FDA and Institutional Review Boards (IRBs) for review and approval, which may adversely impact the cost, timing and/or successful completion of a clinical study. For example, while we have reached agreement with the FDA on the design of the Phase 2/3 pivotal trial for our lead product candidate sepopofarsen, there can be no assurance that there will be no changes to the planned design of this trial or that we will not be required to conduct additional testing for this product candidate. If we experience delays completing—or if we terminate—any of our clinical studies, or if we are required to conduct additional clinical studies, the commercial prospects for our product candidates may be harmed and our ability to generate product revenue will be delayed.

Failures or delays in the commencement or completion of our preclinical studies or ongoing or planned clinical trials of our product candidates could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

Successful completion of clinical trials is a prerequisite to submitting an NDA to the FDA or a MAA to the EMA and, consequently, the ultimate approval and commercial marketing of our product candidates. 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 IRB or ethics committee 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 preclinical 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 IRBs at the sites where the IRBs are overseeing a clinical trial, a data safety monitoring board (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 the clinical trials and preclinical testing of our product candidates are not necessarily predictive of the results of our ongoing and planned clinical trials for our product candidates. If we cannot achieve positive results in our clinical trials for our product candidates, we may be unable to successfully develop, obtain regulatory approval for and commercialize them.

Positive results from the clinical trials and preclinical testing of our product candidates *in vitro* and *in vivo* may not necessarily be predictive of the results from our ongoing and planned clinical trials. For example, the positive results that we observed from our Phase 1/2 clinical trial of sepfarsen may not be repeated in the ongoing Phase 2/3 clinical trial for

this candidate, and the therapeutic activity observed in prior trials may not be replicated in future clinical trials. Similarly, the results observed from our recently-announced interim analysis of QR-421a may not be replicated in the full trial or future trials of this candidate. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in preclinical and early clinical development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including adverse events. For example, in our Phase 1/2 clinical trial of sepfarsen, adverse events observed after longer duration of treatment included mild cystoid macular edema and lens opacities. These events were considered likely related to study medication and are consistent with those seen for other ophthalmic and intravitreal oligonucleotide therapies. While these adverse events did not result in any trial discontinuations, there can be no assurance that adverse events that are more serious will not arise in ongoing or future clinical trials of our product candidates. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval. If we fail to produce positive results in our clinical trials for our lead product candidates, the development timeline and regulatory approval and commercialization prospects for those product candidates, and, correspondingly, our business and financial prospects would be materially adversely affected.

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

We are developing a pipeline of product candidates using our proprietary RNA technologies for severe genetic disorders. We believe that targeting the mRNA to restore the production of functional 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. The mechanism of action of our compounds could be different from what we today hypothesize. Also, we may discover that the molecules we develop 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. For example, while we have discovered and are developing our novel Axiomer RNA editing technology, there can be no assurance that we will be able to leverage our technology to create viable product candidates to advance into the clinic, or develop those candidates to submit for regulatory approval. In addition, product candidates based on RNA technologies may demonstrate different chemical and pharmacological properties in humans than they do in laboratory studies or animals. Even if our product candidates 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 existing treatments in unforeseen, ineffective or harmful ways. Our RNA technologies may provoke an unwanted immune response, or immunogenicity, which 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. This 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 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 our 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 obtain and maintain orphan product exclusivity for sepfarsen, QR-421a, QR-1123 or QR-411, 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. Under Regulation No. (EC) 141/2000 on Orphan Medicinal Products, a medicinal product may be designated as an orphan medicinal product if, among other things, it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European 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. This exclusivity 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, among other things, 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 several of our product candidates 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 safer, more effective or otherwise clinically superior.

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.

We intend to seek Orphan Drug designation for our other product candidates, but we may not obtain such designation.

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

We intend to seek a breakthrough therapy designation for sepfarsen, QR-421a, QR-1123 and QR-411, 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 that any 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 or PRIME designation by the EMA may not actually lead to a faster development, regulatory review or approval process.

We have obtained fast track designation from the FDA for sepfarsen for LCA, QR-421a for Usher syndrome and retinitis pigmentosa and QR-1123 for autosomal dominant retinitis pigmentosa. We also have obtained PRIME designation from the EMA for sepfarsen for LCA due to the p.Cys998X mutation in the CEP290 gene. We may seek fast track designation or PRIME designation 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. To be accepted for PRIME, a drug has to show its potential to benefit patients with unmet needs based on early clinical data. The FDA and EMA have broad discretion whether or not to grant such designations, and even if we believe one or more of our product candidates is eligible for such a designation, we cannot be sure that the FDA or EMA would decide to grant it. Even if we do receive fast track or PRIME designation, we may not experience a faster development process, review or approval compared to conventional FDA or EMA procedures. The FDA and EMA may withdraw such designation if they believe that the designation is no longer supported by data from our clinical development program.

A rare pediatric disease designation may not lead to the receipt of a rare pediatric disease priority review voucher, even if sepfarsen or QR-421a is approved.

The FDA has awarded rare pediatric disease priority review vouchers, or PRVs, to sponsors of drug products intended to treat rare pediatric disease products if the treatment and product application meet certain criteria. Under this program, upon the approval of a qualifying NDA or biologics license application, BLA, for the treatment or prevention of a rare pediatric disease, the sponsor of the application may be eligible for a PRV that can be used to obtain priority review for a subsequent NDA or BLA. The PRV may be sold or transferred an unlimited number of times. The FDA has granted rare pediatric disease designation for sepfarsen and QR-421a for LCA and for Usher syndrome, respectively. The PRV program is now set to expire at the end of September 2020, although a drug that has been designated under the program as of September 30, 2020 may still receive a PRV if it is approved for marketing before October 1, 2022. Therefore, there is no guarantee that we will receive a PRV for sepfarsen or QR-421a even if either is approved by the FDA to treat a rare pediatric disease.

Risks Related to Our Dependence on Third Parties

Our development and commercialization strategy for our product candidates relies in part upon certain patent rights that we license from third parties, and termination of such license could have a materially adverse effect on our business, financial condition, results of operations and prospects.

Some of our RNA technologies rely in part upon certain patent rights that we license from third parties. Pursuant to our license agreements, we are obligated to use commercially reasonable efforts to develop and make available to the public

products or processes, as well as to achieve certain specified development, regulatory and commercial milestones. If we do not meet the specified milestones, the third party may be able to terminate the license agreement. They 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 a license agreement were terminated, it could have a material adverse effect on our business, financial condition, results of operations and prospects.

If third parties on which we depend to conduct our preclinical studies or any clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development programs 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 preclinical studies and clinical trials for our product candidates. We and our clinical investigators and CROs are required to comply with various regulations, including Good Clinical Practices (GCP) which are enforced by the FDA, and guidelines of the Competent Authorities of the Member States of the European Economic Area (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 investigators or 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 be certain 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 (cGMP) requirements, which mandate the methods, facilities and controls used in manufacturing, processing and packaging of a drug product to ensure its safety and identity. Failure to comply with these regulations may require us to repeat preclinical studies 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 preclinical 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 agreements and could cause licensors to terminate the agreements, which would further harm our business, financial condition, results of operations and prospects.

Because we have relied and continue to rely 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 service 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. Although 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 preclinical 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 preclinical 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 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 preclinical, clinical and commercial supplies of our product candidates.

We rely on third parties to supply the materials and components for, and manufacture, our research and development, preclinical and clinical trial supplies. 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, preclinical 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 fails 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 preclinical 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 our product candidates, if approved, could be delayed or terminated.

We are parties to, and we may from time to time in the future pursue, collaborative arrangements for the development and commercialization of our product candidates, if approved. For example, we entered into a collaboration with Ionis Pharmaceuticals, pursuant to which we in-licensed our product candidate QR-1123 in exchange for upfront, milestone and royalty payments. However, the development of QR-1123 depends on our ability to maintain this collaboration, and there can be no assurance that we will realize the intended benefits of this arrangement, nor can there be any assurance that the consideration that we have paid and are obligated to pay in the future, as well as the investments that we have made and intend to make to develop QR-1123, will yield any returns.

In addition, we have executed and continue to consider strategic alternatives that include spinouts, out-licensing or collaborative partnerships to develop and commercialize our RNA technologies or programs. For example, in March 2019, we spun out all dystrophic epidermolysis bullosa activities into a newly formed company, Wings Therapeutics Inc. If any of our collaborative partners in future collaborative arrangements for the commercialization of our product candidates or similar arrangements does not devote sufficient time and resources to the 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 collaboration partner were to breach or terminate its arrangements with us, the commercialization of our product candidates could be delayed, curtailed or terminated.

Much of the potential revenue from current and 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 our product candidates and, as a result, could delay or otherwise negatively affect the commercialization of such product candidate. If any future collaboration partners fail to develop or effectively commercialize our product candidates for any of these reasons, our sales, 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 Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving 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, 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 (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 or using or making any false or fraudulent document 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 (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 of 2010, collectively, the Affordable Care Act, 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, and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members; 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.

Comparable laws and regulations exist in the countries within the European Economic Area (EEA). Although such laws are partially based upon European Union law, they may vary from country to country. Both healthcare and industry specific, as well as general EU and national laws, regulations and industry codes constrain, for example, our interactions with government officials and healthcare practitioners, and the handling of healthcare data. Non-compliance with any of these laws or regulations could lead to criminal or civil liability.

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 have adopted and implemented a Code of Business Conduct and Ethics, 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.

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. For instance, we have a license from Massachusetts General Hospital (MGH) to patent rights that relate to certain RNA targeting technologies for generating functional proteins. 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. For our LCA program we have a world-wide exclusive sublicensable and royalty-bearing license to patent rights owned by the Radboud University Medical Center (Radboud) and to patent rights owned by Inserm Transfert (Inserm) for the commercial exploitation of antisense oligonucleotides that cause exon skipping in *CEP290* pre-mRNA. For our Usher program we have a world-wide exclusive sublicensable and royalty-bearing license to patent rights owned by Radboud, for the commercial exploitation of antisense oligonucleotides that cause exon skipping in *USH2A* pre-mRNA. For our adRP program we have a world-wide exclusive license to patent rights owned by Ionis Pharmaceuticals, Inc. for the commercial exploitation of gapmers that target mutated Rhodopsin (P23H) mRNA.

Our licensing arrangements impose diligence, development, regulatory and commercialization milestones, and royalty, insurance and other obligations on us. If we fail to comply with these obligations, licensors 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 technology, which may then be in-licensed by one or more of our competitors.

If the third parties from whom we license patent rights 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.

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, Ionis, Radboud and Inserm, as well as our other licensors, may not successfully prosecute the patent applications licensed to us. Even if patents are issued or granted, MGH, Ionis, Radboud and Inserm, 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, the license agreements may not provide us with a complete freedom to operate in the respective fields, 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 (U.S. PTO) the European Patent Office (EPO) and other foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign national or international 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 rectified 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. 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 for a significant amount of time. 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. and in most European countries, 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 none of our product candidates, their manufacture, use, sale, offer for sale, or importation into the United States or into any country of the EEA will 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 or litigation in foreign courts or proceedings before foreign patent offices. 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 F508del mutation. Although we believe that the claims of this patent are not infringed, particularly in light of the U.S. Supreme Court decision regarding the patentability of naturally occurring nucleic acids, the patent owner may nonetheless initiate litigation. In addition, we are aware of patent positions related to the use of antisense oligonucleotides in the treatment of DEB, for which we have spun out our product candidate to Wings Therapeutics Inc. (Wings). Wings may not enter into any license agreements relating to these patent positions, and there can be no guarantee that it will enter into such agreements on these positions on commercially reasonable terms, or at all. If Wings does not enter into such license agreements, the patent owner(s) may initiate litigation for potential patent infringement. Any such litigation might cause us to earn substantially less royalty income from Wings than we would otherwise earn, if any. Such litigation would be costly for Wings, and there is no assurance that a court would find in its favor on questions of infringement or validity. In addition, we are aware of patent applications in the European Union relating to methods for performing antisense oligonucleotide-mediated exon skipping in the retina of a subject in need thereof. While we believe that we have reasonable grounds to believe that the patent applications should not be allowed, there can be no assurance that no patents will be granted on these applications. In the event patents are granted on these applications, and the holder of these patents seeks to enforce its patent rights and our defenses against a claim of infringement are unsuccessful, we may not be able to commercialize our product candidates in the European Union, if approved, without first obtaining a license to some or all of these patents, which may not be available on commercially reasonable terms or at all. In addition, the opposition against such patents, or the defense of any claim of infringement, even if successful, is time-consuming and expensive.

Furthermore, in the event a thus far unidentified 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 has 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 could 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 certain 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. For example, the Special 301 Report (April 2019) from the Office of the United States Trade Representative identified a number of countries, including India and China,

where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. As a result, proceedings to enforce our patent rights in certain 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

We face competition from entities that have developed or may develop product candidates for our target indications. 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. An overview of potential competitors is included in Item 4.B: “Business overview - Competition”.

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. Furthermore, in our clinical studies we could be competing for the same patient population, resulting in a smaller population of suitable candidates and possibly delays and additional costs.

If any 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.

Even if any of our product candidates is approved, we currently have no sales, marketing or distribution capabilities or experience. In addition, we intend to consider out-licensing, spinouts or collaborative partnerships to develop and commercialize our RNA technologies or programs. If any 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, 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.

In addition, we have estimated the size of patient populations and market potential for certain of the indications that our product candidates are intended to target. While we have based our estimates on industry and market data that we obtained from sources, including scientific journals, that we believe to be reliable, actual potential may differ from these estimates.

Even if we receive marketing approval for any of our product candidates, it may not achieve broad market acceptance, which would limit the revenue that we generate from its sales.

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

- our product candidates' demonstrated ability to treat patients and to provide patients with incremental therapeutic benefits, as compared with other available treatments;
- the relative convenience and ease of administration of our product candidates, including as compared with other treatments for patients;
- the prevalence and severity of any adverse side effects;
- limitations or warnings contained in the labeling approved for our product candidates by the FDA or the EMA;
- availability of alternative treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies or those of our collaborators;
- our ability to increase awareness of our product candidates 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.

Moreover, commercialization of QR-421a will trigger payments of up to \$ 37.5 million pursuant to our agreement with FFB. Under our collaboration with Ionis related to our QR-1123 product candidate, we will be required to make payments to Ionis upon achievement of development and sales milestones, and royalty payments as a percentage of annual net sales. We may not have sufficient funds to support our milestone payment obligations to FFB and Ionis, which could have a material adverse effect on our business and prospects.

Even if we are able to commercialize any 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 any 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 any product candidate. 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 (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 technology 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, and continue to be, several 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 (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 Affordable Care Act (ACA) 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, and impose additional health policy reforms, any of which could negatively impact our business. The ACA 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.

Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$ 12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance and delaying the implementation of certain ACA-mandated fees. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseparable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. While the Trump Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the Texas District Court Judge issued an order staying the judgment pending appeal, it is unclear how this decision, subsequent appeals and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business. In December 2018, the Centers for Medicare and Medicaid Services, or CMS, published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS has recently published a final rule that would give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to

use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (the Right to Try Act) was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

We expect that these and other healthcare reform measures that 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 drug, which could have an adverse effect on customers for our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Even if any 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 any of our product candidates, it would be subject to extensive ongoing requirements by the FDA, the EMA and 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 (Bribery Act) the U.S. Foreign Corrupt Practices Act (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 our 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 our 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 our product candidates, if approved, from 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. On December 18, 2019, the FDA issued a notice of proposed rulemaking that, if finalized, would allow for the importation of certain prescription drugs from Canada. The Secretary of HHS would make the above certification to Congress upon issuance of a final rule based on this proposal. The FDA also issued a draft guidance document outlining a potential pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The regulatory and market implications of the notice of proposed rulemaking and draft guidance are unknown at this time. 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 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 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 our product candidates, physicians may nevertheless prescribe them to their patients in a manner that is inconsistent with the approved label. 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.

Further changes in the tax laws of the jurisdictions in which we operate could arise as a result of the base erosion and profit shifting (BEPS) project being undertaken by the Organisation for Economic Co-operation and Development (OECD). The OECD, which represents a coalition of member countries that encompass certain of the jurisdictions in which we operate, is undertaking studies and publishing action plans that include recommendations aimed at addressing what they believe are issues within tax systems that may lead to tax avoidance by companies. It is possible that the

jurisdictions in which we do business could react to the BEPS initiative or their own concerns by enacting tax legislation that could adversely affect us or our shareholders through increasing our tax liabilities.

Risks Related to Our Organization, Structure and Operations

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. 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 or services with us at any time without penalty, subject to providing any required advance notice. 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.

We may experience difficulties in managing our growth and expanding our operations.

We have limited experience in drug development. As our product candidates enter and advance through preclinical studies and 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 preclinical or clinical data 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 and any events affecting this location may have material adverse consequences.

Our current operations are primarily 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.

Our international operations subject us to various risks, and our failure to manage these risks could adversely affect our results of operations.

- We face significant operational risks as a result of doing business internationally, such as:
- fluctuations in foreign currency exchange rates; potentially adverse and/or unexpected tax consequences, including penalties due to the failure of tax planning or due to the challenge by tax authorities on the basis of transfer pricing and liabilities imposed from inconsistent enforcement;
- potential changes to the accounting standards, which may influence our financial situation and results;
- becoming subject to the different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- reduced protection of, or significant difficulties in enforcing, intellectual property rights in certain countries;
- difficulties in attracting and retaining qualified personnel;
- restrictions imposed by local labor practices and laws on our business and operations, including unilateral cancellation or modification of contracts;
- rapid changes in global government, economic and political policies and conditions, political or civil unrest or instability, terrorism or epidemics and other similar outbreaks or events, and potential failure in confidence of our suppliers or customers due to such changes or events; and
- tariffs, trade protection measures, import or export licensing requirements, trade embargoes and other trade barriers.

European data collection is governed by restrictive regulations governing the use, processing, and cross-border transfer of personal information.

The collection and use of personal health data in the European Union was governed by the provisions of the Data Protection Directive, which, as of May 25, 2018, has been superseded by the GDPR. These directives impose several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The Data Protection Directive and GDPR also impose strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the Data Protection Directive, the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. While the Data Protection Directive did not apply to organizations based outside the EU, the GDPR has expanded its reach to include any business, regardless of its location, that provides goods or services to residents in the EU. This expansion would incorporate any potential clinical trial activities in EU member states. The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for “sensitive information” which includes health and genetic information of data subjects residing in the EU. GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the European Union to the United States or other regions that have not been deemed to offer “adequate” privacy protections. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States, which may deviate

slightly from the GDPR, may result in fines of up to 4% of global revenues, or €20,000,000, whichever is greater. As a result of the implementation of the GDPR, we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our ordinary shares.

In June 2016, a majority of voters in the United Kingdom voted to withdraw from the European Union in a national referendum, commonly referred to as Brexit. On March 29, 2017, the U.K. Prime Minister formally delivered the notice of withdrawal. In March and April 2019, the United Kingdom and the EU agreed on two extensions of the withdrawal deadline. On October 28, 2019, a third extension of the withdrawal deadline was agreed to, in which the final withdrawal date was moved to 31 January 2020. As such, the withdrawal is in effect at the date of this annual report. . This withdrawal has involved a process of lengthy negotiations between the United Kingdom and EU Member States to determine the future terms of the United Kingdom's relationship with the European Union.

These developments have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in the United Kingdom and Europe. As a result of this uncertainty, global financial markets could experience significant volatility, which could adversely affect the market price of our ADSs. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which European Union rules and regulations to replace or replicate in the event of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict our access to capital. If the United Kingdom and the European Union are unable to negotiate acceptable withdrawal terms or if other EU Member States pursue withdrawal, barrier-free access between the United Kingdom and other EU Member States or among the EEA overall could be diminished or eliminated.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers that could make our doing business in the United Kingdom more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar may be adversely affected by Brexit. After the United Kingdom formally left the European Union on January 31, 2020, a transition period began on February 1, 2020, during which European Union pharmaceutical law remains applicable to the United Kingdom. This transition period is due to end on December 31, 2020. There currently are no indications of the effect Brexit will have on the pathway to obtaining marketing approval for any of our product candidates in the United Kingdom after this transition period ends, or what, if any, role the EMA may have in the approval process.

Inadequate funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have

had to furlough critical FDA and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future shutdowns of other government agencies, such as the SEC, may also impact our business through review of our public filings and our ability to access the public markets.

We are increasingly dependent on information technology systems, and our systems and infrastructure face certain risks, including from cyber security breaches and data leakage.

We increasingly rely upon technology systems and infrastructure, including support provided by our partners and third parties, to support our business. For example, we routinely rely on our technology systems and infrastructure to aid us in the collection, use, storage and transfer, disclosure and other processing of voluminous amounts of data (including confidential, business, personal and other sensitive information). We also rely on systems for manufacturing, regulatory compliance and various other matters.

The increasing use and evolution of technology, including cloud-based computing, and reliance on third parties creates additional opportunities for the unintentional, intentional and/or unauthorized exposure, dissemination and/or destruction of confidential information stored in our technology systems, infrastructure and products. Our computer systems, servers and other technology systems (and those of third parties that we use) are vulnerable to breakdown, interruption, cyber and other security attacks, system malfunction, unauthorized access and other events. Security threats, including cyber and other attacks are becoming increasingly sophisticated, frequent, and adaptive. Any such vulnerability could compromise our technology systems and infrastructure and could expose personal and/or proprietary information (including sensitive personal information) to unauthorized third parties and/or cause permanent loss of such data. While we have invested in the protection of data and information technology, there can be no assurance that our efforts will prevent breakdowns, breaches in our systems or other incidents or ensure compliance with all applicable security and privacy laws, regulations and standards. Such breakdowns can lead to regulatory fines and penalties, business disruption, reputational harm, financial loss as well as other damages. We could also suffer strained relationships, increased costs (for security measures, remediation or otherwise), litigation (including class actions and stockholder derivative actions) or other negative consequences (including a decline in stock price) from breaches, cyber and other security attacks, industrial espionage, ransomware, email or phishing scams, malware or other cyber incidents, which may compromise our system infrastructure or lead to data leakage, either internally or at our third-party providers or other business partners. While we have invested in the protection of data and information technology and in related training, there can be no assurance that our efforts will prevent significant breakdowns, attacks, breaches in our systems or other cyber incidents or ensure compliance with all applicable security and privacy laws, regulations and standards, including with respect to third-party service providers that utilize sensitive personal information, including protected health information on our behalf.

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

As at December 31, 2019 we had € 111,950,000 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 twelve months or less. Savings and deposit accounts generate a small amount of interest income. Any future investments may include term deposits, corporate bonds, money market funds and government securities, all in accordance with our cash management policy. These investments are subject to general credit, liquidity, market and interest rate risks. For example, future interest rates may be negative in the European Union. 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 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.

We may be exposed to significant foreign exchange risk.

We incur portions of our expenses, and may in the future derive revenues, in currencies other than the euro, in particular, the U.S. dollar. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro. Therefore, for example, an increase in the value of the U.S. dollar against the euro could be expected to have a negative impact on our expenditures, although it is our policy to match the currency of our cash and cash equivalents with expected cash out flows as much as practically feasible. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

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 use of our product candidates in preclinical studies, in clinical trials and the sale of any of our product candidates 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 our product candidates. 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 any of our current or 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 any of our current or future product candidates, if approved.

We will need to maintain 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 (NOLs) in the Netherlands is currently limited and may be further limited. Under Dutch income tax law, tax losses incurred up to and including 2018 may be carried forward for a period of nine years. Tax losses incurred as of 2019 may be carried forward for a period of six years. As at December 31, 2019, we had a total of € 218.7 million tax loss carry-forwards available for offset against future taxable profits. The first amount of the tax loss carry-forwards will expire in 2021. 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 annual report.

Risks Related to Ownership of our Ordinary Shares

We cannot predict what the market price of our ordinary shares will be. As a result, it may be difficult for investors to sell our ordinary shares at or above the price at which they purchased them.

An active trading market for our shares may not be sustained. The market value of our ordinary shares may decrease from time to time. As a result of these and other factors, investors may be unable to resell our shares at or above the price at which they purchased them. The lack of an active market may impair investors' ability to sell our shares at the time they wish to sell them or at a price that they consider reasonable. The lack of an active market may also reduce the fair market value of our 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 investors could lose all or part of their investment.

The trading price of our ordinary shares 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. For example, the price of our ordinary shares, which reached its high record of \$ 27.60 per share at the close of the trading on March 16, 2015, decreased as low as \$ 2.75 per share at the close of the trading on December 12, 2017. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this annual report, these factors include:

- the presentation of data at industry conferences by us and/or our competitors;
- the responses to any of our IND applications with the FDA and any of our CTA applications with the EMA;
- any current or future preclinical or 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, the European Union and other jurisdictions;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the level of expenses related to any of our product candidates or preclinical 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 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 depends in part on the research and reports that securities or industry analysts publish about us or our business. In the event securities or industry 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 by our existing shareholders in the public market could cause our share price to fall.

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

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of our common stock or securities convertible into our common stock, including in future financings that we may undertake. On November 7, 2018, the Company filed a shelf registration statement, which permitted: (a) the offering, issuance and sale by the Company of up to a maximum aggregate offering price of \$ 300,000,000 of its ordinary shares, warrants and/or units; and (b) as part of the \$ 300,000,000, the offering, issuance and sale by us of up to a maximum aggregate offering price of \$ 75,000,000 of its ordinary shares that may be issued and sold under a sales agreement with H.C. Wainwright & Co in one or more at-the-market offerings. In March 2020, we terminated this sales agreement with H.C. Wainwright & Co. and entered into a new sales agreement for such at-the-market offerings up to a maximum aggregate offering price of \$75,000,000 of our ordinary shares with Citigroup Global Markets Inc. and Cantor Fitzgerald & Co.

In October 2019, the Company consummated an underwritten public offering of 10,454,545 ordinary shares at an issue price of \$ 5.50 per share. Due to this issuance and any future additional issuances of shares of our common stock or securities convertible into common stock, including pursuant to our shelf registration statement or our ATM facility, our stockholders may experience immediate dilution and, as a result, our stock price may decline.

In addition, under the terms of our collaboration with Ionis Pharmaceuticals Inc, we issued to them 112,473 ordinary shares in November 2018. Under the same collaboration agreement, we issued 371,306 ordinary shares to Ionis in December 2019. In the future, we may also make future milestone payments to Ionis, certain of which will be made in equity and others in cash or equity at our discretion.

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

The holdings of the members of our management board and supervisory board and our principal shareholders and their affiliates, represent significant ownership, in the aggregate, of our outstanding ordinary shares (as set out in “Item 7.A. Major Shareholders”). 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 members of our management board and supervisory board and any sale, merger, consolidation, or sale of all or substantially all of our assets. These shareholders may have interests, with respect to their ordinary shares, that are different from other investors 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 our Company;
- impeding a merger, consolidation, takeover or other business combination involving our Company; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our Company.

Please see “Item 7.A. Major Shareholders” 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.

Because we do not anticipate paying any cash dividends on our ordinary shares 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 have been a listed company since September 2014. Complying with all requirements, particularly since we are no longer an “emerging growth company” that enjoys reduced 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 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, the Dutch Financial Supervision Act and the rules promulgated thereunder, as well as rules of the SEC and NASDAQ and the Dutch Corporate Governance Code, or DCGC, for example, are expected to result in ongoing increases in our legal, audit and financial compliance costs. 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. As we no longer qualify as an “emerging growth company,” we can no longer take advantage of reduced reporting requirements applicable to emerging growth companies. For example, we now must comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. Complying with Section 404 may be costly and management’s attention may be diverted from other business concerns, which could adversely affect our business and results of operations.

We currently do not have an internal audit group, and we will need to continue 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.

Our management board will be required to assess the effectiveness of our internal controls and procedures annually and, in case we become a domestic filer, we will be required to disclose changes to these controls on a quarterly basis. Since we have lost our status as an “emerging growth company” under the JOBS Act in 2019, our independent registered public accounting firm is required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. 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.

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

We report under the 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 required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, our shareholders may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

We 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 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 have granted a perpetual and repeatedly exercisable call option to such protection foundation, for up to such number of preferred shares as equals, at the time of exercise of the call option, the lesser of: (i) the total number of shares equal to our issued share capital at that time minus the number of preferred shares already held by the protection foundation at that time (if any) or (ii) the maximum number of preferred shares that may be issued under our authorized share capital under our articles of association from time to time;
- 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;
- a provision that our management board members and supervisory board members may only be removed or suspended 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 have adopted an anti-takeover measure 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, the number of preferred shares described above. 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 our shareholders' rights.

As a Dutch company we are subject to the Dutch Corporate Governance Code (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), we are 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. This may affect our shareholders' rights and they 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 our shareholders' rights will differ from the rights they 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 (other than those which follow from Dutch law) 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.

Certain U.S. holders of our ordinary shares may suffer adverse tax consequences if we are characterized as a passive foreign investment company for U.S. federal income tax purposes.

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 Item 10.E: “Taxation” for more information.

The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate and may fluctuate considerably given that market prices of technology companies have been especially volatile. In addition, the composition of our income and assets will be affected by how, and how quickly, we spend our cash, including any cash raised pursuant to prior offerings. Based on the average value of our gross assets and composition of our income, we believe that we were not a PFIC for the 2019 taxable year. However, our status as a PFIC

is a fact-intensive determination made on an annual basis, and we cannot provide any assurance regarding our PFIC status for the current, prior or future taxable years.

We do not currently intend to provide the information necessary for U.S. holders to make a “qualified electing fund,” or QEF, election if we are treated as a PFIC for any taxable year, and prospective investors should assume that a QEF election will not be available.

Any U.S. or other foreign judgments that investors 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.

Item 4: Information on the Company

A. History and development of the company

ProQR Therapeutics is dedicated to changing lives through the creation of transformative RNA therapies for the treatment of severe genetic rare diseases with a focus on inherited retinal diseases such as Leber's congenital amaurosis 10, Usher syndrome type 2, and autosomal dominant retinitis pigmentosa. Based on our unique proprietary RNA platform technologies, we are growing our pipeline with patients and loved ones in mind.

ProQR was founded in 2012 by Daniel de Boer, Gerard Platenburg, the late Henri Termeer and Dinko Valerio. Since September 18, 2014, our ordinary shares have been listed on the NASDAQ Global Market under the ticker symbol PRQR. As of December 31, 2019, we had raised € 303 million in gross proceeds from our public offerings of shares and private placements of equity securities. In addition, we have received grants, loans and other funding from patient organizations and government institutions supporting our programs, including from Foundation Fighting Blindness and the Dutch government under the innovation credit program.

Our legal name is ProQR Therapeutics N.V. and we were incorporated in the Netherlands, on February 21, 2012. We reorganized from a private company with limited liability to a public company with limited liability on September 23, 2014. Our company has its statutory seat in Leiden, the Netherlands. The address of its headquarters and registered office is Zernikedreef 9, 2333 CK Leiden, the Netherlands, telephone number +31 88 166 7000. Our US office is located at 245 Main Street, Cambridge, MA 02142, USA. The name and address of our agent for service in the United States is CT Corporation System, 111 Eighth Avenue, New York, NY 10011.

The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers like ProQR that file electronically with the SEC. The address of that site is www.sec.gov. We maintain a corporate website at www.ProQR.com. The information contained on our website or available through our website is not incorporated by reference into and should not be considered a part of this Annual Report on Form 20-F, and the reference to our website in this Annual Report on Form 20-F is an inactive textual reference only.

B. Business overview

We are developing a broad pipeline of potentially life changing RNA therapies for inherited retinal diseases, a group of rare debilitating eye diseases, affecting over two million people in the world, for which there are currently no treatment options available. We believe our RNA platform based on intravitreal delivery may be suitable to repair defective RNA in the retina and stop progression or even reverse vision loss associated with the diseases. As we deepen our relationships with the community of people living with inherited retinal diseases, we believe we are well positioned to bring these medicines to patients independently, and are therefore preparing for commercialization, particularly in the Western world.

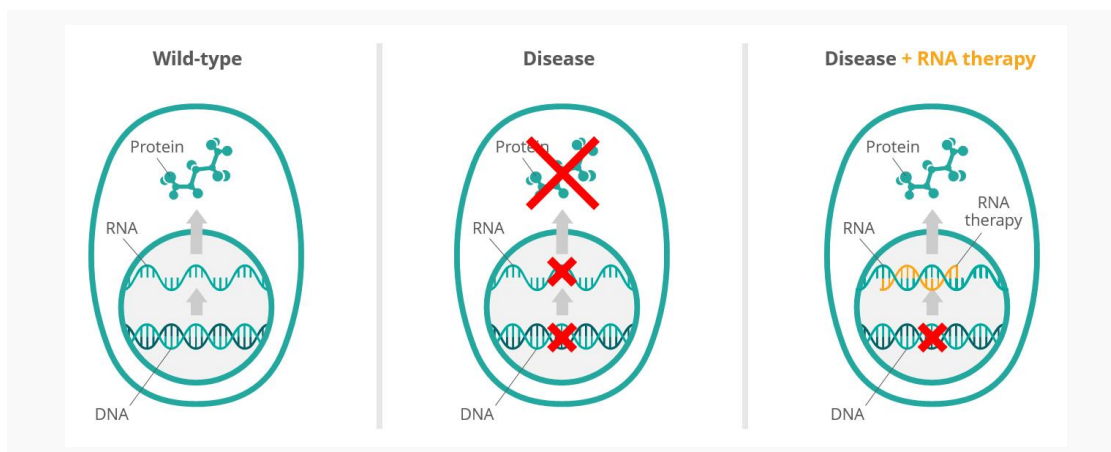
Beyond our clinical portfolio, we discovered and developed a novel proprietary RNA editing platform technology called Axiomer®. Axiomer's editing oligonucleotides, or EONs, are designed to recruit endogenous Adenosine Deaminases Acting on RNA, or ADAR, enzymes to make single nucleotide changes in the RNA in a highly specific and targeted manner at a desired location. We believe our Axiomer platform may be applicable to more than 20,000 disease-causing mutations.

We continuously evaluate opportunities for beneficial collaborations or partnerships to efficiently bring our medicines to patients. In addition, using our discovery engine that is designed to generate a broad pipeline of product candidates, we seek to enter into strategic partnerships for programs that we believe will benefit from such a partnership.

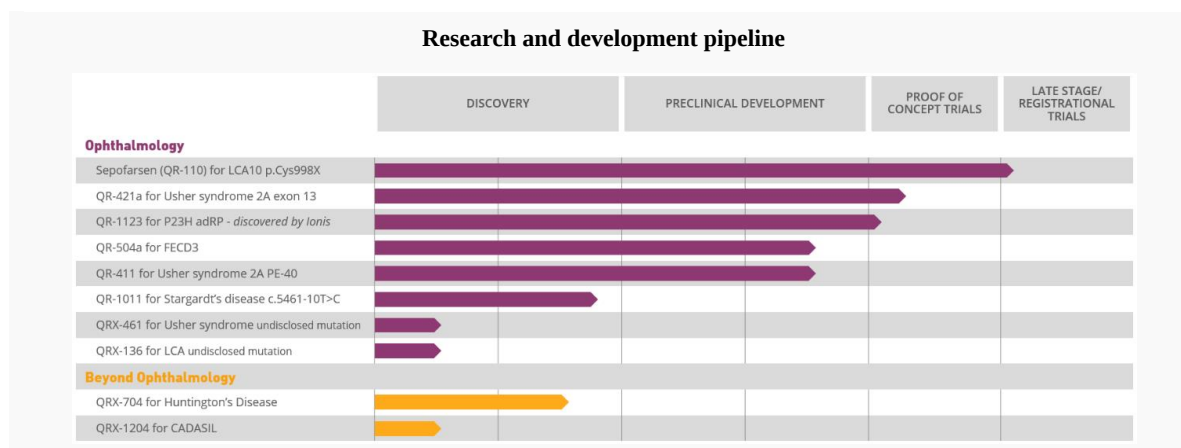
Our RNA Therapies

Our investigational RNA therapies aim to repair defective RNA to stop or reverse genetic diseases. Genetic diseases are caused by mutations in genes in the DNA. The mutation is copied into the RNA that serves as a blueprint for protein production. By designing our RNA therapies to repair the specific mutation in the RNA, the function of the protein can

be restored. This approach allows us to take away the underlying cause of the disease without having to make permanent changes to a patient's DNA.



Our investigational RNA therapies are single-stranded RNA oligonucleotides chemically modified to enhance stability and cellular uptake. While all our compounds are RNA-based, a variety of mechanisms of actions are used, depending on the type of mutation causing the disease. Each RNA therapy is designed to repair a specific RNA mutation and we believe this targeted approach may offer several advantages compared to other therapeutic approaches in the treatment of the rare genetic diseases we target. Our primary focus is on our ophthalmology pipeline that we intend to develop and commercialize. However, given the potential broad applicability of RNA therapies in several other diseases, we also have a discovery effort that seeks to identify molecules for other rare genetic diseases.



Sepofarsen for Leber's Congenital Amaurosis 10

Leber's Congenital Amaurosis (LCA) is the most common genetic cause of childhood blindness, with LCA10 being one of the most severe forms. People with LCA10 typically become blind within the first few years of life and currently there are no approved therapies. The most common mutation is p.Cys998X (also known as c.2991+1655A>G) in the CEP290 gene. Although prevalence rates vary, we estimate this mutation occurs in approximately 2,000 patients in the Western world.

We are developing seprofarsen (formerly named QR-110) for patients who have LCA10 due to the p.Cys998X mutation. Sepofarsen aims to repair the underlying cause in the RNA by splice correction. This RNA splice correction allows the production of a normal (wild-type) CEP290 protein which can restore vision in patients with LCA10. Sepofarsen is administered through intravitreal injections in the eye. Beyond seprofarsen we have an additional discovery-stage program, QRX-136, for another mutation in CEP290.

A Phase 1/2 clinical trial of seprofarsen in adults and children with LCA10 due to the p.Cys998X mutation has been completed. Data from the trial were reported in September 2018, where we demonstrated clinical proof-of-concept as shown by a significant, rapid and sustained improvement in vision in the majority of patients. In January 2019, we reached agreement with the U.S. Food and Drug Administration (FDA) on the design of a proposed Phase 2/3 clinical trial for seprofarsen. This study (Illuminate) was initiated in April 2019 and could serve as the sole registration trial for the program.

Sepofarsen has been granted orphan drug designation by the FDA and European Medicines Agency (EMA) for LCA and received fast track designation by the FDA for LCA10. In 2019, we also received PRIME designation from the EMA for LCA due to the CEP290 p. Cys998X mutation as well as rare pediatric disease designation from the FDA for LCA10.

QR-421a for Usher Syndrome Type 2 and Non-Syndromic Retinitis Pigmentosa

Usher syndrome is the leading cause of combined hearing loss and blindness. Patients are usually born with moderate to severe hearing loss that may worsen over time. The retinal phenotype, known as retinitis pigmentosa, or RP, starts with night blindness followed by progressive loss of peripheral visual fields (tunnel vision) until no vision is left. The retinal phenotype can exist without the hearing loss, this disease is called non-syndromic RP, or nsRP. Both Usher syndrome and non-syndromic nsRP can be caused by mutations in the USH2A gene, which encodes a protein called usherin. To date, there are no therapies approved or product candidates in clinical development that treat the vision loss associated with USH2A mutations.

We are developing QR-421a for patients with USH2A exon 13 mutations. In the Western world, approximately 16,000 patients have vision loss due to mutations in exon 13 of the USH2A gene.

QR-421a is an RNA therapy aimed at modulating the RNA that then results in the expression of functional usherin protein in the eye to maintain and potentially restore vision. This candidate is intended to be administered by intravitreal injections. Beyond QR-421a, we have additional early-stage programs QR-411 for the USH2A PE40 mutation and QRX-461, for another mutation in USH2A.

A Phase 1/2 clinical trial of QR-421a, named *Stellar*, is ongoing in adults with Usher syndrome or nsRP due to exon 13 USH2A mutations. Three-month interim results were reported in March 2020, QR-421a given as a single intravitreal injection was observed to be generally well tolerated with no serious adverse events noted. In the six sham treated subjects, outcome measures demonstrated no consistent pattern of response above the “noise” level. In contrast, two of eight QR 421a-treated patients demonstrated benefit across multiple concordant outcome measures. Based on these early positive findings we will continue the trial as designed with two additional study groups testing different dose levels of QR-421a.

QR-421a and QR-411 received orphan drug designation for the treatment of RP from the FDA and EMA. QR-421a was also granted fast track designation for Usher syndrome type 2 and rare pediatric disease designation for RP caused by USH2A exon 13 mutations by the FDA.

QR-1123 for Autosomal Dominant Retinitis Pigmentosa

Autosomal-dominant retinitis pigmentosa (adRP) is characterized by progressive loss of vision. Symptoms typically start in early teenage years and include night blindness and reduction of peripheral vision, which leads to tunnel vision. Eventually patients lose their central vision and become completely blind during adulthood. In the United States, the P23H mutation in the RHO gene is the most common mutation causing adRP and affects approximately 2,500 patients.

QR-1123 was discovered by Ionis Pharmaceuticals and we in-licensed this candidate in October 2018 to further develop it. QR-1123 is designed for the treatment of P23H adRP by suppressing the formation of the toxic mutant protein. By mutant-specific knockdown, QR-1123 selectively targets the mutant P23H RNA for destruction by RNase H1 cleavage without affecting the wild-type RNA. By reducing the mutant RNA, the resulting toxicity (induced loss of photoreceptors and subsequent loss of vision) can potentially be stopped or reversed.

Currently, a Phase 1/2 clinical trial, named Aurora, is ongoing in adults with adRP due to the P23H mutation. QR-1123 has been granted orphan drug designation for RP due to the P23H mutation and fast track designation by the FDA for adRP.

QR-504a for Fuchs Endothelial Corneal Dystrophy

Fuchs endothelial corneal dystrophy (FECD) is a common age-related, degenerative disorder of the corneal endothelium. FECD can lead to corneal edema, scarring, corneal clouding, and consequential vision loss. Corneal blisters can cause pain in end-stage disease. Current treatment consists of corneal transplant for late-stage disease, an invasive procedure with limitations and associated complications, and therefore a high unmet medical need still remains. The most common genetic cause for FECD are trinuclear repeat (TNR) expansions in the TCF4 gene causing FECD type 3 (FECD3).

We are developing QR-504a as an RNA therapy for the treatment of FECD3. The primary goal of the development plan for QR-504a is to provide a therapy to prevent or slow down the corneal degeneration in patients with FECD3.

We plan to advance the QR-504a program into a first clinical trial in late-stage disease patients. Study PQ-504a-001 is an open label, single-dose, dose escalation, exploratory study to evaluate safety, tolerability, and molecular biomarker(s) in corneal endothelium following a single intravitreal injection in patients with FECD3 scheduled for corneal transplant.

QR-1011 for Stargardt's Disease

Stargardt's disease is the most common inherited macular dystrophy causing progressive loss of central vision, for which there are no treatments currently available. It is associated with mutations in the ABCA4 gene resulting in the loss of photoreceptor cells in the retina. The c.5461-10T>C mutation affects about 7,000 patients in the Western world and leads to aberrant splicing of ABCA4 mRNA. QR-1011 aims to restore normal splicing, leading to the production of wild-type mRNA and protein, thereby stopping or potentially reversing the disease. QR-1011 is currently in the advanced lead optimization phase.

Deep pipeline in Ophthalmology

More than two million people in the World have vision loss due to an Inherited Retinal Disease (IRD), caused by a mutation in the approximately 300 genes that are associated with IRDs. Only a small fraction of those two million patients currently has a treatment available. At ProQR we believe that our RNA therapy platform technology has the potential to treat a large number of the mutations that cause IRDs. Therefore we have set up a dedicated effort to discover potential new treatments for IRDs that currently have no treatment. Although the total IRD population is fragmented in many mutations that cause the disease, we believe our RNA therapies have a set of common characteristics that makes them applicable across many IRD mutations. Today we have novel treatments in various stages of preclinical discovery and development for over 25 different IRD causing mutations. This preclinical pipeline includes molecules for other mutations in Leber's congenital amaurosis, Usher syndrome, Stargardt's disease and beyond. In the coming years we are working to bring several of these molecules into clinical development with the ultimate goal to create transformative RNA therapies where currently no treatment options exist.

Axiomer® RNA Editing Technology

The Axiomer® platform is a novel, proprietary RNA editing technology invented at ProQR. The technology is based on editing oligonucleotides, or EONs, designed to recruit ADAR enzymes (Adenosine Deaminases Acting on RNA) to make single nucleotide changes in the RNA in a highly specific and targeted manner at a desired location. The approach allows the recruitment of endogenous ADARs by using EONs as the sole drug modality, doing away with the need for

overexpression of (artificial) ADAR proteins, guide RNAs or other large, complex components. We continue to build our patent portfolio around this technology.

Recruitment of endogenous RNA-editing enzymes by EONs represents a significant therapeutic opportunity for a new type of drugs that can treat genetic diseases by reversing the underlying mutations. ADARs are present in most human cells and naturally make adenosine-to-inosine (A-to-I) changes in RNA. Since an inosine is interpreted by the cell as a guanosine, an EON-mediated, targeted editing reaction has the potential to effectively modify any chosen adenosine (A) in any RNA to a guanosine (G). This can either restore the original sequence, or bring about an intended de novo A to G change, in order to treat genetic disease. Current estimations point to more than 20,000 G to A mutations in the human population that cause disease.

In vitro and *in vivo* work indicates that the EONs are generally applicable for the correction of mRNA G-to-A mutations. Together with the leading academic experts in RNA editing, we continue to advance our Axiomer RNA editing technology.

Our Strategy

We are dedicated to improving the lives of patients and their loved ones through the development of RNA therapies for severe genetic rare diseases. We believe the strategy as outlined below enables us to build a sustainable independent business which creates value for all stakeholders involved. Key elements of our strategy include:

- **Develop RNA therapies for patients in need.** Through our patient-focused approach, we work to develop best-in-class therapies and to advance the understanding of conditions that we target. As RNA therapies have become an established modality, we are translating new applications in a pipeline of product candidates for patients suffering from rare diseases.
- **Rapidly advance our ophthalmology platform.** The positive results of sepfarsen and QR-421a in Phase 1/2 clinical trials have built confidence in the potential opportunity for RNA therapies in treating genetic eye diseases. Therefore, we have focused our pipeline and plan to rapidly advance programs for diseases with limited or no treatment options. As part of the “ProQR Vision 2023 strategy”, by 2023, we aim to obtain marketing approvals for the first two products in our pipeline for eye diseases, and further build a deep pipeline of ten or more programs beyond those two products, of which we expect three to be in late stage development.
- **Commercialize portfolio of ophthalmic therapies independently.** We plan to commercialize our portfolio of medicines for inherited retinal diseases (IRDs) independently in North America and Europe and seek partners for other geographic areas. While building the commercial infrastructure for a potential commercial launch of sepfarsen, we expect this same infrastructure to serve patients with other IRDs like Usher syndrome or Stargardt’s disease. There are around 30 hub centers specialized in IRD care allowing for an efficient and targeted commercial infrastructure.
- **Leverage our pipeline through strategic consideration of out-licensing, spinouts or collaborative partnerships.** We plan to continue to advance the programs and technologies in our discovery pipeline beyond ophthalmology and selectively engage with partners for development and commercialization of programs and products that we do not intend to independently develop.
- **Expand our Axiomer RNA-editing platform into select therapeutic areas.** Our novel and proprietary RNA editing platform technology, Axiomer, is a new way to use oligonucleotides to edit single nucleotides in the RNA. We believe the Axiomer technology may be applicable to more than 20,000 disease-causing mutations. In 2020 and beyond, we intend to use the platform to develop novel therapies for inherited retinal diseases and continue to validate and create value for the platform through pursuing licensing, partnering and other strategic relationships outside this core therapeutic area.

Patient Focused Approach

ProQR is dedicated to developing best-in-class RNA therapies to improve the lives of patients, families and communities affected by rare and underserved conditions. In order to achieve this goal, ProQR strives to integrate the patient voice into our decision-making throughout the drug development process as we believe that a patient focused strategy is crucial to our success. Therefore, our Patient and Medical Community Engagement (PMCE) team actively collaborates with and listens to the communities we serve to ensure that the patient voice is at the heart of all the work we do here at ProQR.

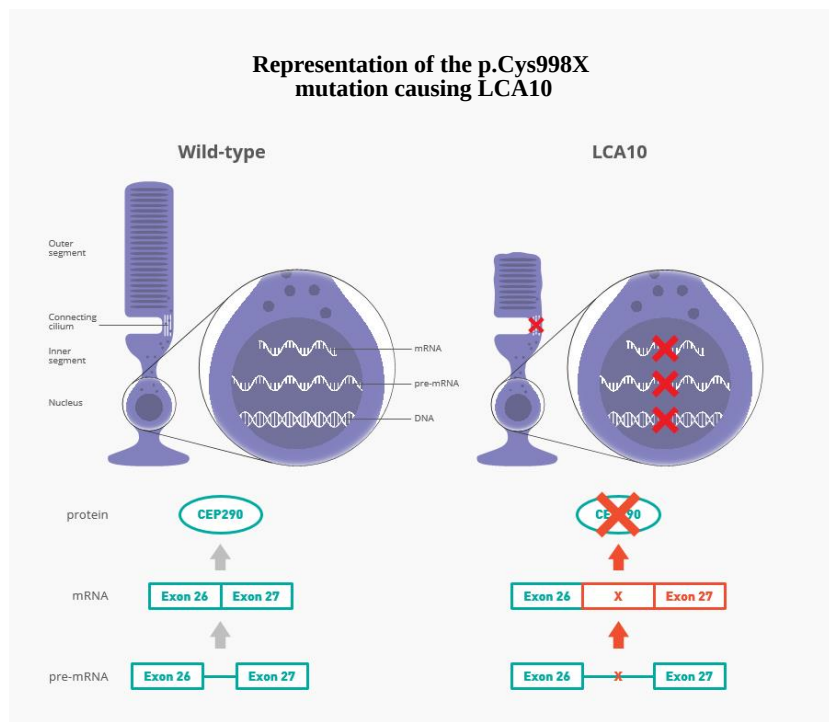
A key initiative at driving this patient voice to the heart of the work we do at ProQR is the newly formed Global Patient & Caregiver Steering Committee. Launched in January 2020, the Steering Committee is a forum for direct patient input on a wide range of topics, to ensure ProQR is meeting the needs of individuals we are striving for a solution.

ProQR recently partnered with Foundation Fighting Blindness in the My Retina Tracker Program, a collaborative, open access program providing no-cost genetic testing and genetic counseling for individuals living in the United States with a clinical diagnosis of an IRD. Genetic testing is crucial to receiving an accurate diagnosis to then move forward with the best care. Through its participation in the program, ProQR hopes to provide IRD patients with easier access to genetic diagnostics, improve access to clinical trials and facilitate therapeutic development in IRDs associated with CEP290, RHO and USH2A genes.

Sepofarsen for Leber's Congenital Amaurosis 10 (LCA10)

LCA Background

Leber's Congenital Amaurosis (LCA) is the most common genetic cause of blindness in childhood. The p.Cys998X mutation (also known as c.2991+1655A>G) in the CEP290 (centrosomal protein of 290 kDa) gene is the most prevalent mutation which generally accounts for the most severe disease phenotype (LCA10). This mutation leads to significant decrease in CEP290 protein within the photoreceptor cells in the retina. Patients affected by this mutation typically lose sight in the first years of life. Clinical features of LCA10 include loss of vision, involuntary eye movement or nystagmus, abnormalities of pupil reactions and no detectable photoreceptor electrical signals on electroretinography (ERG).



LCA Genetics

More than 20 genes have been associated with the genetic defect that causes LCA. The most common mutation is the p.Cys998X in the CEP290 gene causing LCA10. The p.Cys998X mutation is a single nucleotide substitution in the CEP290 gene that creates a new splice site, also called a cryptic splice site, between exon 26 and 27. During the splicing of the pre-mRNA this causes a part of the intron, or pseudoexon, to be included in the mRNA. The pseudoexon contains a premature stop codon, thus the mRNA is not translated into the full length CEP290 protein. CEP290 protein is involved in the formation and stability of the connecting cilium in photoreceptor cells, which facilitates the transport of proteins from the inner segment to the outer segment of the cell. When CEP290 is absent, there is a disturbance in normal protein transport to the outer segments of the photoreceptor cell, which provokes the shortening of the outer segment and its inability to perform its light transducing function.

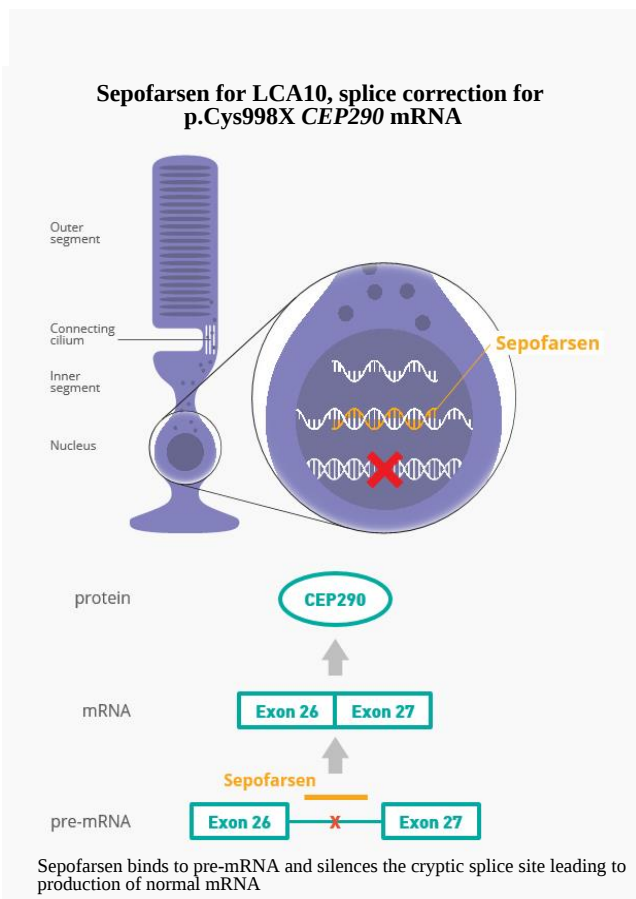
LCA Prevalence and Diagnosis

LCA affects about 15,000 patients in the Western world. Although diagnosis rates vary, our estimations indicate the most common p.Cys998X mutation occurs in approximately 2,000 patients in the Western world.

Patients are initially diagnosed through the presence of clinical symptoms. Nystagmus, rapid involuntary movements of the eyes, tends to be the first symptom visible as well as oculo-digital signs comprising eye poking, pressing, and rubbing. Vision impairment or blindness becomes obvious as age increases. After an ophthalmological examination, LCA is diagnosed. A genetic screening including all known mutations causing LCA is performed to confirm the diagnosis and determine the type of LCA in order to give the patient the most accurate prognosis possible.

Approaches for the Treatment of LCA10

There are currently no disease modifying treatments approved for patients with p.Cys998X associated LCA10 and disease management is currently supportive in nature. The eye is highly suitable for oligonucleotide therapies as it is a contained organ with physical cellular barriers. These natural barriers strongly limit the free entry and exit of cells and larger molecules in and out of the eye, therefore limiting the systemic exposure of locally administered therapies.



Sepofarsen for the Treatment of LCA10

Sepofarsen (formerly named QR-110) is designed to treat LCA10 by splice correction. By binding to the pre-mRNA, sepofarsen aims to silence the cryptic splice site caused by the p.Cys998X mutation. The splicing machinery can thus process the pre-mRNA correctly resulting in normal mRNA and we expect the production of full-length functional wild-type CEP290 protein. Sepofarsen is administered by intravitreal injection.

Sepofarsen received orphan drug designation from the FDA and EMA for the treatment of LCA. Sepofarsen was also granted fast track designation for LCA10 and rare pediatric disease designation by the FDA for LCA10 and PRIME designation by EMA for the treatment of LCA due to the CEP290 p. Cys998X mutation.

Clinical Development for Sepofarsen

The activity seen in our preclinical models of LCA10 provided strong support for the clinical development and therapeutic potential of sepofarsen. The clinical development of sepofarsen began in the second half of 2017 with a Phase 1/2 open-label, multiple dose, dose escalation study to evaluate the safety and tolerability of sepofarsen, study PQ-110-001. This trial was completed in 2019 and enrolled five children (age 8 - 17 years) and six adults (≥ 18 years) who have LCA10 due to one or two copies of the p.Cys998X mutation in the CEP290 gene. Participants received up to four intravitreal injections of sepofarsen into one eye, every three to six months. The study was conducted in three centers with significant expertise in genetic retinal disease in the U.S. and Europe.

The primary objectives of the trial were safety and tolerability. Secondary objectives included the pharmacokinetics and restoration/improvement of visual function and retinal structure through ophthalmic endpoints such as best-corrected visual acuity (BCVA), full-field stimulus testing (FST), optical coherence tomography (OCT), pupillary light reflex (PLR), mobility course and oculomotor instability (OCI).

Safety Data:

Sepofarsen was observed to be well-tolerated with manageable safety findings. In total, eight cases of lens opacities (cataract) were observed (three in the target registration dose cohort and five in high dose cohort). All six of the subjects who had lens replacement surgery regained their pre-cataract vision. Four cases (in three subjects) of retinal findings were observed in the now retired 320/160 μg dose group: two incidences of mild cystoid macular edema were resolved with topical treatment and two incidences of subclinical retinal thinning stabilized within two months of last dose without additional treatment.

Efficacy Data:

The final analysis of efficacy data from PQ-110-001 confirmed clinical proof-of-concept as shown by improvement in BCVA and supported by improvement in performance on the mobility course and mechanistic proof-of-concept was

confirmed by improvement in FST. Importantly, these endpoints showed concordant improvement (Table 1). In approximately 60% of subjects, multiple independent measures of visual function were improved in the treated eye, but not in the contralateral eye.

Table 1. Summary of Efficacy Endpoints

Endpoint	Units	Direction Showing Improvement	Responder Threshold	Change from Baseline at Month 12 Mean (SEM)	
				Treated	Untreated
Overall					
Best corrected visual acuity (ETDRS/BRVT) (n=11)	LogMAR	↓ = improved	≥ -0.3	-0.55 (0.26) p<0.05 vs. CE	-0.122 (0.07)
Full field stimulus red (FST red) (n=10)	cd/m ²	↓ = improved	-0.5	-0.91 (0.18) p<0.01 vs. CE	-0.16 (0.16)
Full field stimulus blue (FST blue) (n=10)	cd/m ²	↓ = improved	-0.5	-0.79 (0.23) p<0.02 vs. CE	-0.02 (0.11)
Mobility course (n=10)	Level	↑ = improved	≥ 2	2.5 (0.98) p=0.1 vs. CE	1.75 (0.75)

Abbreviations: BRVT=Berkeley Rudimentary Vision Test; cd/m²=logarithm of candelas/square meter; ETDRS=Early Treatment Diabetic Retinopathy Study; LogMAR=Logarithm of the Minimum Angle of Resolution, CE=contralateral eye

Measurements of BCVA and functional vision (mobility) confirm vision improvement in these subjects. In addition, clear improvement in FST was seen at both red and blue wavelengths in the treated eye only.

BCVA is an accepted registration endpoint for treatments of retinal diseases, with a generally accepted threshold for clinically meaningful improvement of -0.3 LogMAR (15 letters on an eye chart) in the U.S and -0,2 LogMAR (10 letters) in Europe. At Month 12, this threshold was exceeded in treated, but not untreated eyes, in the overall population, both in adult and pediatric subjects.

Performance on a mobility course was also improved. Concordant improvement in the mechanistic and functional outcome measures confirm that these observations are due to on-target benefits of seprofarsen. Results from the individual endpoints are discussed in more detail below.

Best Corrected Visual Acuity (BCVA)

To assess BCVA, either the ETDRS eye charts or BRVT eye charts (tumbling “E” cards) were used. ETDRS is useful up to and including LogMAR 1.6, and BRVT extends the range to LogMAR 2.9.

Data from the Month 3 and 12 assessment of BCVA for both dose groups and pooled are presented in Table 2 and show that the BCVA improvement in treated eyes started within the first 3 months of treatment and was maintained thereafter. Expectedly, BCVA in contralateral eyes which did not receive treatment did not change appreciably.

Table 2. BCVA at Month 3 and Month 12

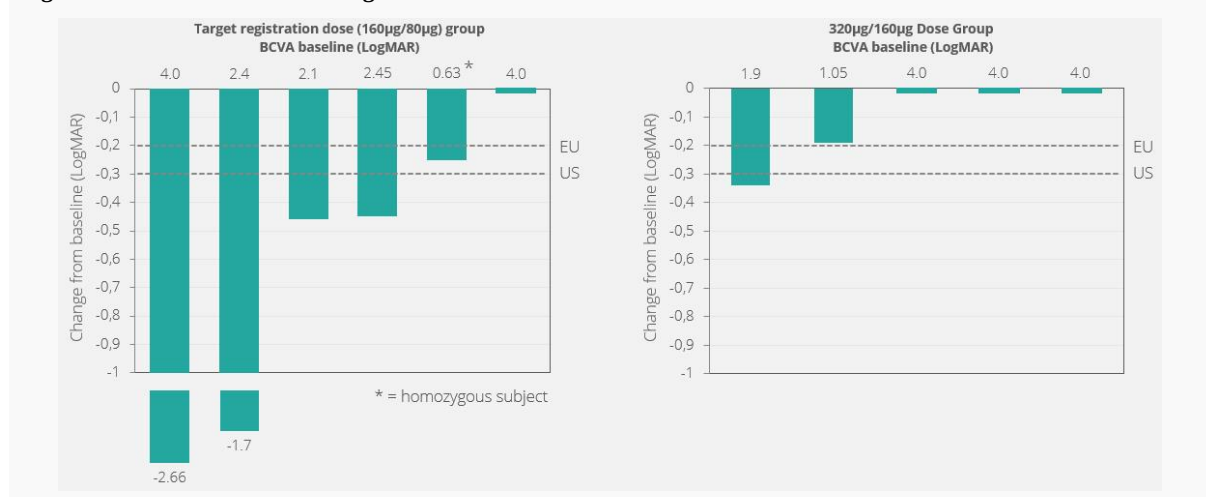
Mean Δ BCVA LogMAR	Treated eye (SEM)		Contralateral eye (SEM)	
	month 3	month 12	month 3	month 12
Pooled analysis (n=11)	-0.50 (0.24)	-0.55 (0.26)	0.0 (0.04)	-0.11 (0.07)
160 μ g/80 μ g (n=6) Target registration dose	-0.81 (0.41)	-0.93 (0.43)	0.01 (0.08)	-0.22 (0.11)
320 μ g/160 μ g (n=5)	-0.13 (0.1)	-0.11 (0.07)	0.0 (0.0)	0.01 (0.04)

Abbreviations: BCVA=Best-corrected visual acuity; LogMAR=logarithm of the minimum angle of resolution; SEM=standard error of the mean

The 160 μ g/80 μ g dose was picked as the target dose for the Phase 2/3 study. This is supported by the results in Table 2.

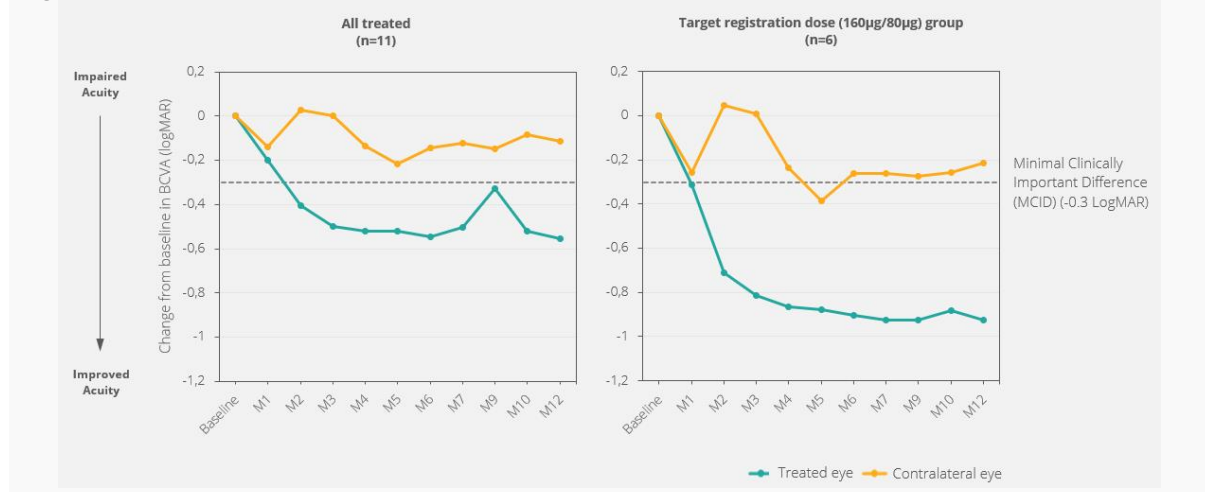
Figure 1 shows the individual BCVA responses from baseline at Month 12. Although the largest responder was at light perception (LP) only, or LogMAR 4.0, the remaining four light perception patients did not have any changes in BCVA (these patients had their greatest responses on FST). These data support the strategy to exclude light perception patients from the Phase 2/3 study. The study population will include patients with hand motion or better vision (LogMAR 3.0 or better). Change from baseline for individual subjects in the target registration dose (160 μ g/80 μ g) and in the 320 μ g/160 μ g dose groups is depicted in Figure 1.

Figure 1. Individual BCVA Change from Baseline at 12 Months



Change from baseline for all subjects pooled and for the target registration (160 μ g/80 μ g) dose group is depicted in Figure 2.

Figure 2. BCVA Changes over Time



Clinically meaningful changes are observed in both the pooled analysis and in the target registration (160µg/80µg) dose group. In the target registration dose group, the mean for the treated eye increased beyond the clinically meaningful threshold after the loading dose and remained stable over 12 months. Clinically meaningful improvements were observed for the treated eye but not for the contralateral eye.

Full-Field Stimulus Test (FST):

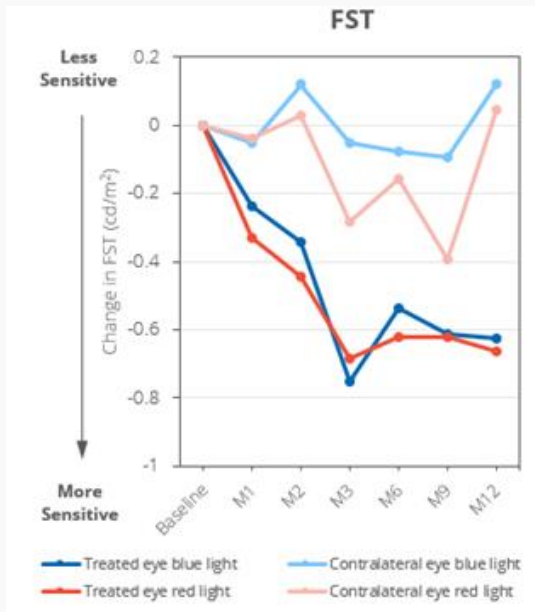
The FST is a sensitive mechanistic outcome measure. This test is similar to a hearing test, but instead of subjects pushing a button when they first hear a progressively louder tone, in FST they push a button when they detect a progressively brighter red or blue light flashed across the entire retina. As FST is a very sensitive test, it was hypothesized that improvement in FST would be the earliest and most sensitive indication that seprofarsen was engaging its target.

Improvements in visual function were supported by a meaningful increase in the ability to detect flashes of red or blue light as determined by the FST test.

In the target registration dose group, 160µg/80µg dose group, the mean change from baseline at twelve months in red light sensitivity was $-0.66 \log \text{ Cd/m}^2$ (SEM 0.14) and improvement in blue light sensitivity was $-0.63 \log \text{ Cd/m}^2$ (SEM 0.31). Three of six subjects showed an improvement of greater than $-0.5 \log \text{ Cd/m}^2$ for blue light, which can be regarded as clinically meaningful. Five of six showed a clinically meaningful improvement for red light. The mean change in the untreated contralateral eye in this group was $0.05 \log \text{ Cd/m}^2$ (SEM 0.17) for red light and $-0.12 \log \text{ Cd/m}^2$ (SEM 0.16) for blue light.

Change over time in FST for the target registration dose group is represented in Figure 3.

Figure 3 Change over Time in FST – target registration dose (160µg/80µg) group



Mobility Course

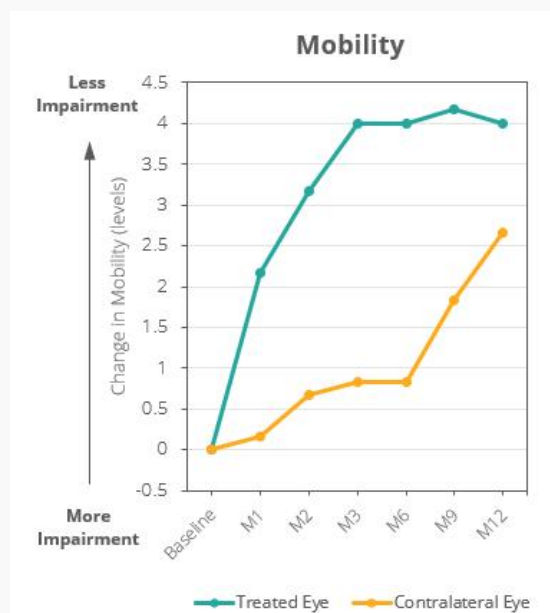
An exploratory mobility course suitable for patients with LCA10 was developed to quantify improvements in functional vision. The tool involves different layouts of increasing complexity, using multiple light levels. In total, the series of courses produces 19 levels, with level 1 being the ability to navigate a short, straight course with a single brightly-backlit obstacle; the other end of the spectrum at level 19 is the ability to navigate a very dimly-lit complex course with multiple obstacles. Improvement is measured by the number of levels a patient is able to navigate.

Most patients demonstrated improvement in functional vision, as assessed using a series of mobility courses at increasing difficulty and multiple light intensities.

In the target registration dose group, the mean change at 12 months of treatment was 4.0 levels (SEM 1.27) with five of six subjects improving by more than 2.0 levels, which can be regarded as clinically meaningful, based on recent gene therapy approval experience. The mean change in the untreated contralateral eye was 2.7 levels (SEM 1.11). We believe this increase was likely due to a training effect. An adjusted mobility course endpoint is being validated in parallel with the Illuminate trial (PQ-110-003).

Change over time in mobility for the 160µg/80µg target registration dose group is represented in Figure 4.

Figure 4 Change over Time in Mobility – target registration (160 µg/80 µg) group



Results from the mobility assessment support the functional significance of the best-corrected visual acuity improvement.

Conclusions from Study PQ-110-001 (Top-line Results)

Sepofarsen was observed to significantly improve vision and the response was durable up to 12 months. Concordant improvements in key secondary outcome measures supported the observed change in vision. In the target registration dose group (160µg/80µg) sepofarsen was well-tolerated with a favorable benefit/risk profile.

Available data from PQ-110-001 confirm clinical proof-of-concept as shown by the significant improvement in BCVA and supported by improvement in performance on the mobility course and FST. Importantly, the three endpoints analyzed showed concordant improvement.

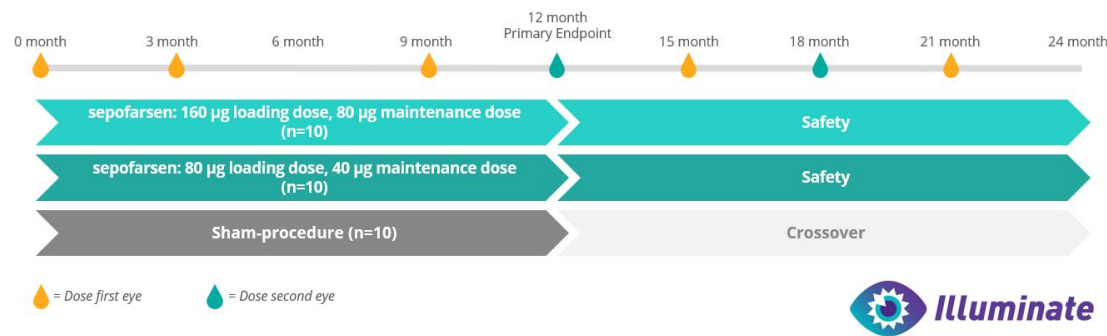
These results support the assumptions underpinning the design of the Phase 2/3 Illuminate study including the target registration dose, the 6-month dosing interval and the inclusion of subjects with vision of hand motion or better.

Next Steps in Clinical Development of Sepofarsen

The *Insight* study, or PQ-110-002, is an open-label extension study to evaluate the safety, tolerability, efficacy and PK of sepofarsen in subjects who completed participation in study PQ-110-001. *Insight* will provide continued access to the investigational product in the treated eye, as well as treatment of the contralateral eye. It is envisaged that the *Insight* study will remain open for as long as the benefit-risk continues to be positive, until drug registration or provision of continued treatment by other means is available. We plan to provide an update on the study during the second half of 2020.

The next study in the clinical development plan, *Illuminate* (PQ-110-003), aims at defining safety and quantifying the treatment effect, relative to masked, sham-treated control subjects, at more than one dose level (160µg/80µg target registration dose level and 80µg/40µg). The Phase 2/3 pivotal study incorporates a blinded interim analysis after at least 18 subjects have been treated for at least three months for sample size re-estimation, to ensure a robust and efficient assessment of sepofarsen in this ultra-rare population. This study is ongoing and is planned to be the sole pivotal study in support of the eventual Marketing Authorization Application (MAA) in the European Union and the New Drug Application (NDA) in the United States. The clinical study design incorporates advice provided by the CHMP and FDA.

The primary endpoint (mean change from baseline in BCVA, based on ETDRS and/or BRVT, of treatment versus sham) will be assessed at 12 months. Thereafter, treatment of the contralateral eye or crossover to active study drug for sham-treated subjects may be considered. We will continue to follow up on subjects for 24 months to assess long-term safety and efficacy. See below a schematic of the *Illuminate* study.



We are planning to start a trial in a pediatric population in parallel to executing the *Illuminate* pivotal study in patients of over 8 years old.

Preclinical Evidence for Sepofarsen

We have conducted in vitro and in vivo preclinical studies that support the clinical development of seprofarsen.

Sepofarsen Assessment in Patient Fibroblasts

Since seprofarsen targets the splicing process, the most direct measurable outcome of activity is the profiling and quantification of CEP290 transcripts (wild-type and mutant) and protein before and after treatment. In preclinical studies, seprofarsen demonstrated restoration of CEP290 wild-type (correctly spliced) mRNA and protein in cultured fibroblast cells of LCA10 patients homozygous and compound heterozygous for the p.Cys998X mutation.

Sepofarsen Activity in Optic Cup Model

Optic cups are a retinal organoid model derived from fibroblasts of an LCA10 patient obtained through skin biopsies. The cells are first reprogrammed into induced pluripotent stem cells, or iPSC, and later differentiated into neural retinal cells, also known as three-dimensional optic cups.

The clinical and molecular relevance of the optic cup model, coupled with the absence of an animal model, makes the optic cup the best model in which to simulate the mechanisms of LCA10 and effectively test the potential of seprofarsen.

LCA10 patient derived optic cups were exposed to seprofarsen. First, we observed that seprofarsen can enter the cells without use of any transfection agents. Second, seprofarsen elicited a dose-dependent restoration of CEP290 wild-type mRNA expression. And third, increased CEP290 mRNA expression was also associated with an increase in functional measures such as percentage of ciliated cells and the length of the cilia.

Retinal Distribution of Sepofarsen

Using labelled seprofarsen administered via intravitreal injection into wild-type mice eyes, we demonstrated that seprofarsen enters the target cells of the retina, including the photoreceptor cells. Sepofarsen has a long tissue half-life based on data obtained in a non-human primate model for a closely related oligonucleotide.

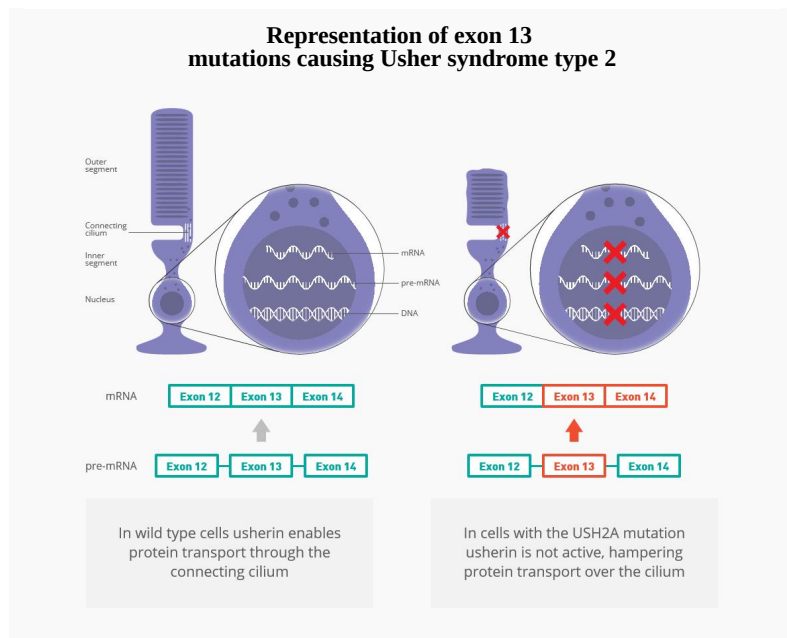
QR-421a for Usher Syndrome Type 2 and Non-syndromic Retinitis Pigmentosa (nsRP)

Usher Syndrome and nsRP Background

Usher syndrome is the leading cause of combined inherited deafness and blindness. Patients with this syndrome generally progress to a stage in which they have very limited central and peripheral vision and are divided in two subgroups. Patients that have Usher syndrome and patients that have non-syndromic retinitis pigmentosa, or nsRP, due to a mutation in the USH2A gene. Patients with Usher syndrome are usually born with moderate to severe hearing loss

that may worsen over time, in addition to developing the vision loss, where patients with nsRP develop only vision loss. Each subgroup is about 50% of the total population.

The retinal phenotype, known as retinitis pigmentosa, or RP, is characterized by photoreceptor degeneration that leads to progressive vision loss. The first visual symptoms typically appear during the second decade of life and start with night blindness due to the start of degeneration of rod photoreceptors. When rod degeneration progresses, patients lose their peripheral visual fields until only a residual central island of vision (tunnel vision) is left. As the disease progresses further, cone photoreceptors degenerate which eventually results in complete blindness.



Usher Syndrome and nsRP Genetics

Usher syndrome type 2 is caused by autosomal recessive mutations in the *USH2A* gene, encoding the protein usherin. Mutations in the *USH2A* gene can disrupt the production of usherin, a protein expressed in photoreceptors where it is required for their maintenance. Usherin is also expressed in the ear, where it is required for normal development of cochlear hair cells and hence, normal hearing. In the eye, defects in usherin cause RP. Mutations in *USH2A* can also cause nsRP, in which patients experience visual loss but do not suffer from hearing loss. Exon 13 mutations represent the most common mutations in the *USH2A* gene.

Disease Prevalence and Diagnosis

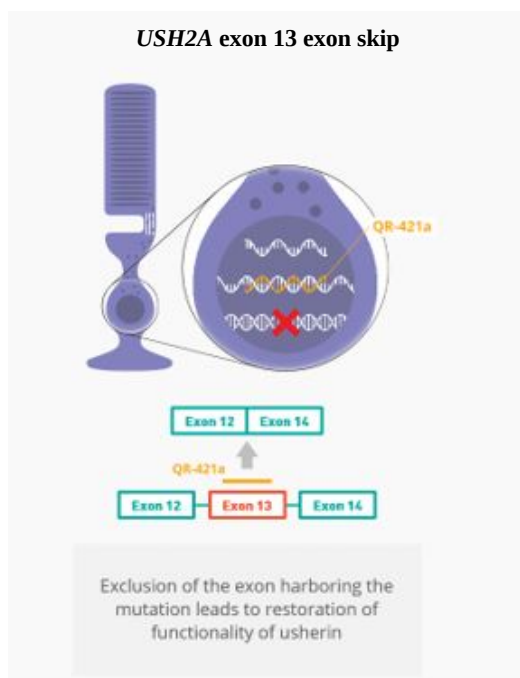
The diagnosis of the disease is based on clinical symptoms and ophthalmologic evaluations. A genetic screening can determine the specific mutation that is causing the disease. The number of patients with vision loss due to *USH2A* exon 13 mutations is estimated to be around 16,000 in the Western world. Lack of access to genotyping may result in significant underdiagnosis in many inherited retinal diseases.

Approaches for the Treatment of Usher Syndrome and nsRP

While the hearing deficit in patients with Usher syndrome type 2 can be at least partially mitigated using hearing aids or cochlear implants, there is no approved treatment for the vision loss associated with *USH2A* mutations. Disease management is supportive in nature. Vitamin A and docosahexaenoic acid (DHA) supplementations have been proposed as pharmacological treatment options. Both therapies have shown a good safety profile but limited clinical benefit. We believe that intravitreal RNA therapy QR-421a is the only product candidates in development for the treatment of patients with RP caused by exon 13 mutations in the *USH2A* gene. Due to the size of the *USH2A* gene, this type of RP is not amenable to a gene therapy approach. Also, given the disease affects both the peripheral and central retina, current gene replacement and gene editing approaches have fundamental limitations as these therapies must be delivered with a surgical procedure to a limited subretinal area. The important deficit in peripheral vision of *USH2A* patients are thereby not addressed.

QR-421a for the Treatment of Usher Syndrome and nsRP

QR-421a is being developed as a treatment for RP caused by mutations in exon 13 of the *USH2A* gene. Mutations in exon 13, including the prevalent c.2299delG mutation, can disrupt the production of usherin, which is required for photoreceptor maintenance. QR-421a aims to induce excision, or skipping, of exon 13 from *USH2A* mRNA leading to an in-frame deletion in the *USH2A* mRNA. Since exon 13 encodes for a repetitive part of the usherin protein, excision of exon 13 is expected to lead to a truncated (partial), however, functional usherin protein. Because of the exon skipping approach, QR-421a is not specific to a single mutation but targets any mutation present in exon 13 of the *USH2A* gene.

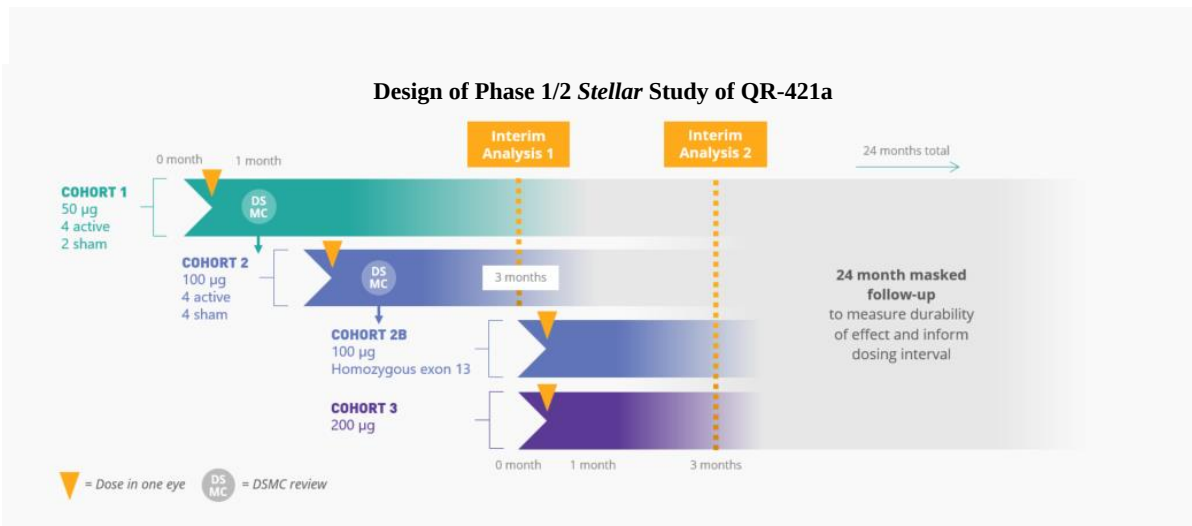


QR-421a received orphan drug designation from the FDA and EMA for the treatment of RP. QR-421a was also granted fast track designation for Usher syndrome type 2 and rare pediatric disease designation for RP caused by *USH2A* exon 13 mutations by the FDA.

Clinical Development of QR-421a

We believe that results of preclinical studies provide support for the clinical development and therapeutic potential of QR-421a. The QR-421a clinical development program has been initiated with the first-in-human *Stellar* study (PQ-421a-001), a Phase 1/2 study designed to evaluate the safety and tolerability of a single IVT injection of QR-421a in subjects with vision loss due to mutations in exon 13 of the *USH2A* gene. Changes in visual function and retinal structure are measured by several endpoints such as visual acuity (BCVA), visual field and optical coherence tomography (OCT). Changes in quality of life for trial subjects will also be evaluated. The study is being conducted at expert sites in North America and Europe.

An extension study, which would permit continued dosing of eligible subjects who complete the *Stellar* trial, is also planned.



In March 2020 findings from a planned interim analysis of the *Stellar* trial were reported. The interim analysis, or IA, was based on nine- and three-month data from the first and second dose cohorts, respectively. The *Stellar* trial is a randomized, single ascending dose, global multicenter, longitudinal, 24-month study, involving active versus sham procedure. The first two cohorts included a total of 14 subjects (ranging from 24-65 years in age), of which eight received a single dose of QR-421a and six received a single sham procedure for masking. Six subjects were enrolled in the 50µg cohort (“low dose”), of which four received treatment and two were randomized to sham; eight patients were enrolled in the 100µg cohort (“mid dose”) of which four received treatment and four were randomized to sham. The population varied in disease characteristics with both Usher syndrome (n=6) and nsRP (n=8) affected subjects included, genetic background with both homozygous (n= 4) and heterozygous (n=10) subjects for *USH2A* exon 13 mutations, and visual impairment at baseline ranging from mild to severe.

Table 1. Baseline Characteristics of Trial Population

Cohort	Genotype	Phenotype	Visual impairment severity	Months of follow up
50µg (n=4)	3 homozygous 1 heterozygous	2 Usher 2 nsRP	2 mild-moderate 2 severe	6-11
100µg (n=4)	0 homozygous 4 heterozygous	2 Usher 2 nsRP	3 mild-moderate 1 severe	3-4
Sham (n=6)	1 homozygous 5 heterozygous	2 Usher 4 nsRP	5 mild-moderate 1 severe	3-9

Safety Data:

Across both cohorts thus far, QR-421a was observed to be generally well tolerated with no serious adverse events noted.

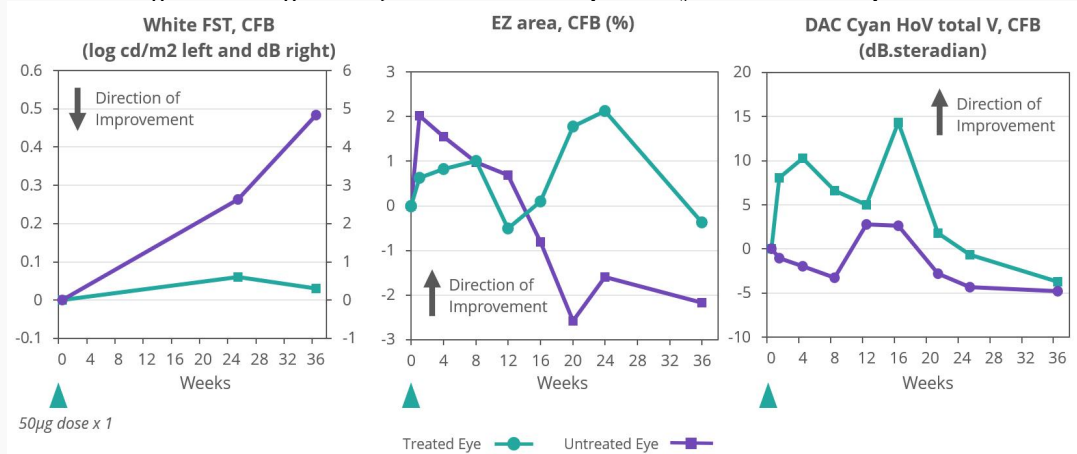
Efficacy Data:

In the six sham treated subjects (two followed for nine months and four for three months), outcome measures demonstrated no consistent pattern of response above the “noise” level. In contrast, two of eight QR-421a-treated

patients (one each in the 50µg and 100µg dose cohorts) demonstrated benefit across multiple concordant outcome measures.

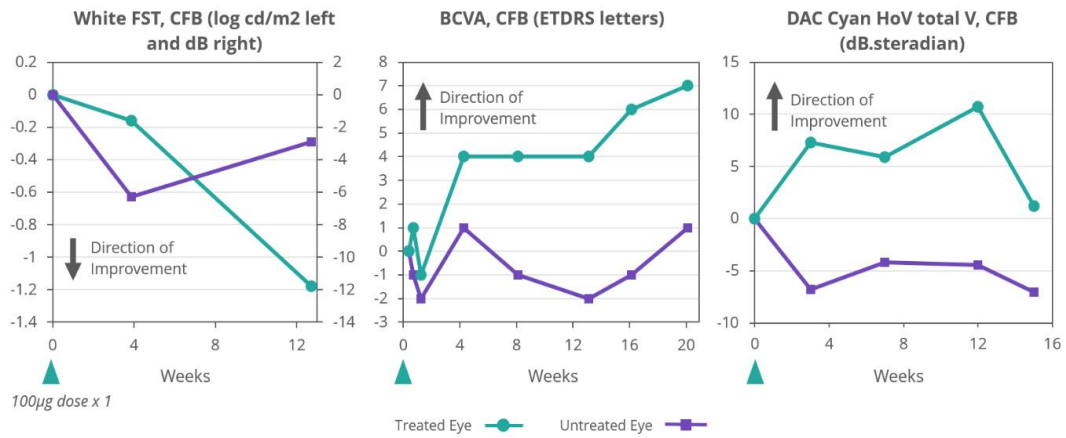
Responder 1: One of four treated patients in the low dose group was classified as a responder, with onset of action observed by the three-month visit. Benefit was maintained for six months or longer, which is consistent with the expected half-life of QR-421a in photoreceptors. This Usher syndrome patient was homozygous for *USH2A* exon 13 mutations and had moderate visual impairment at baseline (peripheral vision affected). Concordant benefit was observed across multiple relevant measures appropriate to the severity of the patient’s disease, including full field stimulus threshold test (FST) [deterioration by 5 dB in untreated eye, treated eye stable], dark adapted chromatic (DAC) perimetry [15 dB.steradian improvement in peripheral sensitivity in treated eye, <5 dB.steradian change in untreated eye], and optical coherence tomography (OCT) assessment of photoreceptor Ellipsoid Zone (EZ area). For FST and OCT, the contralateral, untreated eye demonstrated modest deterioration while the treated eye showed stabilization. For DAC perimetry the untreated eye was unchanged, whereas the treated eye demonstrated improvement.

Figure 1. Change in FST, EZ Area and DAC perimetry over Time in Responder 1



Responder 2: One of four treated patients in the mid dose group was classified as a responder with onset of action observed by three months. This non-syndromic RP patient was heterozygous for *USH2A* exon 13 mutations and had severe visual impairment at baseline (peripheral and central vision affected) with baseline best corrected visual acuity (BCVA) of 33 and 36 letters (approximate Snellen equivalent: 20/250 and 20/200) in the treated and untreated eye, respectively. Concordant benefit was observed across multiple relevant measures appropriate for the stage of disease including FST (improvement by 12 dB in treated eye, no improvement in untreated eye), DAC (up to 10 dB.steradian improvement in treated eye, with deterioration in the untreated eye), and BCVA (7 letter improvement from baseline of 33 letters, which is more than one line on the ETDRS eye chart, compared to no change in the untreated eye).

Figure 2. Change in FST, BCVA and DAC perimetry over Time in Responder 2



Next Steps in Clinical Development of QR-421a

Based on the safety profile and early evidence of efficacy observed to date, we plan to take advantage of the adaptive design, and expand the 100µg cohort with additional subjects who are homozygous for exon 13 mutations. Dose escalation to 200µg (“high dose”) is planned to occur in parallel. An interim analysis of dose- and gene copy-dependent safety and efficacy will be planned once all additional subjects have reached at least three months of treatment.

Preclinical Evidence for QR-421a

We have conducted *in vitro* and *in vivo* preclinical studies that support the clinical development of QR-421a:

- QR-421a induced an *in vitro* concentration-dependent *USH2A* exon 13 skip in human retinal organoids (Figure 1);
- Translation of *ush2a* Δexon 13 mRNA into functional Ush2a protein, as confirmed by visualization of protein in the photoreceptors and ERG b-wave restoration in zebrafish model (Figure 2); and
- QR-421a showed rapid clearance from vitreous with prolonged retention and activity in retina in non-human primates (Figure 3)

Figure 1. Concentration-Dependent Increase of USH2A Exon 13 Skip After One Month of Exposure to QR-421a in c.2299delG Homozygous Patient Retinal Organoids

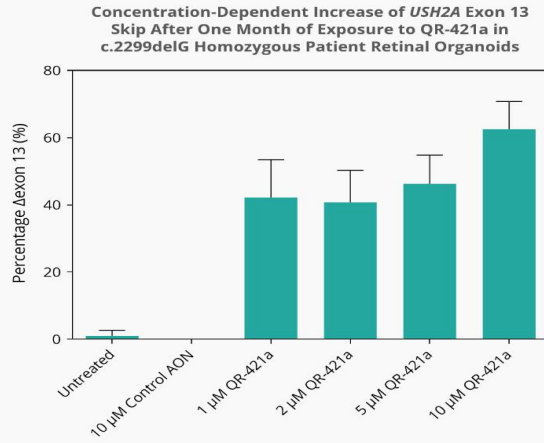


Figure 2. Exon-13 splicing oligo restore ERG in exon-13 mutant fish

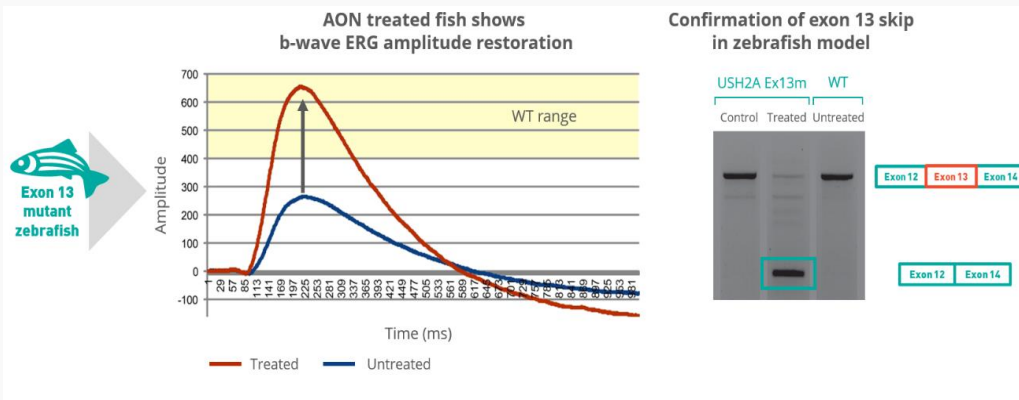
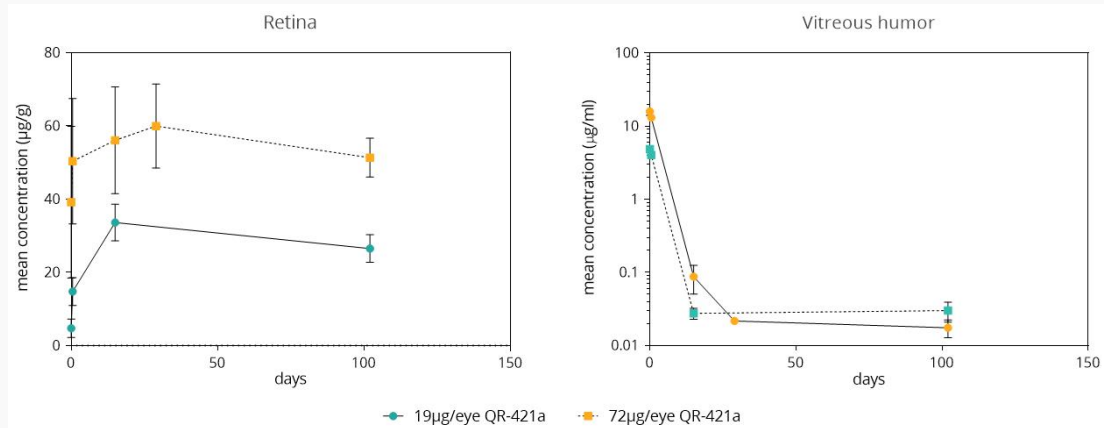


Figure 3. Pharmacokinetics in non-human primates



QR-1123 for Autosomal Dominant Retinitis Pigmentosa (adRP)

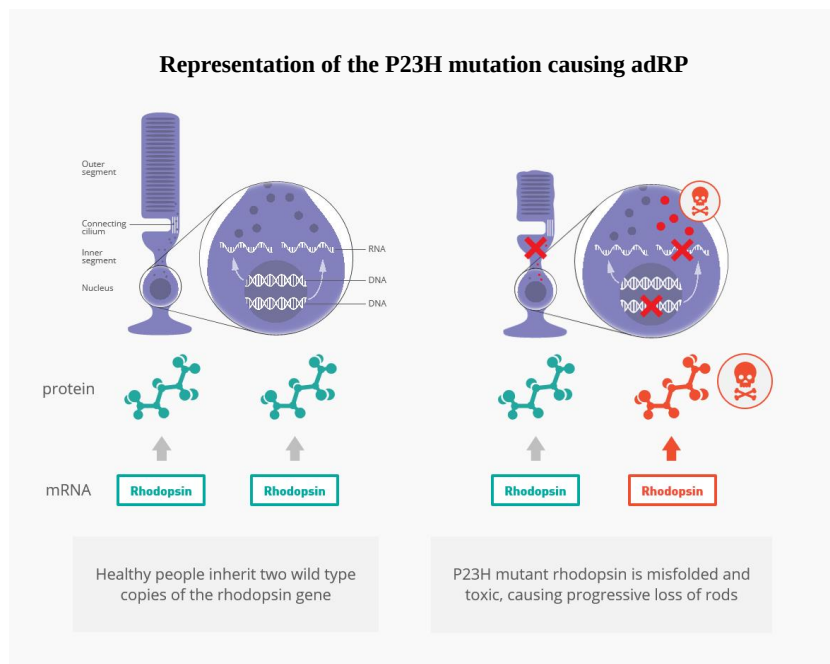
adRP Background

Retinitis pigmentosa (RP) is a group of hereditary retinal diseases in which patients first experience loss of night vision in childhood followed by loss of peripheral vision in young adulthood, and central vision in later life, which ultimately progresses to complete blindness. The worldwide prevalence of RP is about 1 in 4000 for a total of more than 1 million affected individuals. The disease can be inherited as an autosomal-dominant (about 30–40% of cases), autosomal-recessive (50–60%), or X-linked (5–15%) trait.

Autosomal-dominant RP (adRP) is characterized by abnormal, diminished or absent a- and b-waves in the electroretinogram (ERG), reduced peripheral vision (visual field) and the presence of visual defects such as reduced visual acuity and poor photo- and contrast sensitivity. Symptoms typically start in the early teenage years, which include night blindness and reduction of the peripheral vision due to the degeneration of the rod photoreceptors. As the disease progresses, cone photoreceptors are also affected, which translates into loss of central vision and eventually complete blindness in adulthood.

adRP Genetics

Mutations in more than 25 genes can cause adRP, but mutations are most commonly found in the rhodopsin (*RHO*) gene, accounting for approximately 25% of adRP cases. The rhodopsin protein is a light sensitive pigment that is present in the rod photoreceptors in the retina. Rhodopsin, when exposed to light, undergoes conformational changes that are converted into an electrical signal which is sent to the brain where it is interpreted as vision. In the United States, the most prevalent mutation associated with adRP is the P23H mutation (also known as c.68C>A) in the *RHO* gene. The mutant P23H rhodopsin protein is misfolded and toxic to the rod photoreceptor cells causing loss of vision. Although some wild-type protein is being made, there is substantial evidence that the mutant P23H rhodopsin protein elicits a dominant-negative mechanism, such that it diminishes the function of the wild-type protein.

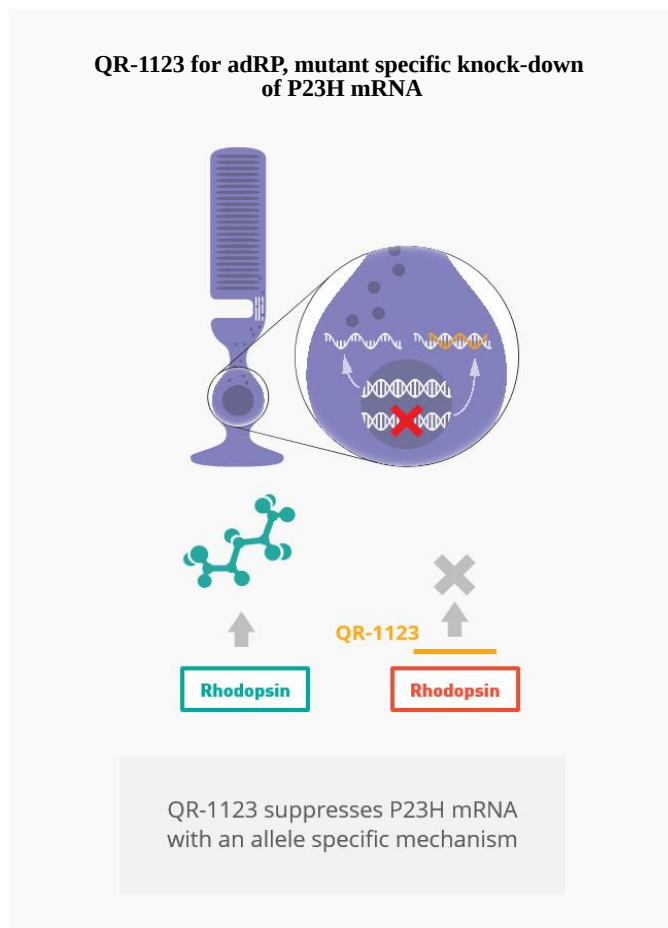


Disease Prevalence and Diagnosis

In the United States the P23H mutation in the *RHO* gene is the most common mutation causing adRP and affects approximately 2,500 patients. The diagnosis of adRP is based on clinical symptoms and ophthalmologic evaluations. A genetic screening can determine what specific mutation is causing the disease.

Approaches for the Treatment of adRP

We believe QR-1123 is the only candidate in development for the treatment of patients with adRP caused by the P23H mutation. Disease management is currently supportive.



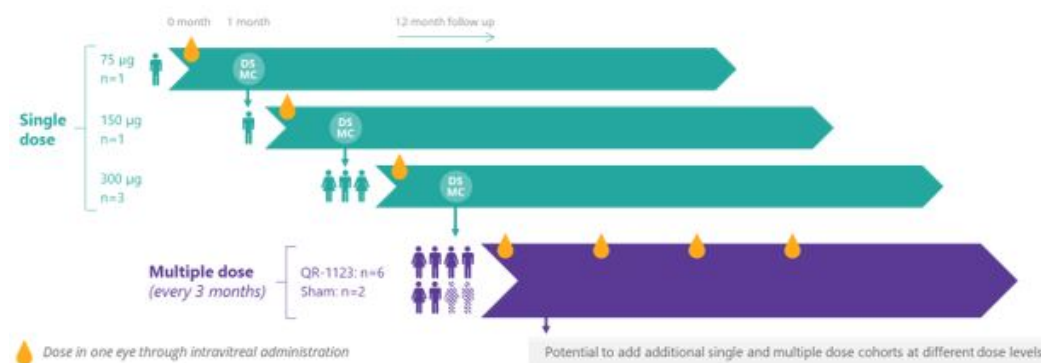
QR-1123 for the Treatment of adRP

QR-1123, discovered by Ionis Pharmaceuticals and in-licensed by ProQR in 2018, is designed for the treatment of P23H adRP. QR-1123 is an allele-specific gapmer that aims to suppress the formation of the mutant protein by selectively targeting the mutant RNA and causing its destruction by RNase H1 cleavage without affecting the wild-type RNA. With reducing the mutant RNA, we believe the toxicity-induced loss of the photoreceptors and subsequent loss of vision can be stopped or potentially reversed.

Clinical Development of QR-1123

Currently a Phase 1/2 clinical trial, named *Aurora*, is ongoing in adults with adRP due to the P23H mutation. *Aurora*, or PQ-1123-001, is a first-in-human study that will initially include up to 35 adults with adRP due to the P23H mutation in the rhodopsin (*RHO*) gene. The trial will include single-dose escalation (open label) groups and multiple-dose escalation (double-masked) groups in which intravitreal injections of QR-1123 or sham procedures will be given in one eye. The objectives of the trial include evaluation of safety and tolerability. Efficacy as measured by improvement of visual function and retinal structure will be assessed through ophthalmic endpoints such as visual acuity, visual field and optical coherence tomography. The trial will be conducted at expert sites in North America.

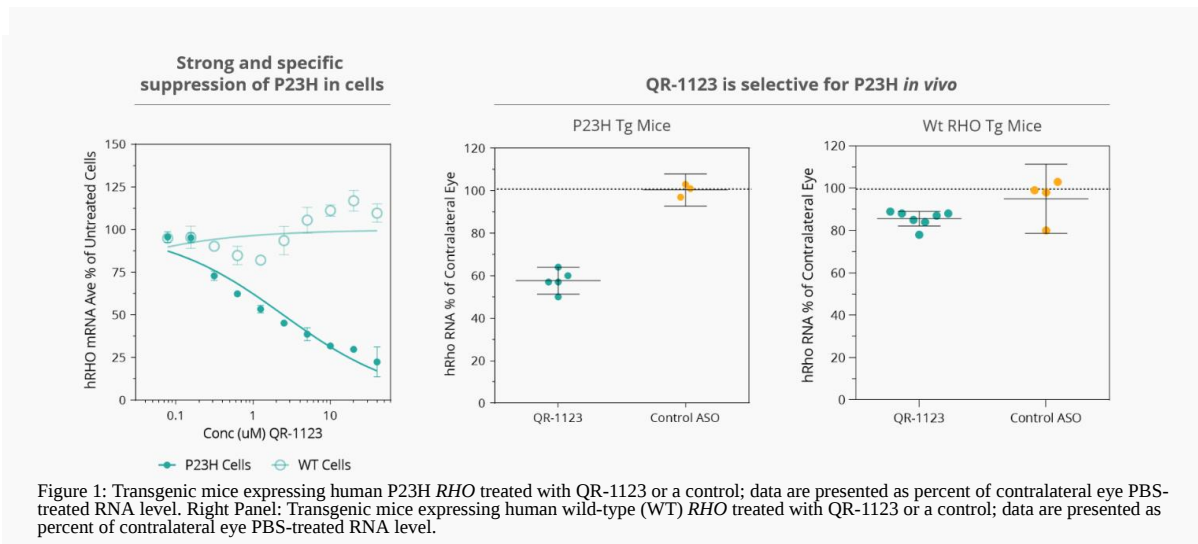
Design of Phase 1/2 *Aurora* Study of QR-1123



Preclinical Evidence for QR-1123

In vitro and *in vivo* experiments have been performed to study the specificity of QR-1123 for the P23H mutant RNA. *In vivo* experiments have been performed to study the effect of QR-1123 on retinal degradation and ERG measurements.

- QR-1123 was observed to selectively target the human P23H mutant rhodopsin mRNA, whilst sparing the human wild-type mRNA in cell models (Figure 1, left panel).
- In mice expressing wild-type *RHO*, no difference in *RHO* mRNA was observed between groups treated with QR-1123 or a control (Figure 1, right panel) while mutant P23H-*RHO* mRNA was reduced after a single QR-1123 injection in the eyes of transgenic mice expressing the mutant mRNA (Figure 1, center panel) confirming the specificity for the P23H allele.
- A rat model of P23H adRP given QR-1123 surrogate had an improved scotopic a-wave response amplitude at all stimulus intensities (Figure 2, left panel). This improved ERG response was not observed in the control-treated eyes (Figure 2, left panel).
- A single IVT administration of QR-1123 retarded the progressive retinal degeneration in a mouse model of P23H adRP (Figure 3, top panel). Importantly, the activity was observed throughout all regions of the retina (Figure 3, lower panel). This shows that QR-1123 has the capability to stop retinal degeneration and indicates that a mechanism based on inhibition of the formation of toxic mutant version of rhodopsin protein has the potential to improve a clinically relevant functional outcome in RP.
- QR-1123 did not have a significant effect on wild-type *RHO* mRNA levels in cynomolgus monkey (Figure 4) suggesting that QR-1123 is specific to the P23H mutant *RHO* mRNA and does not affect the expression of WT *RHO* mRNA.



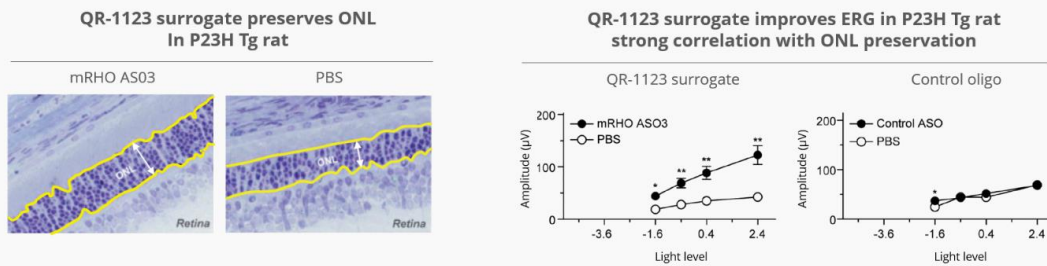


Figure 2: ONL preservation and ERG improvement after QR-1123 treatment. *Left Panel: Representative retinal micrographs of P23H-1 rhodopsin transgenic rat eyes from the PBS or QR-1123 surrogate-treated eye 30 days post IVT injection. Right Panel: Improved ERG response in P23H-1 transgenic rats after a single QR-1123 surrogate treatment with IVT injections at P13 (A) or P14 (B), with ERG measurements made at P48. (A, B). Amplitude versus stimulus intensity curves for scotopic a-waves (circles). The scotopic a-waves of eyes injected with QR-1123 surrogate were significantly greater than PBS-injected contralateral eyes while eyes treated with control were similar to those of PBS-injected contralateral eyes (t-test; *P < 0.05; **P < 0.01; ***P < 0.001; ****P < 0.0001). In the data points without apparent error bars, the error bars are obscured by the symbol.*

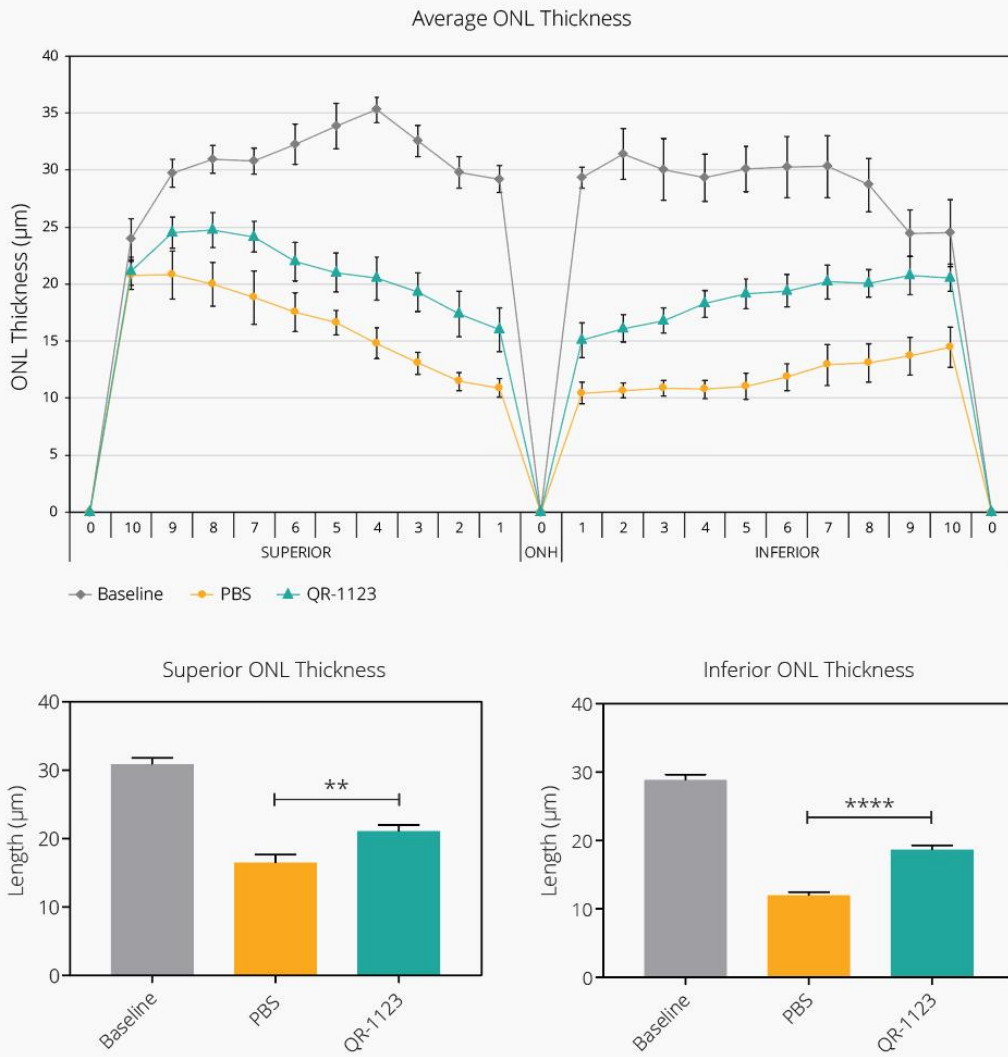


Figure 3: Preservation of ONL in a Tg mouse model after treatment with QR-1123. Top panel: Depicted is a spider diagram of the outer nuclear layer measurements of the entire retina of eyes treated with either PBS (red line) or QR-1123 treated eyes (Green line). Lower Left panel: Average superior region ONL thickness at baseline and in PBS and QR-1123 treated mice. Lower Right panel: Average inferior region ONL thickness at baseline and in PBS and QR-1123 treated mice. Two-tailed t test; **p < 0.01, ****p < 0.0001.

Cynomolgus monkey

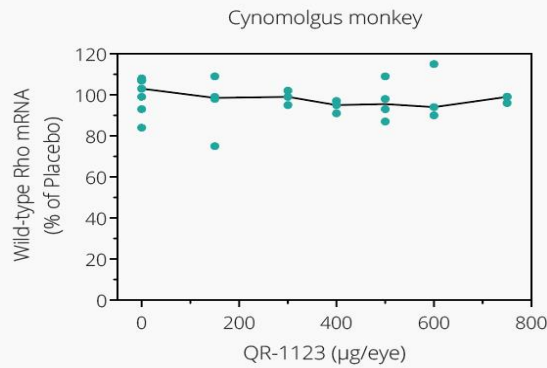
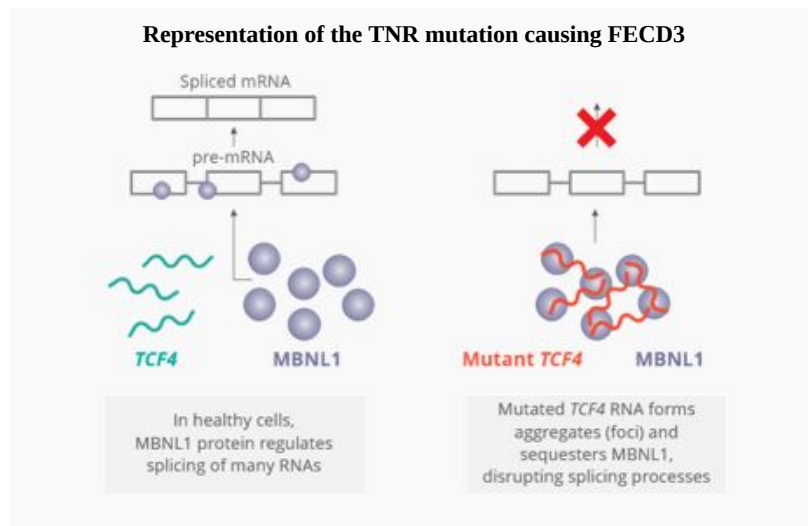


Figure 4: Levels of monkey WT RHO mRNA were measured by qRT-PCR 14 days after IVT injections. The RHO levels of individual animals were normalized to CRX mRNA levels. Values are presented as % of mean of the vehicle group.

QR-504a for Fuchs Endothelial Corneal Dystrophy (FECD)

FECD Background

Fuchs endothelial corneal dystrophy (FECD) is a common age-related, degenerative disorder of the corneal endothelium. FECD leads to severely impaired endothelial cell function resulting in corneal edema, scarring, corneal clouding, and consequential vision loss. Repeated bullae (blister) formation is a major cause of pain in end stage FECD patients.



FECD Genetics

The inheritance pattern of FECD is primarily autosomal dominant and genetic and environmental modifiers such as age and gender are known to affect its prevalence. The genetic basis of the most prevalent form (FECD type 3) has been attributed to CTG TNR expansions in the *TCF4* gene. *TCF4* is a widely expressed gene, yet TNR expansion in *TCF4* only causes disease in the corneal endothelium.

In FECD3, the TNR expansions are transcribed into aggregation-prone RNA molecules, which cause the formation of characteristic nuclear RNA foci. These foci sequester various proteins, such as the essential mRNA splicing factor MBNL1. This sequestration of MBNL1 causes widespread mis-splicing, eventually resulting in FECD3. The number of the TNR repeats has been shown to correlate positively with FECD3 disease severity.

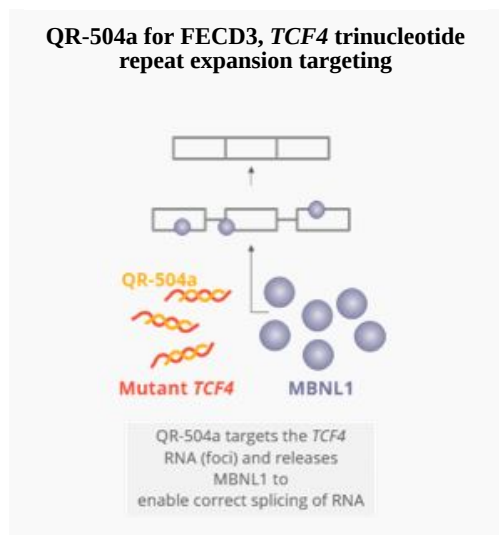
Disease Prevalence and Diagnosis

FECD is a common disorder; it is estimated that FECD affects more than 4% of individuals over the age of 40 in the U.S., and similar prevalence is noted for other global regions. Trinucleotide repeat expansion in the third intron of *TCF4* is strongly associated with FECD, and a repeat length >50 is highly specific for the disease. This group is known as FECD type 3 (FECD3). In the population of European descent, between 73 - 79% of FECD patients were reported to have one or more expanded copies of the CTG repeat expansion allele.

Clinical FECD diagnosis is based on confirmation of confluent central guttae by slit-lamp biomicroscopic examination and concomitant edema, scarring, and loss of vision.

Approaches for the Treatment of FECD

Currently no treatment options are available to address the underlying cause of FECD and disease management is aimed to reduce symptoms. The only effective therapy for late-stage FECD is corneal transplantation. The availability of donors, risk of rejection, and the inherent risk of an invasive procedure are some of the limitations of this procedure. A high unmet medical need exists in this sight-threatening condition. QR-504a is the only product in clinical development for the treatment of patients with FECD3 caused by TNR expansions in intron 3 of the *TCF4* gene.



QR-504a for the Treatment of FECD3

The primary goal of the development plan for QR-504a is to provide a therapy to prevent or slow down the corneal degeneration in patients with FECD3. QR-504a is designed to target the intronic TNRs in the *TCF4* transcript. The aim is to reduce aggregation and the formation of RNA foci in order to normalize the RNA splicing patterns, and prevent or halt corneal degeneration in patients with FECD3.

Clinical Development of QR-504a

We plan to advance the QR-504a program into a Phase 1 first-in-human clinical trial in late-stage disease patients in 2020. Study PQ-504a-001 is an open label, single-dose, dose escalation, exploratory study to evaluate safety, tolerability, and molecular biomarker(s), i.e., target engagement, in corneal endothelium following a single IVT injection of QR-504a in patients with FECD3 scheduled for corneal transplant with parallel lens replacement, i.e., patients at an advanced stage of disease.

Preclinical Evidence for QR-504a

The effects of QR-504a have been studied in primary corneal endothelial cell (CEC) models developed using FECD patient tissue. These models recapitulate the pathology of FECD3, such as displaying RNA foci composed of *TCF4* TNR expansions, which cause cellular toxicity by sequestration of certain essential mRNA splicing factors (e.g., MBNL1), and consequently mis-splicing of other mRNAs, all of which have been correlated to disease causation. In collaboration with Moorfields Eye Hospital and University College London, we are using these CEC models successfully to study and select suitable molecules for the development of a FECD therapy.

We have conducted *in vitro* and *in vivo* preclinical studies that support the clinical development of QR-504a:

- Treatment with the QR-504a surrogate by transfecting CEC models did not only specifically and significantly reduce the nuclear RNA foci incidence, but also led to desequestration of MBNL1 as well as the normalization of splicing toward a 'non-FECD' profile as observed in control cells.

- RNA target engagement of QR-504a was confirmed when directly comparing it to the surrogate AON, as illustrated by the improved reduction of nuclear RNA foci in the FECD3 patient-derived CEC model (**Error! Reference source not found.1**).
- IVT administration of AONs has been shown to result in corneal uptake into the corneal endothelial cells (the target site of pharmacological action for QR-504a) in mice. This was recently confirmed in an ocular biodistribution study in mice, where a single IVT injection of QR-504a showed superior corneal uptake compared to topical administration.

Reduced RNA Foci Incidence in FECD Patient-Derived CECs After Transient Transfection of QR-504a

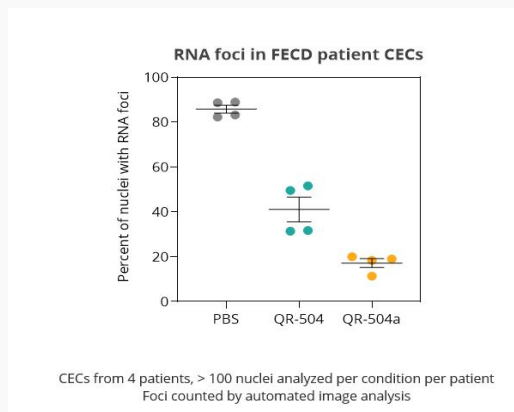


Figure 1: Percentage of nuclei that contain RNA foci after treatment with either PBS (control), QR-504a-surrogate (QR-504) or QR-504a.

Beyond Ophthalmology

Beyond the programs in ophthalmology mentioned above, we have additional early stage programs in our pipeline targeting genetic diseases affecting the central nervous system with high unmet medical need.

QRX-704 for Huntington's Disease

Huntington's disease (HD) is an inherited progressive neurodegenerative disease and one of the most common genetic disorders. Symptoms include involuntary movements, incoordination, impaired speech, cognitive decline and depression. Patients with HD have a shortened life expectancy and there is currently no disease-modifying treatment available. The disease is caused by an expanded repeat of CAG nucleotides in the *HTT* gene, resulting in a mutated huntingtin protein that is cleaved into toxic fragments, which accumulate in nerve cells. QRX-704 is designed to modify *HTT* mRNA to prevent the formation of the toxic fragments, while the huntingtin protein remains functional. QRX-704 is currently in discovery stage.

QRX-1204 for CADASIL

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is a dominantly inherited neurovascular disease characterized by strokes and dementia. There is currently no approved therapy for CADASIL. The disease is caused by mutations in the *NOTCH3* gene that cause the protein to aggregate in the arteries and arterioles leading to arteriopathy. QRX-1204 is designed to remove the mutated exon from the mRNA thereby preventing aggregation while maintaining the signaling function of the protein. QRX-1204 is currently in the lead optimization phase.

Partially Owned Subsidiary Companies

As we focus our operation on the development of RNA medicines for inherited retinal diseases, we have spun-off non-core activities in separate companies that operate independently and are funded externally.

Wings Therapeutics is conducting clinical trials with QR-313 in patients who suffer from dystrophic epidermolysis bullosa. ProQR has a minority ownership in this company and has milestone and royalty rights on the programs. Wings Therapeutics is operated out of Berkeley, California. More information can be found on www.wings-tx.com.

Amylon Therapeutics is focused on the development of medicines for CNS diseases, with a primary focus on HCHWA-D, a genetic form of stroke. ProQR has a majority ownership in the company and has milestone and royalty rights on the programs. Amylon Therapeutics is operated out of Cambridge, Massachusetts. More information can be found on www.amylon-tx.com.

Human Resources

As we believe in passion and commitment, we have built a strong team of 160 ProQRians from all walks of life and around 35 different nationalities, who are up to the challenge and committed to make a difference to the patients we serve. We actively create a caring atmosphere filled with fun and joy, in which we love to work and maintain productive and happy lives. At ProQR we foster empowerment, self-development, creativity and a sense of community.

As an employer, we are a true believer in the value of a workforce in which people from diverse backgrounds are encouraged to develop themselves both personally and professionally. This is reflected in our equal gender balanced leadership team and broader workforce. We believe that happy and energized people, working well together in an environment in which they thrive, will do phenomenal and awesome things.

We are committed to ensure that no employee, candidate or job applicant receives less favorable treatment on the grounds of race, age, disability, pregnancy, religion, gender identity and expression, sexual orientation, marriage or civil partnership status. At ProQR we want to create an inclusive culture where everyone can be valued for who they are and in which individual differences and the contributions in all forms are recognized and valued.

Animal Welfare

It is required by regulatory authorities to demonstrate the safety and, if possible, efficacy of a new drug in animals, before it can be tested in humans. The welfare of animals in our preclinical studies is of great importance to ProQR for reasons of ethics, quality, reliability and applicability of scientific studies. To assure high quality (scientific) research, animal welfare is essential. By actively pursuing the 3R principles (Reduce, Refine and Replace), ProQR is committed to reduce the number of animals needed, minimize discomfort and pain of animals used, and use alternatives to animal research whenever possible.

Animal experiments will be performed only if there are no alternatives such as performing *in silico*, *in-vitro* or *ex-vivo* studies. Study designs will be evaluated with the aim to identify opportunities to reduce the number of animals needed to achieve the objectives of the study. By conducting small pilot (tolerability) studies and by using innovative new technologies and modeling approaches, ProQR further pursues the ambition to reduce, refine and replace animal studies. Approval by the (institutional or national) animal care and use committees is required prior the execution of *in vivo* studies.

External collaborators contracted for the execution of our *in-vivo* preclinical studies (contract research organizations, CROs) are selected based on their expertise, quality and accreditations for laboratory animal care and welfare. CRO facilities are audited by ProQR prior contracting to ensure that the housing, husbandry and animal welfare complies with the highest international standards. Personnel responsible for housing, husbandry and care of the animals must have received adequate and relevant documented education.

In 2015 ProQR became part of an interdisciplinary consortium with Utrecht University (Faculty of Veterinary medicine and Ethics Institute), Radboud University (Medical Center, SYRCLE) and another private company, partly financed by

The Netherlands Organization for Scientific Research, Responsible Innovation grant. The project proposes a more integrated approach towards innovation in the field of animal testing and focuses on translational strategies. ProQR is involved in the work package that aims to deliver step stones for practical guidelines to build robust translational strategies, to design innovative experiments (including animal models) with the aim to develop treatments for rare genetic diseases.

Manufacturing and Supply

We do not currently own or operate manufacturing facilities to produce clinical or commercial quantities of any of our product candidates. We currently contract with drug product manufacturers for the production of seprofarsen solution for intravitreal injection, QR-421a solution for intravitreal injection, QR-1123 for intravitreal injection and QR-504a for intravitreal injection, and we expect to continue to do so to meet the planned clinical requirements of our product candidates.

Currently, each of our active ingredients for our manufacturing activities are supplied by single source suppliers. We have agreements for the supply of such active ingredients with manufacturers that we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. We typically order clinical supplies and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. We have a commercial supply agreement in place for the manufacturing of the active ingredient in seprofarsen. This agreement took effect in July 2019 to cover the process qualification activities, and will remain effective until ten years after the date of first commercial sale of seprofarsen. The termination may be terminated earlier by either party in case of a material breach of the agreement, or by us in case (i) the product or the development thereof is discontinued, (ii) of insufficient supplies of the product, or (iii) of a refusal to implement changes required by regulatory authorities. During the first five years after the first commercial sale, we shall be required to exclusively order our demand of seprofarsen under this agreement, and thereafter only half the demand. Every half year, we shall submit 36 months forecasts of which the first 12 months are a binding take or pay commitment.

We also have clinical 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, amongst others. The contract manufacturing organizations we use manufacture 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, biotechnology, 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, delivery, reliability, convenience of dosing, patient recruitment for clinical studies, 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.

Our competitors are working on similar technologies in the field of RNA repair and RNA editing, but also in the field of gene editing and gene therapy as well as other types of therapies, such as small molecules, protein replacement or antibodies. The industry targeting hereditary ophthalmology indications is driven by gene therapy, gene editing, and other approaches.

Intellectual Property

We strive to protect our technology platforms and our product candidates through a 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 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 delays in granting marketing approval for a patented active ingredient or use of an active ingredient. In Europe, a similar mechanism is available, such that patents may be eligible for a supplementary protection certificate to compensate for the time lost in obtaining marketing authorization for the active ingredient.

Patent Rights Relating to Our LCA Program

With regard to our LCA Program and our lead candidate in the LCA space, seprofarsen, we entered into an exclusive license agreement with the Radboud University Medical Center, Nijmegen, the Netherlands in April 2014 to obtain rights in a patent family with composition of matters claims directed to antisense oligonucleotides for treating LCA and method of use claims relating to modulation of the splicing of the *CEP290* gene product. Patents were granted in Europe (EP 2753694 B1), in the U.S. (US 9,771,580 and US 10,167,470), in Australia (AU 2012305053), and in Eurasia (EA 033653),, and applications are currently pending in the U.S. (continuation application) as well as Brazil and Canada. The term of any patents resulting from these applications would be expected to extend to at least 2032. Furthermore, we entered into an exclusive license agreement with Inserm Transfert SA and Assistance-Publique-Hôpitaux de Paris (AP-HP), Paris, France in January 2018 to obtain rights in a patent family with composition of matters claims directed to antisense oligonucleotides for treating LCA and method of treatment claims relating to modulation of the splicing of the *CEP290* gene product. Patents were granted in the U.S. (US 9,012,425; US 9,487,782; US 9,777,272) and in Europe (EP 2718437 B1) and applications are currently pending in the U.S. (continuation application) and Europe (divisional application). The term of any patents resulting from these applications would be expected to extend to at least 2032.

To further strengthen our position on seprofarsen, we filed our own international patent application in February 2016 to obtain intellectual property rights to a variety of improved antisense oligonucleotides, including seprofarsen, and the use thereof in the treatment of LCA. Patents were granted in South Africa (ZA 2017/05331) and the U.S. (US 10,421,963) and applications are currently pending in the U.S. (continuation application), Europe, Australia, Brazil, Canada, China, Eurasia, India, Israel, Japan, South Korea, Mexico, and New Zealand. The term of any patents resulting from these applications would be expected to extend to at least 2036.

Patent Rights Relating to Our Usher Program

With regard to our Usher Program and our lead candidates in the Usher space, QR-411 and QR-421a, we entered into an exclusive license agreement with the Radboud University Medical Center, Nijmegen, the Netherlands in June 2015 to obtain rights in a patent family with composition of matters claims directed to antisense oligonucleotides for treating Usher syndrome type II and method of use claims relating to modulation of the splicing of the *USH2A* gene product. A patent was granted in the U.S. (US 10,131,910) and applications are currently pending in the U.S. (continuation application) as well as Europe, Canada, Australia, and Israel. The term of any patents resulting from these applications would be expected to extend to at least 2035.

To further strengthen our position on the lead candidates QR-411 and QR-421a, we filed two international patent applications in April 2017 and September 2017, respectively. Both applications were continued in the U.S. and Europe and several other countries. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2037.

Patent Rights Relating to Our Axiomer Program

With regard to our Axiomer program, we filed several national and international patent applications from 2014 to 2019, several of which were continued in national and regional patent applications after the respective international phases. The term of any patents resulting from these applications, if issued, would be expected to extend to at least from 2035 to 2040.

Patent Rights Relating to Our Autosomal Dominant Retinitis Pigmentosa Program

On October 26, 2018, we and Ionis Pharmaceuticals, Inc. entered into a License Agreement, pursuant to which Ionis granted us an exclusive, worldwide, royalty-bearing license to us to develop and commercialize certain pharmaceutical products, including the product designated by Ionis as IONIS-RHO-2.5Rx, which has been re-designated by us as QR-1123, for the prevention or treatment of autosomal dominant retinitis pigmentosa, or adRP, in humans, including patient screening. Ionis also granted to the Company certain sub-license rights. Ionis licensed us non-exclusive rights under a range of technology and manufacturing patent families, as well as an exclusive right to one patent family related to QR-1123. The product patent family contains a granted patent in the U.S. (US 10,426,789) and pending applications in the U.S. (continuation application), Europe, Brazil, Canada, Israel, India, Mexico, and New Zealand.

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 Radboud for LCA

In April 2014 we entered into a Patent License Agreement with Radboud University Medical Center, or Radboud, in the field of antisense oligonucleotide-based therapy for Leber's Congenital Amaurosis, or LCA. Under the terms of this license agreement, we have an exclusive, world-wide royalty-bearing license under certain Radboud patent rights to develop, make, have made, use, sell offer for sale and import of certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of LCA. Pursuant to the terms of the license agreement, we are obligated to

pay Radboud net-sales-related royalties which shall be determined on a product-by-product and country-by-country basis. If we are required to pay any third-party royalties, we may deduct that amount from that which is owed to Radboud. Radboud shall provide human resources, materials, facilities and equipment that are necessary for preclinical and clinical trials and if we do not purchase such trial facilities from Radboud, we are required to pay an increased net-sales-related royalty. In our sole discretion, we may elect to convert our obligation to pay net-sales-related royalties into one of the two lump-sum royalty options depending on whether we elect to convert prior to or after regulatory approval has been filed.

We may sublicense our rights to any third-party provided such sub-license includes the same obligations on the sublicensee as are on us and we promptly furnish Radboud with a copy of the executed sublicensing agreements.

The license agreement will remain in effect until the date on which all patent applications and all granted patents ensuing from such applications have expired or is terminated earlier in accordance with the agreement. Either party may terminate the agreement if the other party is in default of a material obligation under the agreement which has not been cured within 30 days of notice of such default. Either party may also terminate the agreement if the other party declares bankruptcy, dissolves, liquidates or the like. Radboud may also terminate the agreement if we do not pay any amount owed under the agreement and such payment remains overdue for at least 30 days after receiving notice from Radboud of the amount due.

License Agreement with Radboud for Usher syndrome

In June 2015, we entered into another license agreement with Radboud University Medical Center, or Radboud. Under the terms of this license agreement, we have an exclusive, world-wide royalty-bearing license under certain Radboud patent rights to develop, make, have made, use, sell offer for sale and import of certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of Usher syndrome. Pursuant to the terms of the license agreement, we are obligated to pay Radboud net-sales-related royalties which shall be determined on a product-by-product and country-by-country basis. If we are required to pay any third-party royalties, we may deduct that amount from that which is owed to Radboud. Radboud shall provide human resources, materials, facilities and equipment that are necessary for preclinical and clinical trials and if we do not purchase such trial facilities from Radboud, we are required to pay an increased net-sales-related royalty. In our sole discretion, we may elect to convert our obligation to pay net-sales-related royalties into one of the two lump-sum royalty options depending on whether we elect to convert prior to or after regulatory approval has been filed.

We may sublicense our rights to any third-party provided such sub-license includes the same obligations on the sublicensee as are on us and we promptly furnish Radboud with a copy of the executed sublicensing agreements.

The license agreement will remain in effect until the date on which all patent applications and all granted patents ensuing from such applications have expired or is terminated earlier in accordance with the agreement. Either party may terminate the agreement if the other party is in default of a material obligation under the agreement which has not been cured within 30 days of notice of such default. Either party may also terminate the agreement if the other party declares bankruptcy, dissolves, liquidates or the like. Radboud may also terminate the agreement if we do not pay any amount owed under the agreement and such payment remains overdue for at least 30 days after receiving notice from Radboud of the amount due.

License Agreement with Inserm Transfert SA for LCA

In January 2018, we entered into a license agreement with Inserm Transfert SA and Assistance-Publique-Hôpitaux de Paris. Under the terms of the agreement, we have a world-wide, exclusive, royalty-bearing license under patent rights belonging to Inserm Transfert SA and other co-owners to develop, have developed, make, have made, use, have used and sell, have sold or otherwise distribute certain licensed products related to antisense oligonucleotides for treating LCA and method of treatment claims relating to modulation of the splicing of the *CEP290* gene product.

We have the right to grant sublicenses to third parties subject to certain limitations such as the sublicensee's activities do not conflict with the public order or ethical obligations of Inserm Transfert SA or any co-owner and do not tarnish the image of Inserm Transfert SA or any co-owner.

In partial consideration of the rights and licenses granted by the license agreement, we are required to make payments upon the completion of certain milestones: completion of a clinical trial more advanced than First in Man, such as a Phase IIb; and the first marketing authorization or any foreign equivalent for a first product. In further consideration of the rights and license granted under the agreement, we shall pay to Inserm Transfert SA a running royalty on net sales of products sold by us or our sublicensee.

Unless terminated earlier pursuant to termination provisions of Agreement, the license agreement will remain in effect on a country-by-country basis, until the later to occur of the following events (i) the invalidation or expiration of the last to expire or to be invalidated patent rights which covers the manufacture, use or sale of the product in said country or until the expiration of the exclusive commercialization right granted by a regulatory agency to a product as an orphan drug or (ii) five years after the first commercial sale of a product in the country in which the product is sold. The agreement may be terminated by either party in the event of an uncured breach by the non-breaching party. Inserm Transfert SA may terminate the agreement if we become the subject of voluntary or involuntary winding-up proceedings or judicial recovery, if we or our sublicensees interrupt development activities for at least one year, if we or our sublicensees interrupt commercialization for more than twelve months after the first commercialization in a country, if we do not commercialize a product within two years following our obtaining of marketing approval in a country, or if we or our sublicensees do not put a product into commercial use and do not keep products reasonably available to the public within twelve years of the effective date of the agreement.

License Agreement with Ionis Pharmaceuticals, Inc. for adRP

In October 2018, we entered into a license agreement with Ionis Pharmaceuticals, Inc. Under the License Agreement, we are required to make an upfront payment of an aggregate of up to \$ 6.0 million in installments, and certain payments up to an aggregate of \$ 20.0 million upon the satisfaction of certain development and sales milestones. In addition, Ionis is entitled to royalty payments in the double digits of aggregate annual net sales, subject to minimum sales in certain circumstances, and subject to reduced rates in certain circumstances. The royalty term lasts on a product-by-product and country-by-country basis, until the later of the expiration of the patent rights licensed to us and the expiration of regulatory-based exclusivity for such product in such country. The License Agreement may also be terminated by either party based upon certain uncured material breach by, or insolvency of, the other party, or by us at any time with advanced notice.

In connection with the upfront payments and development milestone payments, we also simultaneously entered into a Stock Purchase Agreement with Ionis, pursuant to which we agreed to issue an aggregate of \$ 2.5 million of ordinary shares to satisfy the first installment upfront payment, and the remaining installment of the upfront payment in ordinary shares determined upon the due date of such installment. In addition, the Stock Purchase Agreement provides for the ability for us, at our discretion, to pay the development milestone payments in ordinary shares when such payments are due. We may not issue ordinary shares to Ionis to the extent that such issuance would result in Ionis owning in excess of 18.5% of our issued and outstanding shares, nor may we issue ordinary shares if such issuance, together with previous issuances under the Stock Purchase Agreement, would exceed 19.9% of our outstanding ordinary shares as of the date of the execution of the Stock Purchase Agreement. Under these circumstances, we are required to pay the remainder of the upfront and/or development milestone payments in cash.

In addition, in connection with the Stock Purchase Agreement, we also entered into an Investor Agreement with Ionis, pursuant to which we agreed to register for resale the ordinary shares issued by us under the Stock Purchase Agreement, under the circumstances described in the Investor Agreement. The Investor Agreement also contains customary covenants related to our registration of such shares, preparation of filings in connection therewith and indemnification of Ionis. The Investor Agreement also contains lockup provisions prohibiting the disposition of our ordinary shares issued under the Stock Purchase Agreement for a period of 12 months from the applicable issuance date, as well as voting provisions requiring Ionis to vote its ordinary shares in accordance with the recommendations of our board of directors, in each case subject to certain exceptions.

Other License Agreements

In January 2016, we entered into an agreement with Leiden University Medical Center, or LUMC, which gives us a world-wide, exclusive, royalty-bearing license in the field of amyloid beta related diseases, notably Alzheimer's disease

and HCHWA-D, under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to its CNS program. On September 12, 2017, we spun out this program into Amylon Therapeutics B.V., in which we maintain a majority ownership.

In January 2017, we entered into an agreement with LUMC, which gives us a world-wide, exclusive, royalty-bearing license in the field of Huntington's disease, under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to the HD program.

In February 2019, we entered into an agreement with the University of Rochester, New York, which gives us a world-wide, exclusive, royalty-bearing, sublicensable license in the field of antisense oligonucleotides for use in nucleotide specific RNA editing through pseudouridylation, under certain patent rights of University of Rochester. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to the Axiomer/pseudouridylation program.

In May 2012, we entered into a license agreement with MGH, under which 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. The license is sub-licensable, contains certain diligence obligations and provides for milestone and royalties payments towards MGH.

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.

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, untitled or 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 preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices, or GLP, regulations;
- manufacture of the drug product in accordance with current Good Manufacturing Practice, or GMP, 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;

- satisfactory completion of an FDA audit of clinical trial sites to assess compliance with GCP; and
- review and approval by the FDA of the NDA.

The testing and approval process require 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 preclinical testing stage. Preclinical 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 preclinical 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 preclinical 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 reauthorize the trial 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 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, the parameters to assess efficacy 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. 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. Within 15 calendar days after the sponsor determines that the information qualifies for writing, written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the

product drug. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. 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.

A drug being studied in clinical trials may be made available to individual patients in certain circumstances. Pursuant to the 21st Century Cures Act, or Cures Act, as amended, the manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug, or as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy.

U.S. Review and Approval Processes

The results of product development, preclinical 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; 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 sponsor of an approved NDA is also subject to an annual prescription drug product program fee.

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 patients 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. The FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, program as a condition of approval, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Regulation of Combination Products in the United States

Certain products may be comprised of components that are regulated under separate authorities and by different centers at the FDA. These products are known as combination products. A combination product is comprised of a combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, a device, and a biological product. Under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, 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, device and biological products, or biological and drug products;
- a drug, biological product or device packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, biological product 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, biological product or device packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, biological product or device 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, which is the single mode of action that provides the most important therapeutic action of the combination product, i.e., the mode of action expected to make the greatest contribution to the overall intended therapeutic effects 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's Office of Combination Products addresses issues surrounding combination products and provides guidance regarding 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.

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 an unmet medical need 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. In addition to other benefits, such as the ability to 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.

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.

Breakthrough Designation

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 preclinical 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.

Priority Review

The FDA may grant an NDA a priority review designation, which sets the target date for FDA action on the application for a new molecular entity at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Rare Pediatric Disease Priority Review Voucher

The FDA may grant rare pediatric disease designation for indications in the treatment or prevention of a rare disease or condition that affects fewer than 200,000 individuals in the United States and that is a serious or life-threatening disease that primarily affects individuals aged from birth to 18 years, including age groups often called neonates, infants,

children and adolescents. Under the FDCA, a sponsor who receives approval of an NDA for a product that is for the prevention or treatment of a rare pediatric disease and meets certain additional criteria, may qualify for a rare pediatric disease priority review voucher, or PRV. A PRV can be redeemed to receive priority review under an expedited timeframe for a subsequent marketing application for a different product. A PRV may also be sold or transferred from the initial sponsor to another sponsor and may be further transferred any number of times before it is used. Pursuant to the 21st Century Cures Act, FDA's authority to award rare pediatric disease PRVs has been extended until 2020 and until 2022 for products that receive rare pediatric disease designation by 2020.

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, untitled or warning letters, holds on clinical trials, product 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, guidance, 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 Amendments. The Hatch-Waxman Amendments permit 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, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. 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 preclinical 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—a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug in the United States for this type of disease or condition will be recovered from sales of the product. 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. 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, as amended, 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. The FDCA requires 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 preclinical 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, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose 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 may obtain regulatory approval. In the United States, sales of any products for which we may 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 need 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 pharmaco-economic studies in order to demonstrate the medical need and cost-effectiveness of any 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 of 2010, collectively, the Affordable Care Act, 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 will 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 provision of the Affordable Care Act referred to as 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 for Economic 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 payor, 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 Affordable Care Act 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 Affordable Care Act 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 \$ 10,781 and \$ 21,563 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 Affordable Care Act 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 Affordable Care Act 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 Affordable Care Act 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 Affordable Care Act also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by expanding the population potentially eligible for Medicaid drug benefits. In addition, the Affordable Care Act 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. The Affordable Care Act 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.
- The Affordable Care Act 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”).

- The Affordable Care Act 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 Affordable Care Act 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 annually report this information to CMS which makes it publicly available in a searchable format on a CMS website.
- A new Patient-Centered Outcomes Research Institute was established pursuant to the Affordable Care Act 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 Affordable Care Act created the Independent Payment Advisory Board which 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 Affordable Care Act 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.

Some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In December 2017, President Trump signed into law the Tax Cuts and Jobs Act of 2017, which includes a repeal of the individual mandate under the Affordable Care Act. Additionally, in October 2017, President Trump signed an Executive Order directing federal agencies to review regulations applicable to association health plans and short-term health insurance, and announced that the administration would halt federal subsidies to insurance plans under the Affordable Care Act. It is possible that other repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage and/or in individuals having insurance coverage that provides less generous benefits. Thus, the full impact of the Affordable Care Act, any law replacing elements of it, or the political uncertainty surrounding its repeal or replacement on our business remains unclear. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

European Union Drug Review Approval

In the European Economic Area, or EEA (which is comprised, as of January 31, 2020, of the 27 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, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines, and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions 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. In general, there are three alternative routes to authorize medicinal products at a national level in the European Union:

- *Decentralized Procedure.* Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the Centralized Procedure. The competent authority of the reference member state will lead in the assessment of the application.
- *Mutual Recognition Procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.
- *National Procedure.* Applicants following the national procedure will be granted a marketing authorization that is valid only in a single member state. This procedure is not available for applicants seeking approval in more than one member state.

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 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 of the clinical trial application 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. 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 trial and a copy of the final study report.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. It is expected that the new Clinical Trials Regulation will come into effect in 2020. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new regulation, which will be directly applicable in all Member States (meaning that no national implementing legislation in each Member State is required), aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure using a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

PRIME Designation

PRIME is a voluntary scheme launched by the EMA to enhance support for the development of medicines that target an unmet medical need. The scheme focuses on medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options. These medicines are considered priority medicines by EMA. The scheme is open to medicines under development and for which the applicant intends to apply for an initial marketing authorization application through the Centralized Procedure. This scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation to enable accelerated assessment of medicines applications. Medicines under the PRIME scheme can expect to be eligible for accelerated assessment at the time of application for a marketing authorization. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

Acceptance into the PRIME scheme is based on the medicine's demonstration of potential to benefit patients with unmet medical needs based on early clinical data. Applicants from the academic sector and micro-, small- and medium-sized enterprises (SMEs) can apply earlier on the basis of compelling non-clinical data and tolerability data from initial clinical trials.

Once a candidate medicine has been selected for PRIME, the EMA will:

- appoint a rapporteur from the Committee for Medicinal Products for Human Use (CHMP) or from the Committee on Advanced Therapies (CAT) in the case of an advanced therapy to provide continuous support and help to build knowledge ahead of a marketing-authorization application;
- organize a kick-off meeting with the CHMP/CAT rapporteur and a multidisciplinary group of experts, so that they provide guidance on the overall development plan and regulatory strategy;
- assign a dedicated contact point;
- provide scientific advice at key development milestones, involving additional stakeholders such as health-technology-assessment bodies, to facilitate quicker access for patients to the new medicine; and
- confirm potential for accelerated assessment at the time of an application for marketing authorization.

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 27—European Union Member States. The centralized procedure will continue to apply to the United Kingdom for a transition period following Brexit, which is currently scheduled to run until 31 December 2020. However, after that transition period it is not clear whether the Centralized Procedure will continue to apply to the United Kingdom (although marketing approvals already granted under the Centralized Procedure will continue to apply in the United Kingdom).

Pursuant to Regulation (EC) No. 726/2004, as amended, the Centralized Procedure is mandatory for certain drugs, including 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 that sepfarsen and QR-421a have been granted orphan designation in the EU, they qualify, at the present time, 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 guidance and have published numerous guidelines that may apply to our product candidates. 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, excluding clock stops where additional information or written or oral explanation is to be provided by the applicant in response to the questions of the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 201 days. 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 timeframe of 210 days for assessment will be reduced to 150 days (excluding clock stops) but it is possible that the CHMP can revert to the standard time-limit for the Centralized Procedure if it considers that the application 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, preclinical tests and clinical trials. However, products designated as orphan medicinal products enjoy, upon receiving marketing authorization, a period of ten 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 that qualify for additional protections under Regulation (EC) No. 1901/2006 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 compared to products available for the 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. Orphan drug designations have been granted by the European Commission to sepofoarsen (EU/3/16/1641) QR-421a (EU/3/18/1973), and QR-411 (EU/3/17/1853).

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 ten 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 medicinal product”. A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. This ten year 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, for example 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 concept of ‘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 in the European Union. 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 external 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 an 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.

C. Organizational structure

At December 31, 2019, ProQR Therapeutics N.V. is the ultimate parent company of the following entities:

- ProQR Therapeutics Holding B.V. (the Netherlands, 100%);
- ProQR Therapeutics I B.V. (the Netherlands, 100%);
- ProQR Therapeutics II B.V. (the Netherlands, 100%);
- ProQR Therapeutics III B.V. (the Netherlands, 100%);
- ProQR Therapeutics IV B.V. (the Netherlands, 100%);
- ProQR Therapeutics VI B.V. (the Netherlands, 100%);
- ProQR Therapeutics VII B.V. (the Netherlands, 100%);
- ProQR Therapeutics VIII B.V. (the Netherlands, 100%);
- ProQR Therapeutics IX B.V. (the Netherlands, 100%);
- ProQR Therapeutics I Inc. (United States, 100%);
- Amylon Therapeutics B.V. (the Netherlands, 80%);
- Amylon Therapeutics, Inc. (United States, a 100% subsidiary of Amylon Therapeutics B.V.).

ProQR Therapeutics N.V. is also statutory director of Stichting Bewaarneming Aandelen ProQR (“ESOP Foundation”) and has full control over this entity. ProQR Therapeutics Holding B.V. holds a 20% minority shareholding in Wings Therapeutics Inc.

D. Property, plants and equipment

The Company leases office and laboratory facilities of 2,960 square meters at Zernikedreef in Leiden, the Netherlands, where our headquarters and our laboratories are located. The current lease agreement for these facilities terminates on June 30, 2020. A renewed lease agreement is in place for a 10-year period starting on July 1, 2020, which may be renewed for subsequent 5-year terms. This new lease agreement will increase the number of square meters leased to 4,772. In May 2018, we entered into an agreement to lease office space in the United States, at CIC Cambridge. The office space currently measures 60 square meters and is located at 245 Main Street, Cambridge, MA 02142. We believe that our existing facilities are adequate to meet current needs and that suitable alternative spaces will be available in the future on commercially reasonable terms.

Item 4A: Unresolved staff comments

Not applicable.

Item 5: Operating and Financial Review and Prospects

You should read the following discussion and analysis of our financial condition and results of operations together with the information under Item 3.A: "Selected financial data" and our audited financial statements, including the notes thereto, included elsewhere in this annual report. The following discussion is based on our financial statements prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (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 Item 3.D: "Risk factors".

A. Operating results

Overview

To date, we have financed our operations primarily through our initial public and follow-on offerings, our ATM facility and private placements of equity securities, and to a lesser extent from funding from governmental bodies and patient organizations, including Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) a subsidiary of the Cystic Fibrosis Foundation, Foundation Fighting Blindness (FFB), Netherlands Enterprise Agency (RVO), and EB Research Partnership (EBRP).

In October 2019, the Company consummated an underwritten public offering of 10,454,545 ordinary shares at an issue price of \$ 5.50 per share. The gross proceeds from this offering amounted to € 51,597,000 while the transaction costs amounted to € 3,047,000, resulting in net proceeds of € 48,550,000.

In December 2019, the Company issued 371,306 shares in the aggregate amount of \$ 3,501,000, at \$ 9.43 (€ 8.51) per share to Ionis Pharmaceuticals, Inc. Under the terms of the agreement, the second installment of the upfront payment in ordinary shares to the Company's common stock was made to Ionis upon the dosing of the first patient in the phase 1/2 Aurora clinical trial for QR-1123. The first installment of the upfront payment in ordinary shares to its common stock was made to Ionis upon signing the worldwide license agreement in November 2018. The Company was granted an exclusive worldwide license to QR-1123 and relevant patents. The Company will also make future milestone payments, certain of which will be made in equity and others in cash or equity at the company's discretion, and royalties on net sales of 20% through the royalty term.

At December 31, 2019, we had cash and cash equivalents of € 111,950,000. 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 inception in February 2012. For the years ended December 31, 2019, 2018 and 2017, we incurred net losses of € 56,746,000, € 37,086,000 and € 43,675,000, respectively. At December 31, 2019, we had an

accumulated deficit of € 211,746,000. We expect to continue incurring losses for the foreseeable future as we continue our preclinical studies of our product candidates, continue clinical development of our product candidates sepoparsen, QR-421a and QR-1123, advance QR-504a into clinical development, increase investments in our other research programs, apply for marketing approval of our product candidates and, if approved, build a sales and marketing infrastructure for the commercialization of our product candidates.

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. There have been no material adjustments to prior period estimates for any of the periods included in this annual report.

Our significant accounting policies are fully described in the notes to our financial statements appearing elsewhere in this annual report.

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, 2019 that had a material impact on our financial position, except for IFRS 16 *Leases*.

IFRS 16 Leases

IFRS 16 *Leases* specifies how a company recognizes, measures, presents and discloses leases. The Company has implemented IFRS 16 on January 1, 2019 by applying the modified retrospective method, meaning that the 2018 comparative numbers in the current year financial statements are not restated. Under this standard, all lease contracts are recognized on the Company's balance sheet, except for short-term and low value leases.

Upon implementation of IFRS 16, the Company recognized a lease liability and a corresponding right-of-use asset of € 2,359,000. Because the interest rate implicit in the lease could not be readily determined, future lease payments were discounted using the Company's incremental borrowing rate on the initial application date to determine the lease liability. The weighted average incremental borrowing rate applied is 4.3%. The carrying amounts of the lease liability and right-of-use asset at December 31, 2019 are € 508,000 and € 606,000, respectively.

In the income statement, lease expenditures previously recognized in operating expenses have been replaced by depreciation and interest expenses. In 2019, depreciation expenses on the right-of-use asset amounted to € 1,187,000 and interest expenses on the lease liability amounted to € 48,000. Under IFRS 16, total expenses resulting from lease contracts can be higher in the earlier years of a lease and lower in the later years, because the interest component of total expenses typically decreases over time.

The main impact on the statement of cash flows is an increase in cash flows from operating activities, since the repayments of the principal part of the lease liability are classified in the net cash flow from financing activities. This effect amounts to € 1,261,000 in 2019.

The Company applied the following practical expedients upon implementation of the new standard:

- Applied the short-term lease exemption, meaning that leases with a duration of less than one year are expensed in the income statement on a straight-line basis.
- Applied the low value lease exemption, meaning that leased assets with an individual value of \$ 5,000 or less if bought new are expensed in the income statement on a straight-line basis.

- Applied the option to include non-lease components in the lease liability.

Furthermore, we used the transition option to measure the right-of-use asset based on the recognized lease liability.

Reconciliation of the prior year operating lease commitment to the opening balance sheet

At December 31, 2018, the Company reported a commitment for future minimum lease payments under non-cancellable operating leases of € 2,466,000. The lease liability recognized upon implementation of IFRS 16 on January 1, 2019 amounted to € 2,359,000. The difference of € 107,000 is caused by the effect of discounting future lease payments to determine the lease liability.

A number of new standards, amendments to standards and interpretations are effective for annual periods beginning on after January 1, 2020 and have not been applied in preparing these consolidated financial statements. None of these are expected to have a material impact on the Group in the current or future reporting periods and on foreseeable future transactions. The Group does not plan to adopt these standards early.

JOBS Act and Foreign Private Issuer Exemptions

The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an “emerging growth company.” As of 2019, ProQR no longer qualifies as an emerging growth company, as we reached the maximum term of five years. As such, the Company can no longer apply the exemptions as of 2019 relating to not providing an auditor attestation report on our system of internal control over financial reporting.

As a foreign private issuer, we are not subject to the same requirements that are imposed upon U.S. domestic issuers by the Securities and Exchange Commission, or SEC. Under the Exchange Act, we will be subject to reporting obligations that, in certain respects, are less detailed and less frequent than those of U.S. domestic reporting companies. For example, although we intend to report our financial results on a quarterly basis, we will not be required to issue quarterly reports, proxy statements that comply with the requirements applicable to U.S. domestic reporting companies, or individual executive compensation information that is as detailed as that required of U.S. domestic reporting companies. We will also have four months after the end of each fiscal year to file our annual reports with the SEC and will not be required to file current reports as frequently or promptly as U.S. domestic reporting companies. We may also present financial statements pursuant to IFRS instead of pursuant to U.S. GAAP. Furthermore, although the members of our management and supervisory boards will be required to notify the Dutch Authority for the Financial Markets of certain transactions they may undertake, including with respect to our ordinary shares, our officers, directors and principal shareholders will be exempt from the requirements to report transactions in our equity securities and from the short-swing profit liability provisions contained in Section 16 of the Exchange Act. These exemptions and leniencies will reduce the frequency and scope of information and protections available to you in comparison to those applicable to a U.S. domestic reporting companies.

Financial Operations Overview

Other Income

Other income is incidental by nature and mainly consists of grant income from government-related organizations and charities. (Government) Grants are recognized in other income in the same period in which the related R&D costs are recognized.

Research and Development Costs

Research and development expenses consist principally of:

- salaries for research and development staff and related expenses, including social security costs and share-based compensation expenses;
- costs related to our preclinical and clinical activities and trials;

- costs for production of clinical and preclinical compounds and drug substances by contract manufacturers, including supporting studies such as stability studies and other analysis of the compounds;
- fees and other costs paid to contract research organizations, or CROs, in connection with additional preclinical 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.

Our research and development expenses primarily relate to the following key programs:

- Sepofarsen for the treatment of LCA

The research and development costs relating to our product candidate, sepofarsen, primarily consist of salaries and costs paid to CROs for toxicology and clinical studies, including statistical analyses, and manufacturing of process performance qualification batches. 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.

- QR-421a for the treatment of Usher syndrome

The research and development costs relating to our product candidate, QR-421a, primarily consist of salaries, costs paid to CROs for managing the clinical study, costs for statistical analyses and costs for toxicology studies. 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.

- QR-1123 for the treatment of autosomal dominant Retinitis Pigmentosa

The research and development costs relating to our product candidate, QR-1123, primarily consist of salaries and costs paid to CROs for our clinical study. 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 QR-504a and our innovation unit, which is our internal discovery engine. Our innovation unit has been active in building a pipeline based upon our toolbox of RNA technologies that we have in-licensed or developed in-house. These expenses primarily consist of salaries, costs for production of the preclinical compounds and costs paid to CROs for our preclinical studies.

For the years ended December 31, 2019, 2018 and 2017, we incurred expenses of € 46,491,000, € 29,514,000 € 31,153,000, respectively, on research and development.

Our research and development expenses may vary substantially from period to period based on the timing of our research and development activities. Research and development expenses are expected to moderately increase as we initiate and continue clinical trials for sepofarsen, QR-421a and QR-1123, and advance QR-504a and any other product candidate in preclinical studies. In addition, the COVID-19 outbreak has resulted in the delay of all of our ongoing and scheduled trials, including our ongoing pivotal trial of sepofarsen for LCA10. While we are implementing mitigation procedures designed to enable us to resume our development activities when the disruption resolves, there can be no assurance that these procedures will be successful or that we can avoid a material and adverse disruption to our business.

Any disruption in our development activities may substantially increase our costs in conducting such activities, including as a result of resuming research and development efforts.

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 sepfarsen, QR-421a, QR-1123, QR-504a or any other product candidate that we may develop in the future.

Any of these variables with respect to the development of sepfarsen, QR-421a, QR-1123, QR-504a, 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 such product candidate. For example, if the FDA, EMA or other regulatory authority were to require us to conduct preclinical 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 Costs

Our general and administrative expenses consist principally of:

- salaries for employees other than research and development staff and related expenses, including social security costs and share-based compensation expenses;
- 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.

Since our IPO in September 2014 we have incurred additional costs associated with operating as a public company. These public company-related expenses include costs of additional personnel, additional legal fees, accounting and audit fees, managing directors' and supervisory directors' liability insurance premiums and costs related to investor relations. We expect that our general and administrative expenses will remain fairly stable in upcoming years.

Share-Based Compensation

Share-based compensation reflects the costs of our equity-settled, share option plan, which are measured at the fair value of the options at the grant date, and which are spread in line with each of the separate vesting tranches of the applicable

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 note 12(d) to the financial statements included elsewhere in this annual report for additional information on share-based compensation.

Finance Income

To date, our cash and cash equivalents have been deposited primarily in savings and short-term deposit accounts. Savings and deposit accounts generated a limited amount of interest income. In 2019, 2018 and 2017 we held deposits in US dollars.

Income tax

Due to the operating losses incurred since inception the Company has no income tax provisions as of December 31, 2019, except for the income tax provision for our US subsidiary. Realization of deferred tax assets is dependent on future earnings, if any, the timing and amount of which are uncertain. Accordingly, we have not yet recognized any deferred tax asset related to operating losses. Also, no other transactions have occurred that would lead to a deferred tax position.

Results of Operations

Comparison of the periods ended December 31, 2019 and 2018

The following table sets forth our results of operations for the periods indicated.

	Year ended December 31,		Change
	2019	2018	
	(€ in thousands)		
Other income	1,933	5,761	(3,828)
Research and development costs	(46,491)	(29,514)	(16,977)
General and administrative costs	(12,887)	(12,540)	(347)
Operating result	(57,445)	(36,293)	(21,152)
Finance income and expense	402	(792)	1,194
Results related to associates	429	—	429
Corporate income taxes	(132)	(1)	(131)
Net loss	(56,746)	(37,086)	(19,660)

Other income

Other income is incidental by nature. In 2019, other income included grant income from the Foundation Fighting Blindness (FFB) for the purpose of developing QR-421a. FFB grant income amounted to € 1,312,000 in 2019 compared to € 2,478,000 in 2018.

The EBRP/EBMRF grant agreement was terminated on March 26, 2019 as part of the strategic spin out of the Dystrophic Epidermolysis Bullosa (DEB) activities into a newly formed company, Wings Therapeutics Inc. As such, no grant income was recognized in 2019 related to this grant. In 2018, € 1,301,000 had been recognized as other income.

In addition, in 2018 the Company recognized grant income amounting to € 1,300,000 relating to the Horizon 2020 grant received from the European Commission in May 2015 for the development of eluforsen. No income was recognized relating to this grant in 2019.

Research and development costs

Research and development costs amounted to € 46,491,000 for the year ended December 31, 2019 compared to € 29,514,000 for the year ended December 31, 2018. These costs were primarily related to our product candidates, sepfarsen, QR-421a, QR-1123, QR-504a, QR-313 (in 2018) and our innovation unit. Our research and development expenses are highly dependent on the development phases of our product candidates and are expected to stay largely at the same level, although they may fluctuate significantly from period to period.

The increase in research and development costs in the year ended December 31, 2019 compared to the year ended December 31, 2018 is mainly due to:

- costs we incurred for the Phase 2/3 clinical trial for sepfarsen, which increased in 2019 compared to 2018;
- costs we incurred for the first-in-human clinical trial for QR-421a, which increased in 2019 compared to 2018;
- costs we incurred for the first-in-human clinical trial for QR-1123, which started in 2019;
- increased payments to Ionis Pharmaceuticals, Inc. under the terms of the license agreement for QR-1123;
- increased staff costs as a result of an increase in the number of staff working on (pre-)clinical development of our product candidates. The number of full-time equivalent employees working on research and development increased from 89 at December 31, 2018 to 117 at December 31, 2019;
- 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 our product candidates;
- increased project-related consultancy costs, including regulatory and intellectual property support; and
- increased share-based compensation, reflecting grants of share options to research and development staff made after we adopted our Option Plan in September 2013.

General and administrative costs

General and administrative costs amount to € 12,887,000 for the year ended December 31, 2019 compared to € 12,540,000 for the year ended December 31, 2018. We expect that general and administrative costs will remain fairly stable in upcoming years.

Finance income and expense

We had net finance income of € 402,000 for the year ended December 31, 2019, as compared to net finance expenses of € 792,000 for the year ended December 31, 2018. The financial income and expenses mainly reflect foreign exchange results on cash and cash equivalents denominated in U.S. dollars.

Comparison of the periods ended December 31, 2018 and 2017

Reference is made to our 2018 annual report on form 20-F, filed on March 28, 2019, for a comparison of the periods ended December 31, 2018 and 2017.

B. Liquidity and capital resources

To date, we have financed our operations through our IPO, follow on offerings, ATM facility, private placements of equity securities, convertible loans and funding from governmental bodies and patient organizations.

On November 7, 2018, the Company filed a shelf registration statement, which permitted: (a) the offering, issuance and sale by the Company of up to a maximum aggregate offering price of \$ 300,000,000 of its ordinary shares, warrants and/or units; and (b) as part of the \$ 300,000,000, the offering, issuance and sale by us of up to a maximum aggregate offering price of \$ 75,000,000 of its ordinary shares that may be issued and sold under a sales agreement with H.C. Wainwright & Co in one or more at-the-market offerings. In March 2020, we terminated this sales agreement with H.C. Wainwright & Co. and entered into a new sales agreement for such at-the-market offerings up to a maximum aggregate offering price of \$75,000,000 of our ordinary shares with Citigroup Global Markets Inc. and Cantor Fitzgerald & Co., whom we refer to as the Agents.

Subject to the terms and conditions of the sales agreement, each Agent will use its commercially reasonable efforts to sell the shares from time to time, based upon our instructions. We have no obligation to sell any of the shares, and may at any time suspend sales under the agreement or terminate the agreement in accordance with its terms. We have provided the Agents with customary indemnification rights, and the Agents will be entitled to a fixed commission of 3.0% of the aggregate gross proceeds from the shares sold. The agreement contains customary representations and warranties, and we are required to deliver customary closing documents and certificates in connection with sales of the shares. We may instruct only one Agent to offer and sell shares under the agreement on any single given day.

Sales of the shares under the agreement will be made in transactions that are deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, including sales made directly on the NASDAQ Global Market at market prices, in negotiated transactions at market prices prevailing at the time of sale, or at prices relating to such prevailing market prices, and/or any other method permitted by law.

The description of the agreement set forth above does not purport to be complete and is qualified in its entirety by reference to the full text thereof, which is attached hereto as Exhibits 4.17 and incorporated by reference herein.

Cash Flows

The table below summarizes our statement of cash flows for the years ended December 31, 2019 and 2018.

	Year ended December 31,		
	2019	2018	Change
	(€ in thousands)		
Net cash used in operating activities	(43,970)	(28,493)	(15,477)
Net cash used in investing activities	(580)	(312)	(268)
Net cash generated by financing activities	50,199	86,457	(36,258)
Net increase/(decrease) in cash and cash equivalents	5,649	57,652	(52,003)
Currency effect cash and cash equivalents	721	(171)	892
Cash and cash equivalents at the beginning of the period	105,580	48,099	57,481
Cash and cash equivalents at the end of the period	111,950	105,580	6,370

Net cash used in operating activities increased from € 28,493,000 in the year ended December 31, 2018 to € 43,970,000 in the year ended December 31, 2019. The increase is caused mainly by the higher operating loss, which increased by € 21,152,000 in 2019, compared to 2018. This effect is partly offset by adjustments for share-based payment expenses and depreciation expenses.

Net cash used in investing activities increased from € 312,000 in the year ended December 31, 2018 to € 580,000 in the year ended December 31, 2019. This increase was primarily due to our investments in laboratory equipment and equipment used in our clinical studies. In addition, various leasehold improvements were initiated in 2019.

Net cash generated by financing activities decreased from € 86,457,000 in the year ended December 31, 2018 to € 50,199,000 in the year ended December 31, 2019. In 2018, the Company consummated an underwritten public offering of 6,612,500 ordinary shares at an issue price of \$ 15.75 per share. The gross proceeds from this offering amounted to € 89,983,000 while the transaction costs amounted to € 5,792,000, resulting in net proceeds of € 84,191,000. In 2019,

we raised gross proceeds of € 51,597,000 from the issuance of 10,454,545 ordinary shares. Transaction costs amounted to € 3,047,000, resulting in net proceeds of € 48,550,000.

Reference is made to our 2018 annual report on form 20-F, filed on March 28, 2019, for a comparison of the periods ended December 31, 2018 and 2017.

Cash and Funding Sources

The table below summarizes our main sources of financing for the years ended December 31, 2019, 2018 and 2017.

	Equity Capital	Convertible Loans	Government Borrowing	Total
	(€ in thousands)			
Year ended December 31, 2017	25,685	650	301	26,636
Year ended December 31, 2018	84,191	1,132	264	85,587
Year ended December 31, 2019	48,550	690	2,027	51,267
Total	158,426	2,472	2,592	163,490

In 2019, our primary source of funding was the underwritten public offering of 10,454,545 ordinary shares in October, resulting in net proceeds of € 48,550,000. Our main source of financing in 2018 was our offering in September providing net proceeds of € 84,191,000. In 2017, our sources of financing were our offering in July providing net proceeds of € 4,864,000, our offerings in November providing net proceeds of € 16,683,000 and the sale of shares through our ATM facility providing net proceeds of € 4,138,000.

Convertible loans were issued to Amylon Therapeutics B.V. in 2017, 2018 and 2019 and are interest-bearing at an average rate of 8% per annum. They are convertible into a variable number of ordinary shares within 36 months at the option of the holder or the Company in case financing criteria are met. Any unconverted loans become payable on demand after 24 – 36 months in equal quarterly terms.

In March 2018, we entered into a convertible loan (the “Loan”), pursuant to which we borrowed an aggregate of € 260,000 from the lender. The loan bears interest at a rate of 3% per annum. The outstanding principal and interest under the Loan is convertible into a variable number of ordinary shares at the option of the holder in case financing criteria are met. If these criteria are not met on or before March 1, 2022, the outstanding amount will be fully converted into our ordinary shares.

At December 31, 2019, we had borrowings of € 13,052,000, which consisted of borrowings from a government body (€ 10,315,000) and convertible loans (€ 2,737,000). Cash is denominated in both U.S. dollars and euros

At December 31, 2018, we had borrowings of € 9,386,000, which consisted of borrowings from a government body (€ 7,515,000) and convertible loans (€ 1,871,000). Cash is denominated in both U.S. dollars and euros.

For a description of our financial commitments, see below.

Funding Requirements

We expect that our cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2022. 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, resumption and completion of preclinical 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 Item 3.D: “Risk Factors”.

Capital Expenditures

The following table sets forth our capital expenditures for the years ended December 31, 2019, 2018 and 2017:

	<u>Year ended December 31,</u>		
	<u>2019</u>	<u>2018</u>	<u>2017</u>
	(€ in thousands)		
Purchases of tangible fixed assets	835	312	82

The increase in purchases of tangible fixed assets from € 82,000 in 2017 to € 312,000 in 2018 was primarily due to our investments in laboratory equipment in 2018. Purchases of tangible fixed assets increased further from € 312,000 in 2018 to € 835,000 in 2019. This increase was primarily due to our investments in laboratory equipment and equipment used in our clinical studies. In addition, various leasehold improvements were made in 2019.

Contractual Obligations and Commitments

The table below analyzes ProQR’s undiscounted liabilities into relevant maturity groupings based on the remaining period at December 31, 2019 until the contractual maturity date:

	<u>Less than</u>	<u>Between 1</u>	<u>Between 2</u>	<u>Over 5 years</u>
	<u>1 year</u>	<u>and 2 years</u>	<u>and 5 years</u>	
	(€ in thousands)			
At December 31, 2019				
Borrowings	343	10,054	4,790	322
Lease liabilities	513	—	—	—
Trade payables and other payables	10,142	—	—	—
Total	10,998	10,054	4,790	322

Commitments

Rent

Since 2012, the Company is domiciled in Leiden, the Netherlands. We are currently a party to a lease agreement for laboratory and office space in Leiden. The total commitment for this agreement and a new lease agreement to which the Company had committed as at December 31, 2019 amounts to € 13,377,000.

Patent license agreements

The Company and the Radboud University Medical Center have entered into a Patent License Agreement under which we were granted a world-wide exclusive license pursuant to which we may have certain royalty obligations in relation to our product candidate sepfarsen for Leber's congenital amaurosis.

The Company and the Radboud University Medical Center have entered into a Patent License Agreement under which we were granted a world-wide exclusive license pursuant to which we may have certain royalty obligations in relation to Type II Usher Syndrome.

The Company and the Leiden University Medical Centre have entered into a Patent License Agreement under which we were granted a world-wide exclusive license pursuant to which we may have certain royalty obligations in relation to several CNS diseases.

The Company and Inserm Transfert SA and Assistance-Publique-Hôpitaux de Paris have entered into a Patent License Agreement under which we were granted a world-wide exclusive license pursuant to which we may have certain royalty obligations in relation to our product candidate sepfarsen for Leber's congenital amaurosis.

On October 29, 2018, ProQR signed of an agreement with Ionis Pharmaceuticals to license QR-1123 (formerly "IONIS-RHO-2.5Rx"), an RNA medicine for autosomal dominant retinitis pigmentosa (adRP) caused by the P23H mutation in the rhodopsin (RHO) gene. Under the terms of the agreement, ProQR was granted an exclusive worldwide license to QR-1123 and relevant patents. In 2018, ProQR paid the first installment of an upfront payment in ordinary shares in the aggregate amount of \$ 2,500,000 at \$ 22.23 per share, which represents a 20% premium (based on the volume weighted average price of the previous 20 trading days) to its common stock, to Ionis upon signing the agreement. In 2019, ProQR paid the second installment of the upfront payment in ordinary shares in the aggregate amount of \$ 3,501,000, at \$ 9.43 per share. ProQR will also make future milestone payments, certain of which will be made in equity and others in cash or equity at ProQR's discretion, and royalties on net sales of 20% through the royalty term.

The Company and the General Hospital Corporation (MGH) have entered into a Patent License Agreement pursuant to which we may have certain royalty and milestone payment obligations based on the development or commercialization of eluforsen. The Company and PARI Pharma GmbH entered into an agreement, pursuant to which the Company is granted an exclusive license to the use of PARI's eflow technology for the administration of oligonucleotide-based drugs in the F508del mutation in cystic fibrosis, pursuant to which the company has certain upfront-, development-, and sales-based royalty-payment obligations.

Refer to Item 4.B: "Business Overview" for more details on patent license agreements.

Clinical support agreements

On February 9, 2018, we entered into an agreement with Foundation Fighting Blindness, or FFB, under which FFB will provide funding of \$ 7.5 million to advance QR-421a into the clinic and will receive future milestones.

Pursuant to the terms of the agreement, we are obligated to make a one-time milestone payment to FFB of up to \$ 37.5 million, payable in four equal annual installments following the first commercial sale of QR-421a, the first of which is due within 60 days following the first commercial sale. We are also obligated to make a payment to FFB of up to \$ 15 million if it transfers, sells or licenses QR-421a other than for certain clinical or development purposes, or if we enter into a change of control transaction. However, the payment in the previous sentence may be set-off against the \$ 37.5

million milestone payment. Either FFB or we may terminate the agreement for cause, which includes our material failure to achieve certain commercialization and development milestones. Our payment obligations survive the termination of the agreement.

In August 2014, we entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, a subsidiary of the Cystic Fibrosis Foundation, pursuant to which CFFT agreed to provide the Company with up to \$ 3 million to support the clinical development of eluforsen.

Pursuant to the terms of the agreement, we are obligated to make a one-time milestone payment to CFFT of up to approximately \$ 16 million, payable in three equal annual installments following the first commercial sale of eluforsen, the first of which is due within 90 days following the first commercial sale. We are also obligated to make a one-time milestone payment to CFFT of up to \$ 3 million if net sales of eluforsen exceed \$ 500 million in a calendar year. Lastly, we are obligated to make a payment to CFFT of up to approximately \$ 6 million if we transfer, sell or license eluforsen other than for certain clinical or development purposes, or if we enter into a change of control transaction prior to commercialization. However, the payment in the previous sentence may be set-off against the \$ 16 million milestone payment. Either CFFT or we may terminate the agreement for cause, which includes our material failure to achieve certain commercialization and development milestones. Our payment obligations survive the termination of the agreement.

Research and development commitments

The Company has committed itself to a number of obligations amounting to € 19,472,000 at December 31, 2019 (2018: € 8,114,000). Of these obligations an amount of € 10,234,000 is due in 2020, the remainder is due in 1 to 5 years.

Our commitments are set out in more detail in note 21 and 22 to the financial statements as included elsewhere in this annual report.

C. Research and development, patents and licenses, etc.

See Item 4.B: “Business Overview” and Item 5: “Operating and Financial Review and Prospects”.

D. Trend information

Other than as disclosed elsewhere in this annual report, we are not aware of any trends, uncertainties, demands, commitments or events for the period from January 1, 2019 to December 31, 2019 that are reasonably likely to have a material adverse effect on the Company’s net revenues, income, profitability, liquidity or capital resources, or that caused the reported financial information to be not necessarily indicative of future operating results or financial conditions. For a discussion of trends, see Item 5.A: “Operating results”.

E. Off-balance sheet arrangements

During the periods presented in this annual report, we did not have any off-balance sheet arrangements.

F. Tabular disclosure of contractual obligations

See Item 5.B: “Liquidity and capital resources”.

G. Safe harbor

This annual report contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Refer to “Forward-looking statements” at the beginning of this report.

Item 6: Directors, Senior Management and Employees**A. Directors and senior management**

We have a two-tier board structure consisting of our management board ('raad van bestuur') and a separate supervisory board ('raad van commissarissen'). Below is a summary of relevant information concerning our supervisory board, management board and senior management.

Supervisory Board

The following table sets forth information with respect to each of our supervisory board members and their respective dates of birth. 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 Zernikedreef 9, 2333 CK Leiden, the Netherlands.

Our supervisory board is currently composed of the following members, all of whom are independent under applicable NASDAQ standards and all of whom, with the exception of Mr. Dinko Valerio, are independent under the Dutch Corporate Governance Code (DCGC):

Name	Date of Birth	Position	Member Since	Term expires
Dinko Valerio	August 3, 1956	Member of the Supervisory Board (Chairman)	January 1, 2014	2020
Alison Lawton	September 26, 1961	Member of the Supervisory Board	September 17, 2014	2022
Antoine Papiernik	July 21, 1966	Member of the Supervisory Board	January 1, 2014	2021
James Shannon	June 5, 1956	Member of the Supervisory Board	June 21, 2016	2020
Bart Filius	July 5, 1970	Member of the Supervisory Board	May 21, 2019	2023
Theresa Heggie	November 17, 1960	Member of the Supervisory Board	July 1, 2019	2023

The following sets forth biographical information regarding our Supervisory Board members. There are no family relationships among the members of our Supervisory Board, Management Board or Executive Officers.

Dinko Valerio is one of our founders and currently serves as the chairman of our Supervisory Board. Mr. Valerio has served on our supervisory 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 former 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. In 2017 Mr. Valerio became a board member of Amylon Therapeutics B.V., an 80% owned affiliate of ProQR Therapeutics N.V. Adding to his corporate experience, Mr. Valerio was appointed professor in the field of gene therapy of the hematopoietic system at the University of Leiden in 1992. 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.

Alison Lawton has served on our supervisory board since September 2014. Ms. Lawton is currently Chief Executive Officer, President and Director of Kaleido Biosciences where she was previously President and Chief Operating Officer since Dec 2017. Previously, Ms. Lawton was Chief Operating Officer at Aura Biosciences, Inc, from 2015 to 2017, Ms. Lawton served as Chief Operating Officer at OvaScience Inc., a life sciences company, from January 2013 to January 2014. In addition, from 2014 to 2017, Ms. Lawton served as a biotech consultant for various companies, including as Chief Operating Officer consultant at X4 Pharmaceuticals. Ms. Lawton worked at various positions of increasing responsibility at Genzyme Corporation, or Genzyme, and subsequently at Sanofi-Aventis, following its 2011 acquisition of Genzyme, each a global biopharmaceutical company. Ms. Lawton served as head of Genzyme Biosurgery, where she was responsible for Genzyme's global orthopedics, surgical and cell therapy and regenerative medicine businesses. Prior

to that, Ms. Lawton oversaw Global Market Access at Genzyme, which included Regulatory Affairs, Global Health Outcomes and Strategic Pricing, Global Public Policy, and Global Product Safety & Risk Management. Before joining Genzyme, Ms. Lawton worked for seven years in the United Kingdom at Parke-Davis, a pharmaceutical company. Ms. Lawton serves on the board of directors of Verastem, Inc., a public biopharmaceutical company. She also served on the board of directors of Cubist Pharmaceuticals for three years until its acquisition by Merck & Co., Inc. in 2015. She is past President and Chair of the Board of Regulatory Affairs Professional Society and past FDA Advisory Committee member for Cell and Gene Therapy Committee. She earned her BSc in Pharmacology, with honors, from King's College London.

Antoine Papiernik has served on our supervisory board since January 2014. Mr. Papiernik is managing partner at Sofinnova Partners, which he joined in 1997, and was appointed chairman in 2017. Mr. Papiernik has been an initial investor and active board member in public companies like Actelion, Addex, Auris Medical, Shockwave Medical Inc., Orexo, NovusPharma (then sold to CTI), Movetis (then sold to Shire), Mainstay Medical, Pixium Vision and Stentys, which went public respectively on the Zurich Stock Exchange, the NASDAQ Global Market, 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), Core Valve (sold to Medtronic), Fovea (sold to Sanofi Aventis) Ethical Oncology Science (EOS, sold to Clovis Oncology) and Recor Medical (sold to Otsuka). Mr. Papiernik is also a board member of private companies MedDay Pharmaceuticals, MD Start II, Reflexion Medical, Tissium (previously named Gecko Biomedical), SafeHeal, Highlife, Rgenix and Ablacare. Mr. Papiernik has an MBA degree from the Wharton School of Business, University of Pennsylvania.

James Shannon, MD has served on our Supervisory Board since June 2016. Mr. Shannon has had an extensive career in drug development and pharma. From 2012 until his retirement in 2015, Mr. Shannon was Chief Medical Officer at GlaxoSmithKline. Prior to that he was Global Head of Pharma Development at Novartis and Senior Vice-President, Clinical Development at Sterling Winthrop Pharmaceuticals. He held board positions at companies including Biotie, Circassia, Crucell, Endocyte, MannKind and Cerimon Pharmaceuticals. In 2017 he joined the board of directors of Horizon Pharma. He received his undergraduate and postgraduate degrees at Queen's University of Belfast and is a Member of the Royal College of Physicians (UK). Mr. Shannon currently is Chairman of the Board at myTomonows (NL) and Kyowa Kirin NA (USA) and holds board positions at Mannkind Corp (USA), Horizon Pharma (Ire) and Immodulon (UK).

Bart Filius is Chief Operating Officer (COO) and Chief Financial Officer (CFO) at Galapagos NV. He joined Galapagos in 2014 as CFO and added the role of COO in 2017. Prior to joining Galapagos, Mr. Filius held a variety of executive positions at Sanofi, where he was Vice President, CFO Europe, Country manager for The Netherlands and Vice President for Mergers & Acquisitions. Prior to joining Sanofi, Mr. Filius was a strategy consultant at Arthur D. Little. Mr. Filius has an MBA degree from INSEAD and a bachelor's degree in business from Nyenrode University.

Theresa Heggie currently serves as Senior Vice President, Head of CEMA at Alnylam Pharmaceuticals. She previously served in senior commercial and operating roles at Shire where she built the EMEA rare disease business and led the Global Commercial Operations and, following Shire's acquisition of Jerini, served as its CEO. Earlier in her career, Ms. Heggie held increasingly senior positions in the commercial organizations at Janssen Pharmaceuticals and Baxter Healthcare. Ms. Heggie has also been a board member at SOBI (Swedish Orphan Biovitrum) and currently serves on the board of BioCryst. She received a BSc from Cornell University.

Management Board

The following table sets out information with respect to each of our management board member, his date of birth and his position at the company as of the date of this annual report. The business address of our management board member is our registered office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands.

Name	Date of Birth	Position	Date of Appointment	Term Expires
Daniel de Boer	April 12, 1983	Chief Executive Officer	February 21, 2012	2022

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

Daniel de Boer is our founding Chief Executive Officer since our incorporation in 2012. Daniel is a serial-entrepreneur and passionate advocate for rare disease patients. He assembled a group of successful biotech executives as co-founders and built a team of a 150 experienced scientists and drug developers, devoted to creating RNA therapies for patients in need. Under Daniel's leadership ProQR initiated clinical trials in multiple development programs for rare diseases, and raised over € 300 million in funding, including an IPO on Nasdaq. Daniel is responsible for the overall strategy and general business in the company. Before founding ProQR, Daniel was founder and Chief Executive Officer of RNA Systems, PC Basic and Running IT, companies he led through phases of growth, developing and launching several products in multiple European countries. Daniel was also a co-founder of Amylon Therapeutics, a company developing therapies for genetic brain diseases. In 2018 Daniel was named "Emerging Entrepreneur of the Year" by EY. In 2019, Daniel was selected for the Young Global Leaders program at the World Economic Forum.

Officers

Our management board is supported by our officers. The following table sets forth information with respect to each of the officers, their respective dates of birth and their positions, as of the date of this annual report. The business address of our officers is our registered office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands.

Name	Date of Birth	Position
David Rodman	May 12, 1955	Executive Vice President of Research & Development
Gerard Platenburg	February 24, 1964	Chief Innovation Officer
Smital Shah	April 25, 1976	Chief Business & Financial Officer

David Rodman, MD is our Executive Vice President of Research & Development. David joined ProQR in 2017 having previously served in leadership roles with Novartis Institutes for Biomedical Research (NIBR), Vertex Pharmaceuticals, miRagen Therapeutics and Nivalis Therapeutics. Prior to moving to industry in 2005, David had a distinguished academic career, leading the Center for Genetic Lung Diseases at the University of Colorado and directing the Cystic Fibrosis Care, Teaching and Research efforts at the National Jewish Medical and Research Center in Denver, Colorado. During 12 years in industry, David has had global responsibility for driving innovation in the translation of cutting-edge science into transformational new therapies for rare diseases including CF, pulmonary fibrosis, pulmonary artery hypertension and severe immunologic and inflammatory diseases. At Vertex Pharmaceuticals he directed early- and late-stage CF clinical development programs including Kalydeco®, Orkambi® and VX-661. David received a BA in Economics from Haverford College in 1976, an MD from the University of Pennsylvania in 1980 and completed training in Internal Medicine, Pulmonary and Critical Care Medicine at the University of Colorado. He has served as an advisor to the National Institutes of Health, was elected to the American Society for Clinical Investigation and is a Fellow of the American Heart Association.

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's degree in chemistry and molecular biology from Leiden University in 1987 and pursued PhD work at Leiden University.

Smital Shah has served as our Chief Financial Officer since October 2014 and was promoted to Chief Business and Financial Officer in November 2018, where she is responsible for finance, investor relations and communications, business development and commercial. She joined the board of Pliant Therapeutics in 2019. Smital has a 12-year track record of management and leadership in biopharma companies and investment banking, with particular experience in

financial strategy, capital markets and business development. Prior to joining us Smital was at Gilead Sciences, where she managed their multi-billion dollar debt, cash and investment portfolios. Prior to Gilead, Smital spent several years in investment banking at Leerink Partners and JP Morgan focused on capital raising and strategic transactions in the biotech space. During this time, Smital has helped raise over \$ 1 billion in equity capital and over \$ 7 billion in debt capital for emerging and established biotech companies as well advised on a variety of strategic transactions such as mergers, divestitures, asset sales, dividends, royalty monetizations and corporate partnerships. Previously, she held various R&D focused roles at Johnson & Johnson. Smital has a Bachelors and Masters in Chemical Engineering and an MBA from the University of California at Berkeley.

B. Compensation

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. On May 21, 2019, the general meeting of shareholders adopted the current compensation policy of our company. 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 supervisory board, including the criteria for granting such shares or changes to such grants. The general meeting of shareholders may grant compensation to members of the supervisory board. The supervisory board will be reimbursed for their expenses.

Compensation of the Supervisory Board

The remuneration of the supervisory board members in 2019 is set out in the table below:

	2019			Total
	Short term employee benefits	Post- employment benefits (€ in thousands)	Share-based payment	
Mr. Dinko Valerio	74	—	106	180
Mr. Antoine Papiernik	104	—	—	104
Ms. Alison Lawton	41	—	107	148
Mr. Paul Baart	144	—	—	144
Mr. James Shannon	48	—	109	157
Mr. Bart Filius	30	—	26	56
Ms. Theresa Heggie	19	—	18	37
	460	—	366	826

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 (refer to Note 12(d) to the financial statements included elsewhere in this annual report).

On May 21, 2019, our shareholders approved new compensation principles for the supervisory board. Under the new compensation principles, members of our supervisory board receive a board fee of \$ 35,000 per year and the chairperson receives a board fee of \$ 70,000 per year. In addition, the audit committee chairperson receives \$ 15,000 per year for service on that committee, and each other member of the audit committee receives \$ 7,500 per year for service on that committee. The compensation committee chairperson receives \$ 10,000 per year for service on that committee, and each other member of the compensation committee receives \$ 5,000 per year for service on that committee. The chairperson of the nominating and corporate governance committee receives \$ 8,000 per year for service on that committee, and each other member of the nominating and corporate governance committee receives \$ 4,000 per year for service on that committee. In addition, members of the supervisory board may be granted an additional compensation in cash of \$ 77,500 per year or a grant of options with an underlying value of \$ 155,000 per year.

Compensation of the Management Board

The table below sets out a breakdown of the compensation in 2019 of each current member of the management board:

	2019			Total
	Short term employee benefits	Post-employment benefits	Share-based payment	
Mr. D.A. de Boer	722	10	1,533	2,265

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 (refer to Note 12(d) to the financial statements included elsewhere in this annual report).

For further detail on compensation of members of our supervision board, management board and senior management, see Note 23 to the financial statements included elsewhere in this annual report.

C. Board practices

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 terms of four years. Our articles of association provide that the supervisory board members must retire periodically in accordance with a rotation schedule adopted by the supervisory board. A supervisory board member who retires in accordance with the rotation schedule can be reappointed immediately. 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 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.

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. The management board as a whole and any management board member individually, are authorized to represent us in dealings with third parties. The management board may delegate this authority in whole or in part to employees of the company.

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 elects 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. Our articles of association provide that the management board members must retire periodically in accordance with a rotation schedule adopted by the management board. A management board member who retires in accordance with the rotation schedule may be reappointed immediately for a term of not more than four years at a time.

Service Agreements

We have entered into a service agreement with our CEO. The service agreement contains a termination notice period of two months. The service agreement may be terminated in the event of an urgent reason (*dringende reden*) at any time, without advance notice. The service agreement with Daniel de Boer 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. The service agreement also contains certain restrictive covenants, including post termination non-competition and non-solicitation covenants, which survive for a period of 12 months post-termination.

Committees of the Supervisory Board

We 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

Our audit committee consists of Bart Filius (chairman), Theresa Heggie and James Shannon. Each member satisfies the independence requirements of the NASDAQ listing standards and Rule 10A-3(b)(1) under the Exchange Act, and each

member meets the criteria for independence set forth in best practice provision 2.1.8 of the DCGC. Bart Filius qualifies as an “audit committee financial expert,” as defined by the SEC in Item 16A: “Audit Committee Financial Expert” and as determined by our supervisory board. The audit committee oversees our accounting and financial reporting processes and the audits of our financial statements. The audit committee is 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

Our compensation committee consists of James Shannon (chairman), Dinko Valerio and Alison Lawton. Each member satisfies the independence requirements of the NASDAQ listing standards. In addition, each member meets the criteria for independence set forth in best practice provision 2.1.8 of the DCGC, with the exception of Mr. Dinko Valerio. The compensation committee assists 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 is 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 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.

Our supervisory board may also delegate certain tasks and powers under our Option Plan to the compensation committee.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Dinko Valerio (chairman) and Antoine Papiernik. Each member satisfies the independence requirements of the NASDAQ listing standards. In addition, each member meets the criteria for independence set forth in best practice provision 2.1.8 of the DCGC, with the exception of Mr. Dinko Valerio. The nominating and corporate governance committee assists 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 our officers. The nominating and corporate governance committee is 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.

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.

D. Employees

As at December 31, 2019, we had a total of 154.4 employees (converted to FTE). Of these employees, 118.3 were engaged in research and development and 36.1 in general and administrative. For additional details we refer to note 17 to the financial statements. As far as we know, our employees are not represented by a labor union. We have never experienced any employment related work stoppages, and we consider our relations with our employees to be good.

E. Share ownership

Refer to Item 7.A: “Major shareholders” in this annual report.

Item 7: Major Shareholders and Related Party Transactions

A. Major shareholders

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as at December 31, 2019 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 percentage of shares beneficially owned is based on a total of 49,745,687 ordinary shares outstanding as at December 31, 2019. The numbers 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, or to receive the economic benefit of ownership of the securities. 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 of December 31, 2019, and such securities are considered outstanding for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. 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 N.V., Zernikedreef 9, 2333 CK, Leiden, the Netherlands.

Name and Address of Beneficial Owner	Shares Beneficially Owned	
	Number	Percentage
5% or Greater Shareholders:		
Wellington Management Company LLP ¹	5,495,128	11.0 %
RTW Investments LLC ²	4,779,135	9.6 %
Adage Capital Partners GP, L.L.C. ³	4,571,319	9.2 %
The Goldman Sachs Group, Inc. ⁴	3,506,364	7.0 %
Sofinnova Partners ⁵	2,764,194	5.6 %
Jennison Associates LLC ⁵	2,630,626	5.3 %
Stichting Aescap 2.0 ⁷	2,499,294	5.0 %
Supervisory Board Members and Management Board Members		
Dinko Valerio ⁸	789,831	1.6 %
Antoine Papiernik ⁹	2,764,194	5.6 %
James Shannon ¹⁰	127,942	0.3 %
Alison Lawton ¹¹	76,958	0.2 %
Bart Filius	—	— %
Theresa Heggie	—	— %
Daniel de Boer ¹²	1,347,658	2.7 %
All supervisory board members and management board members as a group (7 persons)¹⁴	5,106,583	10.3 %

- Information is based on a report on Schedule 13G/A jointly filed with the SEC on January 28, 2020 by Wellington Management Group LLP, Wellington Group Holdings LLP, Wellington Investment Advisors Holdings LLP and Wellington Management Company LLP. These shares are owned of record by clients of certain investment advisers including Wellington Management Company LLP (together, the “Wellington Investment Advisers”), of which Wellington Management Group LLP is the parent holding company. Wellington Investment Advisors Holdings LLP controls directly, or indirectly through Wellington Management Global Holdings, Ltd., the Wellington Investment Advisers. Wellington Investment Advisors Holdings LLP is owned by Wellington Group Holdings LLP. Wellington Group Holdings LLP is owned by Wellington Management Group LLP. The registered office of Wellington Management Company LLP is c/o 280 Congress Street, Boston, MA 02210.
- Information is based on a report on Schedule 13G/A filed by RTW Investments, LP on February 14, 2020. These shares are held by RTW Master Fund, Ltd. and one or more private funds managed by RTW Investments, LP. The registered office of RTW Investments, LP is 412 West 15th Street, Floor 9, New York, New York 10011.
- Adage Capital Partners GP L.L.C. (“ACPGP”) is the general partner of Adage Capital Partners, L.P. (“ACP”). Adage Capital Advisors, L.L.C. (“ACA”) is the managing member of ACPGP and general partner of ACP. The address of Adage Capital Partners, L.P. is 200 Clarendon Street, 52nd floor, Boston, Massachusetts 02116. This information is based on a report on Schedule 13G/A filed by Adage Capital Partners GP L.L.C. on February 12, 2020.
- Information is based on a report on Schedule 13G/A filed by The Goldman Sachs Group, Inc. (“GS Group”) and Goldman Sachs & Co. LLC (“Goldman Sachs”). GS Group is the parent holding company of Goldman Sachs. The business address of these entities is 200 West Street, New York, NY 10282.
- Information is based on a report on Schedule 13G/A filed by Sofinnova Capital VII FCPR (“SC VII”), Sofinnova Partners SAS (“SP SAS”), and the managing partners of SP SAS, Dennis Lucquin, Antoine Papiernik, Henriette Richter, Monique Saulnier and Graziano Seghezzi on February 14, 2019. Consists of 2,764,194 shares, except that SC VII, the holder of these shares, may be deemed to have sole or shared power to dispose of these shares, and the aforementioned managing partners of SP SAS 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, 75002, Paris, France. "

- 6 Jennison Associates LLC, "Jennison" furnishes investment advice to several investment companies, insurance separate accounts, and institutional clients "Managed Portfolios". As a result of its role as investment adviser of the Managed Portfolios, Jennison may be deemed to be the beneficial owner of the shares of the Company's Common Stock held by such Managed Portfolios. Prudential Financial, Inc. "Prudential" indirectly owns 100% of equity interests of Jennison. As a result, Prudential may be deemed to have the power to exercise or to direct the exercise of such voting and/or dispositive power that Jennison may have with respect to the Company's Common Stock held by the Managed Portfolios. Jennison does not file jointly with Prudential, as such, shares of the Company's Common Stock reported on Jennison's Schedule 13G may be included in the shares reported on the Schedule 13G filed by Prudential. The registered office of Jennison Associates LLC is 466 Lexington Ave., New York, NY 10017. Information is based on a report on Schedule 13G/A filed by Jennison Associates LLC on February 7, 2020.
- 7 Information is based on a report on Schedule 13G filed on January 27, 2020 by Stichting Aescap 2.0 ("Aescap 2.0"), Privium Fund Management B.V. ("Privium"), as the fund manager of Aescap 2.0, Inspirational Visions BV ("Inspirational Visions") and Patrick Johan Hendrik Krol ("Krol"), the portfolio manager for Privium and the managing director of Inspirational Visions. Consists of 2,480,883 ordinary shares directly held by Aescap 2.0 and 18,411 ordinary shares directly held by Inspirational Visions. The address of each of Stichting Aescap 2.0, Privium Fund Management B.V. and Patrick Johan Hendrick Krol is Gustav Mahlerplein 3, 1082 MS Amsterdam, The Netherlands. The address of Inspirational Visions BV is 1083 HN Amsterdam, The Netherlands.
- 8 Consists of 388,457 ordinary shares and options to acquire 96,411 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2019. Also includes 304,963 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 Ondernemingsweg 240, 1422 DZ, Uithoorn, the Netherlands.
- 9 Consists of 2,764,194 ordinary shares held by Sofinnova Capital VII FCPR. Antoine Papiernik may be deemed to have shared voting and investment power with respect to such shares as a managing partner of Sofinnova Partners SAS, the management company of Sofinnova Capital VII FCPR.
- 10 Consists of 61,538 ordinary shares and options to acquire 66,404 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2019.
- 11 Consists of options to acquire 76,958 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2019.
- 12 Consists of options to acquire 642,349 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2019, and 705,309 ordinary shares held by Appel BV and JDG BV.
- 13 Consists of 4,224,461 ordinary shares and options to acquire 882,122 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2019.

Holdings by U.S. Shareholders

As at December 31, 2019, 99.99% of our ordinary shares were held by record holders in the United States, which excludes shareholders whose shares were held in nominee or street name by brokers.

B. Related party transactions

Since January 1, 2019, there have been no material transactions that are unusual in their nature or conditions with any of our related parties, except for transactions as set out in note 23 to the financial statements as included elsewhere in this report.

Registration Rights Agreement

We have entered 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, as summarized below.

Demand registration rights. Certain of our shareholders that are party to the Registration Rights Agreement, dated as of September 17, 2014, among us and the other parties thereto (the “RRA Shareholders”) are entitled to request that we effect up to an aggregate of two demand registrations under the Registration Rights Agreement, and no more than two demand registrations within any twelve-month period, covering the RRA Shareholders’ ordinary shares (“registrable securities”) that total at least one-third of the outstanding registrable securities and which have an anticipated aggregate net offering price of at least \$ 10 million. In addition, when we are eligible to use Form F-3, RRA Shareholders holding an aggregate of at least 30% of the registrable securities and which have an anticipated aggregate net offering price of at least \$ 5 million have the right to request that we file a registration statement on Form F-3. These demand registration rights are subject to certain customary conditions and limitations, including customary underwriter cutback rights and deferral rights.

Piggyback registration rights. If we propose to register any ordinary shares (other than in registration statements covering share options under our equity incentive plans, a Rule 145 transaction or a dividend reinvestment plan), the RRA Shareholders are entitled to notice of such registration and to include their registrable securities in that registration. The managing underwriter has the right to limit the number of registrable securities included in a piggyback registration if the managing underwriter believes it would interfere with the successful marketing of the ordinary shares.

Subject to limited exceptions, the Registration Rights Agreement provides that we must pay all registration expenses in connection with a demand, piggyback or shelf registration. The Registration Rights Agreement contains customary indemnification and contribution provisions. The registration rights summarized above terminate upon the earliest of the occurrence of a sale event of our company, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all of each RRA Shareholder’s shares without limitation during a three-month period without registration, or the fifth anniversary of our initial public offering.

C. Interests of experts and counsel

Not applicable.

Item 8: Financial Information

A. Consolidated Statements and Other Financial Information

Consolidated financial statements

Consolidated financial statements are filed as part of this annual report, starting page F-1.

Legal proceedings

From time to time we could be involved in legal proceedings that arise in the ordinary course of business. As at December 31, 2019, we believe no proceedings exists of which the outcome, if determined adversely, will have a material adverse effect on our financial position. During the period covered by the audited and approved financial statements contained herein, we have not been a party to or paid any damages in connection with litigation that has had a material adverse effect on our financial position. Any future litigation may result in substantial costs and be a distraction to management and employees. No assurance can be given that future litigation will not have a material adverse effect on our financial position. Refer to Item 3.D: “Risk factors.”

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. 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 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.

B. Significant Changes

There have been no significant changes since the date of the annual financial statements.

Item 9: The Offer and Listing

A. Offering and listing details

See "Item 9.C The Offer and Listing - Markets."

B. Plan of distribution

Not applicable.

C. Markets

Since September 18, 2014, our ordinary shares have been listed on the NASDAQ Global Market under ticker symbol "PRQR".

D. Selling shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the issue

Not applicable.

Item 10: Additional Information

A. Share capital

Not applicable.

B. Memorandum and articles of association

General

We were incorporated on February 21, 2012 as a private company with limited liability (*'besloten vennootschap met beperkte aansprakelijkheid'*) under Dutch law. In connection with our initial public offering in 2014, our shareholders resolved to amend our articles of association and to convert into a public company with limited liability by means of a Deed of Amendment and Conversion, pursuant to which, we converted to a public company with limited liability (*'naamloze vennootschap'*) under the laws of the Netherlands. In connection with this conversion, our legal name changed from ProQR Therapeutics B.V. to ProQR Therapeutics N.V. On 22 June 2016 the articles of association were amended to (i) add certain places where general meeting of shareholders may be held and (ii) amend the term 'annual report' to 'report of the Management Board' to comply with the Implementation Act Annual Accounts Directive (*'Uitvoeringswet richtlijn jaarrekening'*) (Bulletin of Acts and Decrees (*'Staatsblad'*) 2015, 349), pursuant to which act this term has been amended accordingly. On 19 February 2018, the articles of association were amended to (i) to increase the authorized share capital, and (ii) to delete the requirement of a deed for the issuance of shares.

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 Zernikedreef 9, 2333 CK Leiden, the Netherlands.

At December 31, 2019, our authorized share capital is € 7,200,000, divided into 90,000,000 ordinary shares and 90,000,000 preferred shares, each with a nominal value of € 0.04-

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

We have listed our ordinary shares in registered form and our shares are not certificated. We have appointed American Stock Transfer & Trust Company, LLC as our agent to maintain our shareholders register and to act as transfer agent, registrar and paying agent for the ordinary shares. Our ordinary shares are traded on the NASDAQ Global Market in book-entry form.

Articles of Association and Dutch Law

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

Anti-Takeover Measure

To enable us to pursue our business strategy and the successful development of our product pipeline and to protect our interests and those of our stakeholders (including shareholders, employees and patient populations), our business strategy, our continuity and our independence against actual and potential threats, we have adopted an anti-takeover measure by granting a perpetual and repeatedly exercisable call option to a 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 equals, at the time of exercise of the call option, the lesser of: (i) the total number of shares equal to our issued share capital at that time, minus the number of preferred shares already held by the protection foundation at that time (if any) or (ii) the maximum number of preferred shares that may be issued under our authorized share capital under our articles of association from time to time. The protection foundation's articles of association provide that it will act to promote and protect the best interests of us, our business and our stakeholders, including patient populations that may benefit from our products and pipeline, 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 is 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, and may also be issued against the Company's reserves if so requested by the foundation. 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.

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 Pre-emptive 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 of shareholders 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.

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 of shareholders 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”, is an irrevocable and repeatedly exercisable right to subscribe for preferred shares.

On September 15, 2014, our general meeting of shareholders adopted 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 five years from the date of such resolution.

On May 16, 2018, our general meeting of shareholders adopted a resolution pursuant to which the aforesaid authorizations to issue shares and to limit and exclude preemptive rights was renewed. In this renewed authorization the Management Board was delegated the authority to resolve, subject to approval of the Supervisory Board, to, in accordance with applicable laws and NASDAQ listing rules and for a period of 5 years from the date of the resolution of the general meeting of shareholders: (a) issue ordinary shares up to 100% of the Company's authorized share capital for general purposes as reflected above and issuances under Company's stock option plans with the proviso that the issuances under stock option plans is limited to 15% of the Company's issued share capital (minus any treasury shares) at the date of AGM ; (b) grant rights to subscribe for ordinary shares as described under (a); and (c) limit or exclude the pre-emptive rights of holders of ordinary shares, which delegation shall include the authority to determine the price and further terms and conditions of any such share issuance or grants.

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 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 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.

On May 10, 2017, our general meeting of shareholders adopted a resolution pursuant to which our management board will be authorized to acquire up to 10 % of our issued share capital plus, in case of a material reorganization of the capital structure of the Company an additional 10%, on NASDAQ or by other means 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 of shareholders, 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 of shareholders 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 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 disproportionate 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, bringing to market 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 make our products available to the patient populations that may benefit from such products and to maintain a suitable pipeline of products that may be beneficial for relevant patient populations;
- 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, Schiphol Airport (municipality Haarlemmermeer), The Hague, Oegstgeest, Leidschendam, Katwijk, Noordwijk or in Wassenaar, 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 eight 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 of shareholders 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 of shareholders. 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 of shareholders. 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 management board member present at the meeting and, if none of them is

present, the general meeting of shareholders 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 of shareholders may decide at his discretion to admit other persons to the meeting. The chairman of the general meeting of shareholders 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 of shareholders 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 of shareholders 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 of shareholders 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, a report of the management board 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.

In Dutch public takeover practice, depending on the circumstances, an asset sale transaction is sometimes used as a way to squeeze out minority shareholders, for example, after a successful public offer, or tender offer, through which the offeror acquires a supermajority, but less than all, of the shares. In such a scenario, the business of the target company would be sold to an offeror, a buyer or a special purpose vehicle, followed by the liquidation of the target company. The purchase price would be distributed to all shareholders in proportion to their respective shareholding as liquidation proceeds, thus separating the business from the company in which minority shareholders participated.

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.

C. Material contracts

Except as otherwise disclosed in this annual report (including the Exhibits), we are currently not, and have not been in the two years preceding publication of this annual report, party to any material contract, other than contracts entered into in the ordinary course of business.

D. Exchange controls

Cash dividends payable on our ordinary shares may be officially transferred from the Netherlands to non-residents and converted into any other currency without legal restrictions imposed by Dutch law, except that for statistical purposes such payments and transactions must be reported to the Dutch Central Bank, and furthermore, no payments, including dividend payments, may be made to jurisdictions subject to sanctions adopted by the government of the Netherlands and implementing resolutions of the Security Council of the United Nations.

E. Taxation

Taxation in the Netherlands

General

The following is a general summary of certain material Dutch 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 Dutch 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 Dutch 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 Dutch Income Tax Act 2001) or statutory directors ('*bestuurders*') or supervisory directors ('*commissarissen*') of a company resident in the Netherlands; 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 national tax legislation and published regulations in the Netherlands, 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.

(a) Dividend Withholding Tax

Dividends distributed by us generally are subject to Dutch 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 Dutch 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 to the extent such proceeds exceed the average paid-in capital of those shares as recognized for purposes of Dutch 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 Dutch dividend withholding tax, has been made or will be made; and
- partial repayment of the paid-in capital, recognized for purposes of Dutch 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, Dutch dividend withholding tax.

Individuals and corporate legal entities who are resident or deemed to be resident in the Netherlands for Dutch tax purposes ('Dutch Resident Individuals' and 'Dutch Resident Entities' as the case may be), can generally credit the Dutch 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 if the ordinary shares are attributable to a Dutch permanent establishment of such non-resident holder.

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

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

established in Aruba, Curacao, St. Maarten, the BES islands or in a state which has concluded a double tax treaty with the Netherlands)

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

Pursuant to legislation to counteract “dividend stripping”, a reduction, exemption, credit or refund of Dutch dividend withholding tax is denied if the recipient of the dividend is not the beneficial owner as described in the Dutch Dividend Withholding Tax Act 1965 (in Dutch: ‘*Wet op de dividendbelasting 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 Dutch 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.

(b) Taxes on Income and Capital Gains

(i) Dutch Resident Individuals

If a holder of ordinary shares is a Dutch Resident Individual, any benefit derived or deemed to be derived from the ordinary shares is taxable at the progressive income tax rates (with a maximum of 51.75%), if:

- (a) the ordinary shares are attributable to an enterprise from which the Dutch 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 Dutch 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*’). Irrespective of the actual income and capital gains realized, the annual taxable benefit of all the assets and allowable liabilities of a Dutch Resident Individual holder of ordinary shares who is taxed under this regime is set at a deemed return based on the fair market value of the assets reduced by the allowable liabilities on January 1 of each year. Depending on the aggregate amount of the fair market value of the assets reduced by the liabilities, the deemed return ranges from 1.935% up to 5.60% (2019). This deemed return is subject to income tax at a flat rate of 30%. Taxation only occurs if and to the extent the fair market value of the assets reduced by the liabilities exceeds a threshold (heffingsvrij vermogen) of € 30,360 (or € 60,720 in case of a fiscal partnership). The deemed return will be adjusted annually.

(ii) Dutch Resident Entities

Any benefit derived or deemed to be derived from the ordinary shares held by Dutch Resident Entities, including any capital gains realized on the disposal thereof, will generally be subject to Dutch corporate income tax at a rate of 25% (a corporate income tax rate of 19% applies with respect to taxable profits up to € 200,000).

(iii) 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 realized on the disposal or deemed disposal of the ordinary shares, provided that:

- (a) such holder is neither a resident nor deemed to be resident in the Netherlands for Dutch tax purposes and, if such holder is an individual, such holder does not qualify for the application of the rules of the Dutch Income Tax Act 2001 as they apply to residents of the Netherlands;
- (b) 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 or has a deemed enterprise for activities performed as statutory director ("bestuurder") or supervisory director ("commissaris") of a company resident of the Netherlands; and
- (c) 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.

(c) Gift and Inheritance Taxes

(i) 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.

(ii) Non-residents of the Netherlands

No Dutch 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:

- (a) 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
- (b) 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 Dutch gift and inheritance taxes, amongst others, a person that holds the Dutch 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 Dutch gift tax, amongst others, a person not holding the Dutch 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.

(d) Other Taxes and Duties

No Dutch VAT and no Dutch 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.

(e) Residence

A shareholder will not become resident or deemed resident in the Netherlands for tax purposes by reason only of holding 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 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 will hold our 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 of 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 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 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 contrary position concerning the tax consequences of the 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 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 if the trust 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 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 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.

(a) 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 the holding period requirement as well as the absence of certain risk reduction transactions.

A 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 a case-by-case basis. 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.

(b) 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 that does not make such an 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.

Net Investment Income 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 Net Investment Income Tax to its income and gains in respect of its investment in our ordinary shares.

(c) 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 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 (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 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, unless the shareholder makes a purging election (which allows a shareholder to purge the continuing PFIC taint by either making a deemed sale election or a deemed dividend election).

Based on the average value of our gross assets and composition of our income, we believe that we were not a PFIC during the 2019 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.

If we are a PFIC, and you are a U.S. holder, then a special tax regime will apply unless you make a mark-to-market election (described below). We do not currently intend to provide the information necessary for U.S. holders to make qualified electing fund elections if we are treated as a PFIC for any taxable year. That special tax regime will apply to any “excess distribution” by us to you (generally, your 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). (In determining the average annual distribution, the portion of any excess distribution from a prior year that was allocated to the prior-year PFIC period is disregarded.) That special regime will also apply to any gain realized on the sale or other disposition of the ordinary shares. Under this special 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.”

A U.S. holder may elect mark-to-market treatment, which may alleviate some of the adverse consequences of PFIC status. 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 and not offset by prior mark-to market losses. 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 on that market, the mark-to-

market election will be available to a U.S. holder. U.S. Holders should consult their tax advisors to determine whether the mark-to-market election would be available and, if so, what the consequences of making that election would be in their particular circumstances.

If we are 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, 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 (and with respect to any of our subsidiaries that also may be determined to be PFICs), 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. U.S. investors are urged to consult their own tax advisers with respect to the 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 ownership and disposition of our ordinary share.

(d) 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.

(e) 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 SET OUT ABOVE IS INCLUDED FOR GENERAL INFORMATION ONLY AND MAY NOT BE APPLICABLE DEPENDING UPON A HOLDER'S PARTICULAR SITUATION. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE RELEVANT TO A HOLDER. EACH HOLDER IS URGED TO CONSULT THEIR TAX ADVISOR WITH RESPECT TO THE TAX CONSEQUENCES TO THEM OF THE OWNERSHIP AND DISPOSITION OF THE SHARES INCLUDING TAX CONSEQUENCES UNDER STATE, LOCAL AND OTHER TAX LAWS AND THE POSSIBLE TAX EFFECTS OF CHANGES IN THE UNITED STATES FEDERAL AND OTHER TAX LAWS.

F. Dividends and paying agents

Not applicable.

G. Statement by experts

Not applicable.

H. Documents on display

We are subject to certain reporting requirements of the Exchange Act. As a foreign private issuer, we are exempt from the rules under the Exchange Act prescribing certain disclosure and procedural requirements for proxy solicitations, and our officers, directors and principal shareholders are exempt from the reporting and “short swing” profit recovery provisions contained in Section 16 of the Exchange Act, with respect to their purchases and sales of shares. In addition, we are not required to file reports and Financial Statements with the Commission as frequently or as promptly as companies that are not foreign private issuers whose securities are registered under the Exchange Act. However, we are required to file with the Commission, within four months after the end of each fiscal year, an Annual Report on Form 20-F containing Financial Statements audited by an independent accounting firm. We publish unaudited interim financial information after the end of each quarter. We furnish this quarterly financial information to the Commission under cover of a Form 6-K.

It is possible to read and copy documents referred to in the 2015 Form 20-F that have been filed with the SEC at the SEC’s public reference room located at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms and their copy charges. ProQR SEC filings are also publicly available through the SEC’s website at www.sec.gov.

I. Subsidiary information

Not applicable.

Item 11: 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 management policy is focused on optimizing the net interest result of funds invested in deposits while accepting limited risk (minimum ratings of P-1 or A2 for short-term and long-term, respectively by Moody’s and A-1 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, primarily with respect to the U.S. Dollar. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro. We have exposure associated with the time delay between entering into a contract, budget or forecast and the realization thereof. To minimize economic exposure related to currency fluctuations, currencies on the balance sheet will be matched to the cash flows on an annual basis to ensure the availability of at least 12 months of liquidity per currency per the approved budget. The impact of fair value measurements on the financial statements is limited.

At December 31, 2019 there was a net asset in U.S. Dollars of € 39,004,000 (2018: € 26,928,000). Foreign currency denominated receivables and trade payables are short term in nature (generally 30 to 45 days). As a result foreign exchange rate movements on receivables and trade payables, during the years presented had an immaterial effect on the financial statements.

Our interest rate risk exposure is limited due to the use of loans with fixed rates. At December 31, 2019, we had several loans with a fixed interest rate, totaling € 13,052,000 (2018: € 9,386,000).

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 banks which meet our defined minimum credit ratings.

Liquidity Risk

Management forecasts our liquidity requirements to ensure that there is sufficient cash to meet operational needs. We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2022. 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.

Item 12: Description of Securities other than Equity Securities

A. Debt securities

Not applicable.

B. Warrants and rights

Not applicable.

C. Other securities

Not applicable.

D. American depositary shares

Not applicable.

Part II

Item 13: Defaults, Dividend Arrearages and Delinquencies

No matters to report.

Item 14: Material Modifications to the Rights of Security Holders and Use of Proceeds

No matters to report.

Item 15: Controls and Procedures

A. Disclosure controls and procedures

Under the supervision and with the participation of our Chief Executive Officer (CEO) and Chief Business and Financial Officer (CFO), the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) has been evaluated as of the end of the period covered by the Annual Report (December 31, 2019). The term "disclosure controls and procedures" means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms and that such information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosures.

Based on that evaluation, the Chief Executive Officer and Chief Business and Financial Officer have concluded that these disclosure controls and procedures are effective as at December 31, 2019.

B. Management's annual report on internal control over financial reporting

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

The Company's internal control over financial reporting is a process designed to provide reasonable, but not absolute, assurance regarding the reliability of financial reporting and the preparation of the consolidated financial statements in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting is not intended to provide absolute assurance that a misstatement of our financial statements would be prevented or detected.

In connection with the preparation of the Company's annual consolidated financial statements, management has undertaken an assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2019. Based on this assessment, management concluded that the Company's internal control over financial reporting was effective as at December 31, 2019.

C. Attestation report of the registered public accounting firm

This Annual Report includes an attestation report of the company's registered public accounting firm on the effectiveness of the Company's internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of ProQR Therapeutics N.V.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of ProQR Therapeutics N.V. and subsidiaries (the "Company") as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2019, of the Company and our report dated March 31, 2020 expressed an unqualified opinion on those financial statements and included an emphasis of matter regarding the potential effects of the coronavirus disease 2019 (COVID-19) on the operations of the Company.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's annual report on internal control over financial reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

/s/ Deloitte Accountants B.V.

Amsterdam, The Netherlands
March 31, 2020

D. Changes in internal control over financial reporting

During the year ended December 31, 2019, there have been no changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 16A: Audit Committee Financial Expert

Currently, Bart Filius qualifies as an “audit committee financial expert,” as defined by the SEC and as determined by our supervisory board. In addition, he satisfies the independence requirements of the NASDAQ listing standards and Rule 10A-3(b)(1) under the Exchange Act and the criteria for independence set forth in best practice 2.1.8 of the DCGC.

Item 16B: Code of Ethics

We have adopted a Code of Business Conduct and Ethics applicable to all of our management board and supervisory board members and our employees, including our CEO, CFO, controller or principal accounting officers, or other persons performing similar functions, which is a “code of ethics” as defined by the SEC. The full text of the Code of Business Conduct and Ethics is posted on our company website at www.ProQR.com.

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 within five working days to the extent required by the rules and regulations of the SEC.

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

Item 16C: Principal Accountant Fees and Services

The information required is included in note 24 to the financial statements.

Item 16D: Exemptions from the Listing Standards for Audit Committees

Not applicable.

Item 16E: Purchases of Equity Securities by the Issuer and Affiliated Purchasers

In 2019, no purchases of our registered equity securities were made by us or on our behalf or on the behalf of any affiliated purchaser.

Item 16F: Change in Registrant’s Certifying Accountant

None.

Item 16G: Corporate Governance

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. 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 ("DCGC") or Dutch law. Accordingly, our shareholders may not be afforded the same protection as provided under NASDAQ corporate governance rules to the extent the DCGC or 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.

Item 16H: Mine Safety Disclosure

Not applicable.

Part III

Item 17: Financial Statements

Financial Statements are filed as part of this annual report, starting on page F-1.

Item 18: Financial Statements

Financial Statements are filed as part of this annual report, starting on page F-1.

Item 19: Exhibits

Index of Exhibits

Exhibit No.	Description
1.1	Amended Articles of Association of the Registrant effective as of June 22, 2016 (incorporated by reference to Exhibit 1.1 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2016 (File No. 001-36622) filed on March 31, 2017)
1.2	Amended Articles of Association of the Registrant effective as of February 19, 2018 (incorporated by reference to Exhibit 1.2 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2018 (File No. 001-36622) filed on March 28, 2019)
2.1	Form of Registration Rights Agreement by and between the Registrant and the shareholders party thereto (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151) filed on September 8, 2014)
4.1#	ProQR Therapeutics B.V. Stock Option Plan and forms of notice of grant thereunder (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151) filed on August 14, 2014)
4.2#	ProQR Therapeutics N.V. Stock Option Plan and forms of notice of grant thereunder (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151) filed on September 8, 2014)
4.3#	Form of Management Services Agreement by and between the Registrant and Daniel Anton de Boer (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151) filed on September 8, 2014)
4.4	Form of Call Option Agreement by and between the Registrant and Stichting Continuity ProQR Therapeutics (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151) filed on September 16, 2014)
4.5#	Form of Indemnification Agreement for the Managing Directors, Supervisory Directors and officers of the Registrant (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151) filed on September 8, 2014)
4.6	English translation of Lease Agreement by and between the Registrant and The Netherlands Organisation for applied scientific research TNO ("TNO"), dated as of January 1, 2016, for the Registrant's facility in Zernikedreef in Leiden, the Netherlands (incorporated by reference to Exhibit 4.13 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2016 (File No. 001-36622) filed on March 31, 2017)
4.7††*	English translation of Lease Agreement by and between the Registrant and Leeds Investment I B.V., dated as of September 30, 2019
4.8†	License Agreement between Radboudumc as Licensor, and the Registrant as Licensee dated as of April 17, 2014 (incorporated by reference to Exhibit 4.14 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2016 (File No. 001-36622) filed on March 31, 2017)
4.9†	License Agreement between Inserm Transfert SA, Assistance-Publique- Hôpitaux de Paris, and the Registrant as Licensee dated January 17, 2018 (incorporated by reference to Exhibit 4.15 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2018 (File No. 001-36622) filed on March 28, 2019)

Exhibit No.	Description
4.10†	Letter Agreement between Foundation For Fighting Blindness Clinical Research Institute and ProQR Therapeutics IV B.V. dated as of February 9, 2018 (incorporated by reference to Exhibit 4.16 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2018 (File No. 001-36622) filed on March 28, 2019)
4.11†	License Agreement between Ionis Pharmaceuticals, Inc. and the Registrant dated as of October 26, 2018 (incorporated by reference to Exhibit 4.17 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2018 (File No. 001-36622) filed on March 28, 2019)
4.12†	Stock Purchase Agreement between Ionis Pharmaceuticals, Inc. and the Registrant dated as of October 26, 2018 (incorporated by reference to Exhibit 4.18 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2018 (File No. 001-36622) filed on March 28, 2019)
4.13†	Investor Agreement between Ionis Pharmaceuticals, Inc. and the Registrant dated as of October 26, 2018 (incorporated by reference to Exhibit 4.19 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2018 (File No. 001-36622) filed on March 28, 2019)
4.14††*	Asset Purchase Agreement by and between the Registrant and Wings Therapeutics, Inc., dated as of May 22, 2019
4.15††*	Subscription Agreement by and between the Registrant and Wings Therapeutics, Inc., dated as of May 22, 2019
4.16††*	Supply and Services Agreement, by and between the Registrant and Nitto Denko AVECIA Inc., dated as of July 12, 2019
4.17*	Sales Agreement, by and between the Registrant and Citigroup Global Markets, Inc. and Cantor Fitzgerald & Co., dated as of March 31, 2020
4.18*	Description of the Registrant's Securities
8.1*	Subsidiaries of the Registrant
12.1*	Certification by Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
12.2*	Certification by Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
13.1**	Certification by Principal Executive Officer and Principal Financial Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
15.1*	Consent of Deloitte Accountants B.V., Independent Registered Public Accounting Firm
15.2*	Opinion of Allen & Overy LLP (Dutch counsel to the Company) relating to the sales agreement prospectus and consent included therein
101.INS*	XBRL Instance Document.
101.SCH*	XBRL Taxonomy Extension Schema Document.
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.

Exhibit No.

Description

101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.

* Filed herewith

** Indicates that the exhibit is being furnished and will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liability of that section. Such exhibit will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing.

† Confidential treatment has been granted as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

†† Certain confidential portions of this exhibit (indicated by brackets and asterisks) have been omitted from this exhibit.

Indicates management contract or compensatory plan or arrangement.

Signatures

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

Leiden, March 31, 2020

PROQR THERAPEUTICS N.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: Chief Executive Officer

By: /s/ Smital Shah

Name: Smital Shah

Title: Chief Business and Financial Officer

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Report of the Independent Registered Public Accounting Firm

To the shareholders and the Board of Directors of ProQR Therapeutics N.V.,

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of financial position of ProQR Therapeutics N.V. and subsidiaries (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of profit or loss and comprehensive income, changes in equity and cash flows for each of the three years in the period ended December 31, 2019, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, in conformity with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 31, 2020, expressed an unqualified opinion on the Company's internal control over financial reporting.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Emphasis of Matter

As discussed in Note 25 to the financial statements, the Company has described the potential effects of the coronavirus disease 2019 (COVID-19) on the operations of the business. Our opinion is not modified in respect of this matter.

/s/ Deloitte Accountants B.V.

Amsterdam, The Netherlands
March 31, 2020

We have served as the Company's auditor since 2013.

PROQR THERAPEUTICS N.V.
Consolidated Statement of Financial Position

		December 31, 2019	December 31, 2018
(€ in thousands)			
Assets			
Property, plant and equipment	7	2,440	1,864
Investments in associates	8	429	—
Non-current assets		2,869	1,864
Social security and other taxes	9	850	1,243
Prepayments and other receivables	10	1,866	1,544
Cash and cash equivalents	11	111,950	105,580
Current assets		114,666	108,367
Total assets		117,535	110,231
Shareholders' equity			
Share capital		2,159	1,726
Share premium		287,214	235,744
Reserves		16,702	10,888
Accumulated deficit		(211,746)	(155,443)
Equity attributable to owners of the Company	12	94,329	92,915
Non-controlling interests		(496)	(230)
Total equity		93,833	92,685
Liabilities			
Borrowings		12,709	9,386
Non-current liabilities	13	12,709	9,386
Borrowings		343	—
Lease liabilities	21	508	—
Trade payables		445	135
Current income tax liability	19	64	—
Social security and other taxes		108	—
Pension premiums		2	7
Deferred income		711	545
Other current liabilities		8,812	7,473
Current liabilities	14	10,993	8,160
Total liabilities		23,702	17,546
Total equity and liabilities		117,535	110,231

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

PROQR THERAPEUTICS N.V.

Consolidated Statement of Profit or Loss and Comprehensive Income

		Year Ended December 31,		
		2019	2018	2017
(€ in thousands)				
Other income	15	1,933	5,761	1,495
Research and development costs	16	(46,491)	(29,514)	(31,153)
General and administrative costs		(12,887)	(12,540)	(10,840)
Total operating costs		(59,378)	(42,054)	(41,993)
Operating result		(57,445)	(36,293)	(40,498)
Financial income and expense	18	402	(792)	(3,175)
Results related to associates	8	429	—	—
Result before corporate income taxes		(56,614)	(37,085)	(43,673)
Corporate income taxes	19	(132)	(1)	(2)
Result for the year		(56,746)	(37,086)	(43,675)
Other comprehensive income (attributable to equity holders of the Company)				
<i>Items that will never be reclassified to profit or loss</i>		—	—	—
<i>Items that are or may be reclassified to profit or loss</i>				
Foreign operations – foreign currency translation differences		43	(28)	151
Total comprehensive loss		(56,703)	(37,114)	(43,524)
Result attributable to				
Owners of the Company		(56,480)	(36,894)	(43,637)
Non-controlling interests		(266)	(192)	(38)
		(56,746)	(37,086)	(43,675)
Share information				
Weighted average number of shares outstanding	20	41,037,244	34,052,520	25,374,807
Earnings per share for result attributable to the equity holders of the Company (expressed in Euro per share)				
Basic and diluted loss per share		€ (1.38)	€ (1.08)	(1.72)

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

PROQR THERAPEUTICS N.V.

Consolidated Statement of Changes in Equity

	Attributable to Equity Holders of the Company							Total Equity (€ in thousands)
	Share Capital (€ in thousands)	Share Premium (€ in thousands)	Equity Settled Employee Benefit Reserve (€ in thousands)	Translation Reserve (€ in thousands)	Accumulated Deficit (€ in thousands)	Total (€ in thousands)	Non-controlling Interests (€ in thousands)	
Balance at January 1, 2017	934	123,597	4,353	(15)	(75,733)	53,136	—	53,136
Result for the year	—	—	—	—	(43,637)	(43,637)	(38)	(43,675)
Other comprehensive income	—	—	—	151	—	151	—	151
Recognition of share-based payments	—	—	4,024	—	—	4,024	—	4,024
Issue of ordinary shares	343	25,342	—	—	—	25,685	—	25,685
Issue of treasury shares	180	(180)	—	—	—	—	—	—
Shares options exercised	—	4	—	—	—	4	—	4
Balance at December 31, 2017	1,457	148,763	8,377	136	(119,370)	39,363	(38)	39,325
Result for the year	—	—	—	—	(36,894)	(36,894)	(192)	(37,086)
Other comprehensive income	—	—	—	(28)	—	(28)	—	(28)
Recognition of share-based payments	4	2,185	3,224	—	—	5,413	—	5,413
Issue of ordinary shares	265	83,926	—	—	—	84,191	—	84,191
Shares options lapsed	—	—	(97)	—	97	—	—	—
Shares options exercised	—	870	(724)	—	724	870	—	870
Balance at December 31, 2018	1,726	235,744	10,780	108	(155,443)	92,915	(230)	92,685
Result for the year	—	—	—	—	(56,480)	(56,480)	(266)	(56,746)
Other comprehensive income	—	—	—	43	—	43	—	43
Recognition of share-based payments	15	3,145	5,948	—	—	9,108	—	9,108
Issue of ordinary shares	418	48,132	—	—	—	48,550	—	48,550
Shares options lapsed	—	—	(44)	—	44	—	—	—
Shares options exercised	—	193	(133)	—	133	193	—	193
Balance at December 31, 2019	2,159	287,214	16,551	151	(211,746)	94,329	(496)	93,833

The accompanying notes are an integral part of these financial statements. Specific reference is made to note 12.

PROQR THERAPEUTICS N.V.
Consolidated Statement of Cash Flows

	Year Ended December 31,		
	2019	2018	2017
	(€ in thousands)		
Cash flow from operating activities			
Result for the year	(56,746)	(37,086)	(43,675)
Adjustments for:			
Amortization and depreciation	7	2,052	992
Share-based compensation	12	9,108	5,413
Financial income and expense	18	(402)	792
Results related to associates	8	(429)	—
Net foreign exchange gain / (loss)		43	(28)
Changes in working capital	1,783	1,295	164
Cash used in operations	<u>(44,591)</u>	<u>(28,622)</u>	<u>(35,096)</u>
Corporate income tax paid	(64)	(1)	(2)
Interest received	758	130	147
Interest paid	(73)	—	—
Net cash used in operating activities	<u>(43,970)</u>	<u>(28,493)</u>	<u>(34,951)</u>
Cash flow from investing activities			
Purchases of property, plant and equipment	(580)	(312)	(121)
Net cash used in investing activities	<u>(580)</u>	<u>(312)</u>	<u>(121)</u>
Cash flow from financing activities			
Proceeds from issuance of shares, net of transaction costs	12	48,550	84,191
Proceeds from exercise of share options		193	870
Proceeds from borrowings	13	2,027	264
Proceeds from convertible loans	13	690	1,132
Repayment of lease liability	13	(1,261)	—
Net cash generated by financing activities	<u>50,199</u>	<u>86,457</u>	<u>26,640</u>
Net increase/(decrease) in cash and cash equivalents	<u>5,649</u>	<u>57,652</u>	<u>(8,432)</u>
Currency effect cash and cash equivalents		721	(171)
Cash and cash equivalents at the beginning of the year	11	105,580	48,099
Cash and cash equivalents at the end of the year	<u>11</u>	<u>111,950</u>	<u>105,580</u>

The accompanying notes form an integral part of these financial statements.

PROQR THERAPEUTICS N.V.

Notes to the Consolidated Financial Statements

1. General Information

ProQR Therapeutics N.V. (“ProQR” or “the Company”), is a development stage company domiciled in the Netherlands that primarily focuses on the development and commercialization of novel therapeutic medicines.

Since September 18, 2014, the Company’s ordinary shares are listed on the NASDAQ Global Market under ticker symbol PRQR.

The Company was incorporated in the Netherlands, on February 21, 2012 and was reorganized from a private company with limited liability to a public company with limited liability on September 23, 2014. The Company has its statutory seat in Leiden, the Netherlands. The address of its headquarters and registered office is Zernikedreef 9, 2333 CK Leiden, the Netherlands.

At December 31, 2019, ProQR Therapeutics N.V. is the ultimate parent company of the following entities:

- ProQR Therapeutics Holding B.V. (the Netherlands, 100%);
- ProQR Therapeutics I B.V. (the Netherlands, 100%);
- ProQR Therapeutics II B.V. (the Netherlands, 100%);
- ProQR Therapeutics III B.V. (the Netherlands, 100%);
- ProQR Therapeutics IV B.V. (the Netherlands, 100%);
- ProQR Therapeutics VI B.V. (the Netherlands, 100%);
- ProQR Therapeutics VII B.V. (the Netherlands, 100%);
- ProQR Therapeutics VIII B.V. (the Netherlands, 100%);
- ProQR Therapeutics IX B.V. (the Netherlands, 100%);
- ProQR Therapeutics I Inc. (United States, 100%);
- Amylon Therapeutics B.V. (the Netherlands, 80%);
- Amylon Therapeutics, Inc. (United States, a 100% subsidiary of Amylon Therapeutics B.V.)

ProQR Therapeutics N.V. is also statutory director of Stichting Bewaarneming Aandelen ProQR (ESOP Foundation) and has full control over this entity. ProQR Therapeutics Holding B.V. holds a 20% minority shareholding in Wings Therapeutics Inc.

As used in these consolidated financial statements, unless the context indicates otherwise, all references to “ProQR”, the “Company” or the “Group” refer to ProQR Therapeutics N.V. including its subsidiaries and the ESOP Foundation.

2. Basis of preparation

(a) Statement of compliance

These consolidated financial statements have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB).

(b) Basis of measurement

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.

(c) Functional and presentation currency

These consolidated financial statements are presented in euro, which is the Company's functional currency. All amounts have been rounded to the nearest thousand, unless otherwise indicated.

(d) Going Concern

The management board of ProQR has, upon preparing and finalizing the 2019 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 expects the Company to be a going concern based on its existing funding, taking into account the Company's current cash position and the projected cash flows based on the activities under execution on the basis of ProQR's business plan and budget.

(e) Use of estimates and judgements

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

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.

Information about assumptions and estimation uncertainties that may have a significant risk of resulting in a material adjustment is included below.

(i) Research and development expenditures

Research expenditures are currently not capitalized but are reflected in the income statement because the criteria for capitalization are not met. At each balance sheet date, the Company estimates the level of service performed by the vendors and the associated costs incurred for the services performed.

Although we do not expect the estimates to be materially different from amounts actually incurred, the understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in reporting amounts that are too high or too low in any particular period.

(f) Changes in accounting policies

IFRS 16

IFRS 16 *Leases* specifies how a company recognizes, measures, presents and discloses leases. The Company has implemented IFRS 16 on January 1, 2019 by applying the modified retrospective method, meaning that the 2018 comparative numbers in the current year financial statements are not restated. Under this standard, all lease contracts are recognized on the Company's balance sheet, except for short-term and low value leases.

Upon implementation of IFRS 16, the Company recognized a lease liability and a corresponding right-of-use asset of € 2,359,000. Because the interest rate implicit in the lease could not be readily determined, future lease payments were discounted using the Company's incremental borrowing rate on the initial application date to determine the lease liability. The weighted average incremental borrowing rate applied is 4.3%. The carrying amounts of the lease liability and right-of-use asset at December 31, 2019 are € 508,000 and € 606,000, respectively.

In the income statement, lease expenditures previously recognized in operating expenses have been replaced by depreciation and interest expenses. In 2019, depreciation expenses on the right-of-use asset amounted to € 1,187,000 and interest expenses on the lease liability amounted to € 48,000. Under IFRS 16, total expenses resulting from lease contracts can be higher in the earlier years of a lease and lower in the later years, because the interest component of total expenses typically decreases over time.

The main impact on the statement of cash flows is an increase in cash flows from operating activities, since the repayments of the principal part of the lease liability are classified in the net cash flow from financing activities. This effect amounts to € 1,261,000 in 2019.

The Company applied the following practical expedients upon implementation of the new standard:

- Applied the short-term lease exemption, meaning that leases with a duration of less than one year are expensed in the income statement on a straight-line basis.
- Applied the low value lease exemption, meaning that leased assets with an individual value of \$ 5,000 or less if bought new are expensed in the income statement on a straight-line basis.
- Applied the option to include non-lease components in the lease liability.

Furthermore, we used the transition option to measure the right-of-use asset based on the recognized lease liability.

Reconciliation of the prior year operating lease commitment to the opening balance sheet

At December 31, 2018, the Company reported a commitment for future minimum lease payments under non-cancellable operating leases of € 2,466,000. The lease liability recognized upon implementation of IFRS 16 on January 1, 2019 amounted to € 2,359,000. The difference of € 107,000 is caused by the effect of discounting future lease payments to determine the lease liability.

Other new Standards and Interpretations, which became effective as of January 1, 2019, did not have a material impact on our financial statements.

3. Significant Accounting Policies

The Company has consistently applied the following accounting policies to all periods presented in these consolidated financial statements.

(a) Basis of consolidation

(i) Subsidiaries

Subsidiaries are entities controlled by the Company. The Company controls an entity when it has power over the entity, is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. The Company reassesses whether or not it controls an entity if facts and circumstances indicate that there are changes to one or more of these elements. The financial statements of subsidiaries are included in the consolidated financial statements from the date on which control commences until the date on which control ceases.

(ii) Non-controlling interests ("NCI")

NCI are measured at their proportionate share of the acquiree's identifiable net assets at the acquisition date. Changes in the Company's interest in a subsidiary that do not result in a loss of control are accounted for as equity transactions.

(iii) Loss of control

When the Company loses control over a subsidiary, it derecognizes the assets and liabilities of the subsidiary, and any non-controlling interests and other components of equity. Any resulting gain or loss is recognized in profit or loss. Any interest retained in the former subsidiary is measured at fair value when control is lost.

(iv) Transactions eliminated on consolidation

Intra-group balances and transactions, and any unrealized income and expenses arising from intra-group transactions, are eliminated. Unrealized gains arising from transactions with equity-accounted investees are eliminated against the investment to the extent of the Company's interest in the investee. Unrealized losses are eliminated in the same way as unrealized gains, but only to the extent that there is no evidence of impairment.

(v) Associates

Associates are entities over which the Company has significant influence. Significant influence is the power to participate in the financial and operating policy decisions of the investee but is not control or joint control over those policies.

Investments in associates are accounted for in the consolidated financial statements using the equity method of accounting. Equity accounting involves recording the investment in associates initially at cost, and recognizing the Company's share of the post-acquisition results of associates in the consolidated income statement and the Company's share of post-acquisition other comprehensive income in consolidated other comprehensive income. The cumulative post-acquisition movements are adjusted against the carrying amount of the investments in associates in the consolidated statement of financial position.

When the Company's share of losses in an associate equals or exceeds its interest in the associate, the Company does not recognize further losses unless it has incurred or guaranteed obligations in respect of the associate.

(b) Classes of financial instruments

Financial instruments are both primary financial instruments, such as receivables and payables, and financial derivatives. For the Company's 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.

(c) Foreign currencies

(i) Foreign currency transactions

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions.

Monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rate at the reporting date. Non-monetary assets and liabilities denominated in foreign currencies that are measured at fair value are translated into the functional currency at the exchange rate when the fair value was determined. Foreign currency differences are generally recognized in profit or loss. Non-monetary items that are measured based on historical cost in a foreign currency are not translated.

(ii) Foreign operations

The assets and liabilities of foreign operations are translated into euro at exchange rates at the reporting date. The income and expenses of foreign operations are translated into euros at the exchange rates at the dates of the transactions. Foreign currency differences are recognized in OCI and accumulated in the translation reserve, except to the extent that the translation difference is allocated to NCI.

(d) Recognition of other income

Other income includes amounts earned from third parties and is 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 Company and the amount of the income can be measured reliably. The grants are recognized in other income on a systematic basis over the period the Company recognizes as expenses the related costs for which the grants are expected to compensate.

(e) Government grants — WBSO

The WBSO (“afdrachtvermindering speur- en ontwikkelingswerk”) is a Dutch fiscal facility that provides subsidies to companies, knowledge centers 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 recognized on a net basis within the labor costs.

(Government) Grant income is not recognized until there is reasonable assurance that the Company will comply with the conditions attached to them. (Government) Grants are recognized in profit or loss on a systematic basis over the period the Company recognizes as expenses the related costs for which the grants are intended to compensate.

(f) Employee benefits

(i) Short-term employee benefits

Short-term employee benefits are expensed as the related service is provided. A liability is recognized for the amount expected to be paid if the Company has a present legal or constructive obligation to pay this amount as a result of past service provided by the employee and the obligation can be estimated reliably.

(ii) Share-based payment transactions

The grant-date fair value of equity-settled share-based payment awards granted to employees is generally recognized as an expense, with a corresponding increase in equity, over the vesting period of the awards. The amount recognized as an expense is adjusted to reflect the number of awards for which the related service and non-market performance conditions are expected to be met, such that the amount ultimately recognized is based on the number of awards that meet the related service conditions at the vesting date. For share-based payment awards with non-vesting conditions, the grant-date fair value of the share-based payment is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes.

(iii) Pension obligations

The Company operates defined contribution pension plans for all employees funded through payments to insurance companies. 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 employees have rendered the service entitling them to the contributions. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in the future payments is available.

(g) Taxation

Income tax expense represents the sum of the tax currently payable and deferred tax. It is recognized in profit or loss except to the extent that it relates to a business combination, or items recognized directly in equity or in OCI.

(i) 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.

(ii) 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 realized, 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.

(h) Property, plant and equipment

(i) Recognition and measurement

Items of property, plant and equipment are measured at cost less accumulated depreciation and any accumulated impairment losses. If significant parts of an item of property, plant and equipment have different useful lives, then they are accounted for as separate items (major components) of property, plant and equipment. Any gain or loss on disposal of an item of property, plant and equipment is recognized in profit or loss.

(ii) Depreciation

Depreciation is calculated to write off the cost of items of property, plant and equipment less their estimated residual values using the straight-line method over their estimated useful lives and is recognized in profit or loss. Leased assets are depreciated over the shorter of the lease term and their useful lives unless it is reasonably certain that the Company will obtain ownership by the end of the lease term.

The estimated useful lives of property, plant and equipment for current and comparative periods are as follows:

<input type="checkbox"/> Buildings and leasehold improvements:	5-10 years;
<input type="checkbox"/> laboratory equipment:	5 years;
<input type="checkbox"/> other:	3-5 years.

Depreciation methods, useful lives and residual values are reviewed at each reporting date and adjusted if appropriate.

(i) Impairment of assets

At the end of each reporting period, the Company reviews the carrying amounts of its non-current assets, including right-of-use 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.

The recoverable amount is the higher of fair value less costs of disposal 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.

(j) 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 and subsequently measured at amortized cost or fair value on the basis of the entity's business model for managing the financial assets and the contractual cash flow characteristics of the financial assets.

Specifically:

- debt instruments that are held within a business model whose objective is to collect the contractual cash flows, and that have contractual cash flows that are solely payments of principal and interest on the principal amount outstanding, are measured subsequently at amortized cost, and
- all other debt investments and equity investments are measured subsequently at fair value through profit or loss (FVTPL).

The Company applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for all trade receivables. To measure the expected credit losses, trade receivables have been grouped based on shared credit risk characteristics and the days past due. Trade receivables are written off when there is no reasonable expectation of recovery. Indicators that there is no reasonable expectation of recovery include, amongst others, the failure of a debtor to engage in a repayment plan with the group, and a failure to make contractual payments for a period of greater than 120 days past due. Impairment losses on trade receivables and contract assets are presented as net impairment losses within operating profit. Subsequent recoveries of amounts previously written off are credited against the same line item.

(k) 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.

(l) 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 financial instruments

Compound financial instruments issued by the Group comprise convertible notes denominated in euro that can be converted to share capital at the option of the holder, when the number of shares to be issued is fixed and does not vary with changes in fair value.

The liability component of a compound financial instrument is recognized initially at the fair value of a similar liability that does not have an equity conversion option. The equity component is recognized initially at the difference between the fair value of the compound financial instrument as a whole and the fair value of the liability component. Any directly attributable transaction costs are allocated to the liability and equity components in proportion to their initial carrying amounts.

Subsequent to initial recognition, the liability component of a compound financial instrument is measured at amortized cost using the effective interest method. The equity component of a compound financial instrument is not remeasured.

Interest related to the financial liability is recognized in profit or loss. On conversion, the financial liability is reclassified to equity and no gain or loss is recognized.

Other financial liabilities

Other financial liabilities, including borrowings, are initially measured at fair value, net of transaction costs incurred, and are subsequently measured at amortized 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 amortized 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.

(m) Leases

The Company has applied IFRS 16 as of January 1, 2019, using the modified retrospective approach. Therefore, comparative information has not been restated and is presented applying IAS 17. The details of accounting policies under both IAS 17 and IFRS 16 are presented separately below.

Policies applicable from January 1, 2019

At inception of the contract, the Company assesses whether a contract is or contains a lease. The Company recognizes a right-of-use asset and a corresponding lease liability with respect to all lease arrangements in which it is the lessee, except for short-term leases (defined as leases with a lease term of 12 months or less) and leases of low value assets (such as tablets and personal computers, small items of office furniture and telephones). For these leases, the Company recognizes the lease payments in operating costs on a straight-line basis over the term of the lease unless another systematic basis is more representative of the time pattern in which economic benefits from the leased assets are consumed.

The lease liability is initially measured at the present value of the lease payments that are not paid at the commencement date, discounted by using the interest rate implicit in the lease. When the interest rate implicit in the lease cannot be readily determined, the Company uses its incremental borrowing rate.

Lease payments included in the measurement of the lease liability comprise:

- Fixed lease payments (including in-substance fixed payments), less any lease incentives receivable;
- Variable lease payments that depend on an index or rate, initially measured using the index or rate at the commencement date;
- The amount expected to be payable by the Company under residual value guarantees;
- The exercise price of purchase options, if the Company is reasonably certain to exercise the options; and
- Payments of penalties for terminating the lease, if the lease term reflects the exercise of an option to terminate the lease.

The lease liability is presented as a separate line in the consolidated statement of financial position.

The lease liability is subsequently measured by increasing the carrying amount to reflect interest on the lease liability (using the effective interest method) and by reducing the carrying amount to reflect the lease payments made.

The Company remeasures the lease liability (and makes a corresponding adjustment to the related right-of-use asset) whenever:

- The lease term has changed or there is a significant event or change in circumstances resulting in a change in the assessment of exercise of a purchase option, in which case the lease liability is remeasured by discounting the revised lease payments using a revised discount rate.
- The lease payments change due to changes in an index or rate or a change in expected payment under a guaranteed residual value, in which cases the lease liability is remeasured by discounting the revised lease payments using an unchanged discount rate (unless the lease payments change is due to a change in a floating interest rate, in which case a revised discount rate is used).

- A lease contract is modified and the lease modification is not accounted for as a separate lease, in which case the lease liability is remeasured based on the lease term of the modified lease by discounting the revised lease payments using a revised discount rate at the effective date of the modification.

The right-of-use asset comprises the initial measurement of the corresponding lease liability, lease payments made at or before the commencement day, less any lease incentives received and any initial direct costs. It is subsequently measured at cost less accumulated depreciation and impairment losses.

Whenever the Company incurs an obligation for costs to dismantle and remove a leased asset, restore the site on which it is located or restore the underlying asset to the condition required by the terms and conditions of the lease, a provision is recognized and measured under IAS 37. To the extent that the costs relate to a right-of-use asset, the costs are included in the related right-of-use asset, unless those costs are incurred to produce inventories.

Right-of-use assets are depreciated over the shorter period of lease term and useful life of the underlying asset. If a lease transfers ownership of the underlying asset or the cost of the right-of-use asset reflects that the Company expects to exercise a purchase option, the related right-of-use asset is depreciated over the useful life of the underlying asset. The depreciation starts at the commencement date of the lease.

The right-of-use asset is presented under Property, Plant and Equipment in the consolidated statement of financial position, in the category Buildings and leasehold improvements.

As a practical expedient, IFRS 16 permits a lessee not to separate non-lease components, and instead account for any lease and associated non-lease components as a single arrangement. The Company has used this practical expedient.

Policies applicable before January 1, 2019

(i) Determining whether an arrangement contains a lease

At inception of an arrangement, the Company determines whether such an arrangement is or contains a lease.

At inception or on reassessment of an arrangement that contains a lease, the Company separates payments and other consideration required by such an arrangement into those for the lease and those for other elements on the basis of their relative fair values. If the Company concludes for a finance lease that it is impracticable to separate the payments reliably, then an asset and a liability are recognized at an amount equal to the fair value of the underlying asset. Subsequently, the liability is reduced as payments are made and an imputed finance cost on the liability is recognized using the Company's incremental borrowing rate.

(ii) Leased assets

Assets held by the Company under leases that transfer to the Company substantially all of the risks and rewards of ownership are classified as finance leases. The leased assets are measured initially at an amount equal to the lower of their fair value and the present value of the minimum lease payments. Subsequent to initial recognition, the assets are accounted for in accordance with the accounting policy applicable to that asset.

Assets held under other leases are classified as operating leases and are not recognized in the Company's statement of financial position.

(iii) Lease payments

Payments made under operating leases are recognized in profit or loss on a straight-line basis over the term of the lease. Lease incentives received are recognized as an integral part of the total lease expense, over the term of the lease.

Minimum lease payments made under finance leases are apportioned between the finance expense and the reduction of the outstanding liability. The finance expense is allocated to each period during the lease term so as to produce a constant periodic rate of interest on the remaining balance of the liability.

4. New standards and interpretations not yet adopted

A number of new standards, amendments to standards and interpretations are effective for annual periods beginning after January 1, 2020 and have not been applied in preparing these consolidated financial statements. There are no standards that are not yet effective and that would be expected to have a material impact on the Company in the current or future reporting periods and on foreseeable future transactions. The Company does not plan to adopt these standards early.

5. Financial Risk Management

5.1 Financial risk factors

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.

Financial 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

Market risk is the risk that changes in market prices – such as foreign exchange rates, interest rates and equity prices – will affect the Company's income or the value of its holdings of financial instruments. The objective of market risk management is to manage and control market risk exposures within acceptable parameters, while optimizing the return.

Foreign exchange risk

Foreign exchange risk arises from future commercial transactions and recognized assets and liabilities in foreign currencies, primarily with respect to the U.S. dollar. The Company has an exposure associated with the time delay between entering into a contract, budget or forecast and the realization thereof. The Company operates a foreign exchange policy to manage the foreign exchange risk against the functional currency based on the Company's cash balances and the projected future spend per major currency.

At year-end, a substantial amount of our cash balances are denominated in U.S. Dollars. This amount reflects our current expectation of future expenditure in U.S. dollars.

At December 31, 2019 there was a net asset in U.S. dollars of € 39,004,000 (2018: € 26,928,000). Foreign currency denominated receivables and trade payables are short term in nature (generally 30 to 45 days). As a result, the foreign exchange results recognized in 2019 and 2018 are mainly caused by the cash balance denominated in U.S. dollars.

A reasonably possible weakening of the U.S. dollar by 10% against the functional currency of the Company at December 31, 2019 would have increased our net loss by € 3,900,000 (2018: € 2,693,000). A 10% strengthening of the U.S. dollar against the functional current of the Company would have an equal but opposite effect on our net loss. The analysis assumes that all other variables, in particular interest rates, remain constant.

Price risk

The market prices for the production of preclinical and clinical materials and services as well as external contracted research may vary over time. Currently, the commercial prices of any of the Company's product candidates is uncertain.

When the development products near the regulatory approval date or potential regulatory approval date, the uncertainty of the potential sales price decreases. The Company is not exposed to commodity price risk.

Furthermore, the Company does not hold investments designated for sale, therefore are not exposed to equity securities price risk.

Cash flow and fair value 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 several loans with fixed interest rates, totaling €13,052,000 at December 31, 2019 (2018: € 9,386,000). Details on the interest rates and maturities of these loans are provided in Note 13.

(b) 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 held at ABN Amro, Rabobank and Wells Fargo. Our cash management policy is focused on preserving capital, providing liquidity for operations and optimizing yield while accepting limited risk (Short-term credit ratings must be rated A-1/P-1/F1 at a minimum by at least one of the Nationally Recognized Statistical Rating Organizations (NRSROs) specifically Moody's, Standard & Poor's or Fitch. Long-term credit rating must be rated A2 or A at a minimum by at least one NRSRO).

At December 31, 2019 and December 31, 2018, substantially all of our cash and cash equivalents were held at three large institutions, Rabobank, ABN Amro and Wells Fargo. All institutions are highly rated (ratings of Aa3, A1 and A2 for Rabobank, ABN Amro and Wells Fargo respectively) with sufficient capital adequacy and liquidity metrics.

There are no financial assets past due date or impaired. No credit limits were exceeded during the reporting period.

(c) 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 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 analyzes ProQR's undiscounted liabilities into relevant maturity groupings based on the remaining period at year-end until the contractual maturity date:

	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years
(€ in thousands)				
At December 31, 2019				
Borrowings	343	10,054	4,790	322
Lease liabilities	513	—	—	—
Trade payables and other payables	10,142	—	—	—
Total	10,998	10,054	4,790	322
At December 31, 2018				
Borrowings	—	797	8,984	—
Trade payables and other payables	8,160	—	—	—
Total	8,160	797	8,984	—

5.2 Capital risk management

The Company's objectives when managing capital are to safeguard the Company's ability to continue as a going concern in order to provide returns for shareholders, benefits for other stakeholders and to maintain an optimal capital structure to reduce the cost of capital.

In order to maintain or adjust the capital structure, the Company may adjust the amount of dividends paid to shareholders (although at this time the Company does not have retained earnings and is therefore currently unable to pay dividends), return capital to shareholders, issue new shares or sell assets to reduce debt.

The total amount of equity as recorded on the balance sheet is managed as capital by the Company.

5.3 Fair value measurement

For financial instruments that are measured on the balance sheet at fair value, IFRS 13 requires disclosure of fair value measurements by level of the following fair value measurement hierarchy:

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

The carrying amount of all financial assets and financial liabilities is a reasonable approximation of the fair value and therefore information about the fair values of each class has not been disclosed.

6. 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 sales revenues since inception.

Substantially all non-current assets of the Company are located in the Netherlands. 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.

7. Property, plant and equipment ('PP&E')

	Buildings and leasehold improvements (€ in thousands)	Laboratory equipment (€ in thousands)	Other (€ in thousands)	Total (€ in thousands)
Balance at January 1, 2018				
Cost	1,856	2,004	1,309	5,169
Accumulated depreciation	(802)	(1,069)	(793)	(2,664)
Carrying amount	1,054	935	516	2,505
Additions	18	281	13	312
Depreciation	(296)	(419)	(238)	(953)
Disposals	—	—	—	—
Movement for the period	(278)	(138)	(225)	(641)
Balance at December 31, 2018				
Cost	1,874	2,285	1,322	5,481
Accumulated depreciation	(1,098)	(1,488)	(1,031)	(3,617)
Carrying amount	776	797	291	1,864
Effect of initial application of IFRS 16 <i>Leases</i> (note 21)	2,359	—	—	2,359
Balance at January 1, 2019				
Cost	4,233	2,285	1,322	7,840
Accumulated depreciation	(1,098)	(1,488)	(1,031)	(3,617)
Carrying amount	3,135	797	291	4,223
Additions	141	694	—	835
Depreciation	(1,485)	(433)	(134)	(2,052)
Effect of lease modification (note 21)	(566)	—	—	(566)
Disposals	—	—	—	—
Movement for the period	(1,910)	261	(134)	(1,783)
Balance at December 31, 2019				
Cost	3,808	2,979	1,322	8,109
Accumulated depreciation	(2,583)	(1,921)	(1,165)	(5,669)
Carrying amount	1,225	1,058	157	2,440

The depreciation charge for 2019 is included in the research and development costs for an amount of € 1,583,000 (2018: € 725,000) and in the general and administrative costs for an amount of € 469,000 (2018: € 228,000).

Buildings and leasehold improvements include a right-of-use asset relating to the lease of our Leiden office and laboratory space, with a carrying amount of € 606,000 at December 31, 2019 (2018: € nil).

8. Investments in associates

In May 2019, the Company acquired a non-controlling stake in Wings Therapeutics Inc. as part of the strategic spin out of the Dystrophic Epidermolysis Bullosa (DEB) activities. Wings Therapeutics Inc. was formed and financed by EB Research Partnership (EBRP), the largest global non-profit dedicating to treating and curing EB. Wings Therapeutics

focuses on developing therapies for DEB and continues to conduct the ongoing clinical trial with QR-313 targeting exon 73 as well as progress other RNA molecules that are designed for other mutations that cause DEB.

	<u>Investment in associate</u> (€ in thousands)
Balance at January 1, 2018 and December 31, 2018	—
Investment in associate	949
Share in result	(520)
Balance at December 31, 2019	429

9. Social Security and Other Taxes

	<u>December 31, 2019</u>	<u>December 31, 2018</u>
	(€ in thousands)	
Value added tax	557	311
Wage tax	293	932
	<u>850</u>	<u>1,243</u>

All receivables are considered short-term and due within one year.

10. Prepayments and Other Receivables

	<u>December 31, 2019</u>	<u>December 31, 2018</u>
	(€ in thousands)	
Prepayments	1,526	645
Other receivables	340	899
	<u>1,866</u>	<u>1,544</u>

All receivables are considered short-term and due within one year.

11. Cash and Cash Equivalents

	<u>December 31, 2019</u>	<u>December 31, 2018</u>
	(€ in thousands)	
Cash at banks	111,950	105,580
Bank deposits	—	—
	<u>111,950</u>	<u>105,580</u>

The cash at banks is at full disposal of the Company.

12. Shareholders' Equity

(a) Share capital

	<u>Number of shares 2019</u>	<u>Number of shares 2018</u>	<u>Number of shares 2017</u>
	<u>Ordinary</u>	<u>Ordinary</u>	<u>Ordinary</u>
Balance at January 1	43,149,987	36,425,014	23,346,856
Issued for cash	10,454,545	6,612,500	8,573,975
Issued for services	371,306	112,473	—
Exercise of share options	46,900	226,098	1,034
Treasury shares issued (transferred)	(46,900)	(226,098)	4,503,149
Balance at December 31	<u>53,975,838</u>	<u>43,149,987</u>	<u>36,425,014</u>

The authorized share capital of the Company amounting to € 7,200,000 consists of 90,000,000 ordinary shares and 90,000,000 preference shares with a par value of € 0.04 per share. At December 31, 2019, 53,975,838 ordinary shares were issued and fully paid in cash, of which 4,230,151 were held by the Company as treasury shares (2018: 4,277,051).

In 2017, the Company has issued 976,477 shares pursuant to its current at-the-market offering program, resulting in proceeds of € 4,138,000, net of € 127,000 of offering expenses.

On June 28, 2017, the Company agreed to the issuance of 1,200,000 ordinary shares to institutional investors at an issue price of \$ 5.00 (€ 4.40) per share in a registered direct offering with gross proceeds of € 5,278,000. The closing of the offering was effected on July 3, 2017. Transaction costs amounted to € 414,000, resulting in net proceeds of € 4,864,000.

In November 2017, the Company consummated an underwritten public offering and concurrent registered direct offering of 6,397,498 ordinary shares at an issue price of \$ 3.25 (€ 2.76) per share. The gross proceeds from both offerings amounted to € 17,671,000 while the transaction costs amounted to € 988,000, resulting in net proceeds of € 16,683,000.

In September 2018, the Company consummated an underwritten public offering and concurrent registered direct offering of 6,612,500 ordinary shares at an issue price of \$ 15.75 per share. The gross proceeds from this offering amounted to € 89,983,000 while the transaction costs amounted to € 5,792,000, resulting in net proceeds of € 84,191,000.

In November 2018, the Company issued 112,473 shares in the aggregate amount of \$ 2,500,000, at \$ 22.23 (€ 19.46) per share to Ionis Pharmaceuticals, Inc. Under the terms of the agreement, an upfront payment in ordinary shares to its common stock was made to Ionis upon signing the worldwide license agreement. The Company was granted an exclusive worldwide license to QR-1123 and relevant patents. The Company will also make future milestone payments, certain of which will be made in equity and others in cash or equity at the company's discretion, and royalties on net sales of 20% through the royalty term.

On November 7, 2018, the Company filed a shelf registration statement, which permitted: (a) the offering, issuance and sale by the Company of up to a maximum aggregate offering price of \$ 300,000,000 of its ordinary shares, warrants and/or units; and (b) as part of the \$ 300,000,000, the offering, issuance and sale by us of up to a maximum aggregate offering price of \$ 75,000,000 of its ordinary shares that may be issued and sold under a sales agreement with H.C. Wainwright & Co in one or more at-the-market offerings.

In October 2019, the Company consummated an underwritten public offering of 10,454,545 ordinary shares at an issue price of \$ 5.50 per share. The gross proceeds from this offering amounted to € 51,597,000 while the transaction costs amounted to € 3,047,000, resulting in net proceeds of € 48,550,000.

In December 2019, the Company issued 371,306 shares in the aggregate amount of \$ 3,501,000, at \$ 9.43 (€ 8.51) per share to Ionis Pharmaceuticals, Inc. Under the terms of the agreement, the second installment of the upfront payment in ordinary shares to the Company's common stock was made to Ionis upon the dosing of the first patient in the phase 1/2 Aurora clinical trial for QR-1123.

(b) Equity settled employee benefit reserve

The costs of share options for employees, members of the Supervisory Board and members of the Management Board 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'. On September 25, 2017, we established a Dutch foundation named Stichting Bewaarneming Aandelen ProQR for holding shares in trust for employees, members of the Management Board and members of the Supervisory Board of the Company and its group companies who from time to time will exercise options under the Company's equity incentive plans.

(c) Translation reserve

The translation reserve comprises all foreign currency differences arising from the translation of the financial statements of foreign operations.

(d) Share options

The Company operates an equity-settled share-based compensation plan which was introduced in 2013. Options may be granted 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 € 5,948,000 in 2019 (2018: € 3,224,000), of which € 3,323,000 (2018: € 2,167,000) was recorded in general and administrative costs and € 2,625,000 (2018: € 1,057,000) was recorded in research and development costs based on employee allocation.

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.

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:

- the exercise price of the option;
- the expected life of the option;
- the current value of the underlying shares;
- the expected volatility of the share price;
- the dividends expected on the shares; and
- the risk-free interest rate for the life of the option.

The fair value of the options is estimated at the date of grant using the Black-Scholes option-pricing model, with on average the following assumptions:

	Options granted in 2019	Options granted in 2018	Options granted in 2017
Risk-free interest rate	2.430 %	2.223 %	1.913 %
Expected dividend yield	— %	— %	— %
Expected volatility	80.2 %	80.9 %	88.7 %
Expected life in years	5 years	5 years	5 years

The resulting weighted average grant date fair value of the options amounted to € 7.71 in 2019 (2018: € 2.02). The stock options granted have a 10-year life following the grant date and are assumed to be exercised five years from date of grant for all awards.

Movements in the number of options outstanding and their related weighted average exercise prices are as follows:

	2019		2018		2017	
	Number of options	Average exercise price	Number of options	Average exercise price	Number of options	Average exercise price
Balance at January 1	4,511,512	€ 4.24	3,331,875	€ 4.78	2,205,989	€ 4.88
Granted	1,237,506	€ 11.77	1,570,366	€ 3.11	1,199,447	€ 4.63
Forfeited	(119,338)	€ 9.35	(142,467)	€ 4.29	(72,527)	€ 5.56
Exercised	(46,900)	€ 4.18	(226,098)	€ 4.02	(1,034)	€ 3.54
Expired	(7,326)	€ 8.76	(22,164)	€ 6.42	—	€ —
Balance at December 31	5,575,454	€ 5.80	4,511,512	€ 4.24	3,331,875	€ 4.78
Exercisable at December 31	2,521,477		1,683,731		1,148,893	

The options outstanding at December 31, 2019 had an exercise price in the range of € 1.11 to € 20.34 (2018: € 1.11 to € 20.34) and a weighted-average contractual life of 7.2 years (2018: 7.6 years).

The weighted-average share price at the date of exercise for share options exercised in 2019 was € 12.47 (2018: € 15.36).

Please refer to Note 23 for the options granted to key management personnel.

13. Non-current liabilities

(a) Borrowings

	December 31, 2019	December 31, 2018
	(€ in thousands)	
Innovation credit	7,191	5,164
Accrued interest on innovation credit	3,124	2,351
Convertible loans	2,473	1,783
Accrued interest on convertible loans	264	88
Total borrowings	13,052	9,386
Current portion	(343)	—
	12,709	9,386

Innovation credit (“Innovatiekrediet”)

On June 1, 2012, ProQR was awarded an Innovation credit by the Dutch government, through its agency RVO of the Ministry of Economic Affairs, for the Company’s cystic fibrosis program. Amounts were drawn under this facility in the course of the years 2013 through 2017. The credit covers 35% of the costs incurred in respect of the program up to € 5,000,000.

The credit is interest-bearing at a rate of 10% per annum. In October 2018 ProQR received a conditional waiver of the € 5,000,000 Innovation credit. Consequently, the repayment of the total loan of € 8,085,000 including interest, will be waived if conditions are met, which will be reviewed annually for 3 years.

On December 10, 2018 ProQR was awarded an Innovation credit for the seprofarsen program. Amounts will be drawn under this facility from 2018 through 2021. The credit of € 4,755,000 through December 31, 2021 will be used to conduct the Phase 2/3 clinical study and efforts to obtain regulatory and ethical market approval (NDA/MAA) of seprofarsen for LCA10, of which € 2,230,000 had been received at December 31, 2019. The credit, including accrued interest of 10% per annum, is repayable depending on obtaining market approval.

The assets which are co-financed with the granted innovation credits are subject to a right of pledge for the benefit of RVO.

Convertible loans

Convertible loans were issued to Amylon Therapeutics B.V. in 2017, 2018 and 2019 and are interest-bearing at an average rate of 8% per annum. They are convertible into a variable number of ordinary shares within 36 months at the option of the holder or the Company in case financing criteria are met. Any unconverted loans become payable on demand after 24 – 36 months in equal quarterly terms.

In March 2018, the Company entered into a convertible loan (the “Loan”), pursuant to which we borrowed an aggregate of € 260,000 from the lender. The loan bears interest at a rate of 3% per annum. The outstanding principal and interest under the Loan is convertible into a variable number of ordinary shares at the option of the holder in case financing criteria are met. If these criteria are not met on or before March 1, 2022, the outstanding amount will be fully converted into our ordinary shares.

14. Current Liabilities

	December 31, 2019	December 31, 2018
	(€ in thousands)	
Borrowings	343	—
Lease liabilities	508	—
Trade payables	445	135
Current income tax liability	64	—
Social securities and other taxes	108	—
Pension premiums	2	7
Deferred income	711	545
Accrued expenses and other liabilities	8,812	7,473
	10,993	8,160

At December 31, 2019 and 2018, current liabilities included deferred income resulting from funds received for our research and innovation programs. Accrued expenses and other liabilities consisted principally of accruals for services provided by vendors not yet billed, payroll-related accruals and other miscellaneous liabilities.

15. Other income

	2019	2018	2017
	(€ in thousands)		
Grant income	1,778	5,378	870
Rental income from property subleases	—	174	625
Other income	155	209	—
	1,933	5,761	1,495

Other income is incidental by nature. On February 9, 2018, the Company entered into a partnership agreement with Foundation Fighting Blindness (FFB), under which FFB has agreed to provide funding of \$ 7,500,000 for the preclinical and clinical development of QR-421a for Usher syndrome type 2A targeting mutations in exon 13. FFB grant income amounted to € 1,312,000 in 2019 compared to € 2,478,000 in 2018.

On June 5, 2018, the Company entered into a partnership agreement with EB Research Partnership (EBRP) and EB Medical Research Foundation (EBMRF) under which EBRP and EBMRF have agreed to provide funding of \$ 5,000,000 for the clinical development of QR-313 for Dystrophic Epidermolysis Bullosa targeting mutations in exon 73. The EBRP/EBMRF grant agreement was terminated on March 26, 2019 as part of the strategic spin out of the Dystrophic Epidermolysis Bullosa (DEB) activities into a newly formed company, Wings Therapeutics. As such, no grant income was recognized in 2019 related to this grant. In 2018, € 1,301,000 had been recognized as other income.

In 2015, the European Commission (EC) through its Horizon 2020 program awarded us and our academic partners a grant of € 5,997,000 to support the clinical development of eluforsen (ProQR: € 4,627,000). Horizon 2020 is one of the largest research and innovation programs in the European Union with nearly € 80 billion in available funding for qualified projects from 2014 to 2020. This program has ended at December 31, 2017 and the final amount of € 1,300,000 was recognized as other income in 2018.

16. Research and Development Costs

Research and development costs amounted to € 46,491,000 in 2019 (2018: € 29,514,000, 2017: € 31,153,000) and comprise allocated employee costs, the costs of materials and laboratory consumables, the costs of external studies including, amongst others, clinical studies and toxicology studies and external research, license- and IP-costs and allocated other costs.

17. Employee Benefits

	2019	2018	2017
	(€ in thousands)		
Wages and salaries	13,187	11,558	11,855
Social security costs	1,433	1,346	1,285
Pension costs — defined contribution plans	910	868	860
Equity-settled share based payments	5,948	3,224	4,024
	21,478	16,996	18,024
Average number of employees for the period	139.8	127.7	139.9

Employees per activity at December 31 (converted to FTE):

	December 31, 2019	December 31, 2018	December 31, 2017
Research and Development	118.3	89.2	96.2
General and Administrative	36.1	29.6	34.0
Total number of employees at December 31 (converted to FTE)	154.4	118.8	130.2

Of all employees 143.1 FTE are employed in the Netherlands (2018: 112.8 FTE).

Included in the wages and salaries for 2019 is a credit of € 714,000 (2018: € 1,294,000, 2017: € 723,000) with respect to WBSO subsidies.

18. Financial Income and Expense

	2019	2018	2017
	(€ in thousands)		
Interest income:			
Current accounts and deposits	763	189	90
Interest costs:			
Interest on loans and borrowings	(1,083)	(810)	(596)
Foreign exchange result:			
Net foreign exchange benefit/(loss)	722	(171)	(2,669)
	402	(792)	(3,175)

19. Income Taxes

The calculation of the tax charge is as follows:

	2019	2018	2017
	(€ in thousands)		
Income tax based on domestic rate	14,261	9,106	10,918
Tax effect of:			
Different tax rates in foreign jurisdictions	17	—	—
Non-deductible expenses	(1,501)	(818)	(634)
Stock issue expenditures that are deductible	843	1,448	—
Change in unrecognized deductible temporary differences	(7)	(25)	(25)
Current year losses for which no deferred tax asset was recognized	(13,703)	(9,712)	(10,261)
Under-provision in previous years	(42)	—	—
Income tax charge	(132)	(1)	(2)
Effective tax rate	— %	— %	— %

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. Consequently, the Company has not recognized a deferred tax asset related to operating losses.

As per December 31, 2019, the Company has a total amount of € 218.7 million (2018: € 162.6 million, 2017: € 123.9 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.

20. 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.

	2019	2018	2017
Result attributable to equity holders of the Company (€ in thousands)	(56,480)	(36,894)	(43,637)
Weighted average number of shares outstanding	41,037,244	34,052,520	25,374,807
Basic (and diluted) earnings per share (€ per share)	€ (1.38)	€ (1.08)	€ (1.72)

(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.

21. Leases

The Company leases office and laboratory facilities of 2,960 square meters at Zernikedreef in Leiden, the Netherlands, where our headquarters and our laboratories are located. The current lease agreement for these facilities ends on June 30, 2020. A renewed lease agreement is in place for a 10-year period starting on July 1, 2020, which may be extended for subsequent 5-year terms. This new lease agreement will increase the number of square meters leased to 4,772 and contains no significant dismantling requirements.

The lease liability and the corresponding right-of-use asset for the Leiden office and laboratory facilities initially recognized on January 1, 2019 both amounted to € 2,359,000. In September 2019, the lease agreement was modified, resulting in a reduction in the carrying amount of the right-of-use asset of € 566,000 and a reduction in the lease liability of € 590,000. The modification consisted of a change in the termination date from December 31, 2020 to June 30, 2020, as a result of the new lease commencing on July 1, 2020.

The following table summarizes the relevant disclosures in relation to our leases in 2019:

	2019
	(€ in thousands)
Depreciation charge for right-of-use asset	1,187
Interest expense on lease liability	48
Expense relating to short-term leases	189
Total cash outflow for leases	1,310
Additions to right-of-use assets during the period	—

The carrying amount of the right-of-use asset at the end of the reporting period is disclosed in note 7 Property, Plant & Equipment.

A maturity analysis of our lease liability is included in note 5 Financial Risk Management under (c) Liquidity risk. The total undiscounted commitment for the new lease agreement to which the Company had committed at December 31, 2019 amounts to € 12,864,000. This amount does not include potential commitments that may arise from contractual extension options, as the Company is not reasonably certain that any extension options will be exercised.

The lease expenditure charged to the income statement in 2018 amounted to € 1,813,000 (2017: € 2,103,000).

The Company leased out a part of its office in the U.S. and the Netherlands during 2017 and early 2018. In 2019, total sublease income amounted to € nil (2018: € 174,000, 2017: € 625,000). In 2018 and 2017, sublease income was recorded in other income.

22. Commitments and Contingencies

(a) Claims

There are no claims known to management related to the activities of the Company.

(b) Patent license agreements

On October 26, 2018, we and Ionis Pharmaceuticals, Inc. entered into a License Agreement, pursuant to which Ionis granted an exclusive, worldwide, royalty-bearing license to us to develop and commercialize certain pharmaceutical products, including the product designated by Ionis as IONIS-RHO-2.5Rx, which has been re-designated by us as QR-1123, for the prevention or treatment of retinitis pigmentosa in humans, including patient screening. Ionis also granted to the Company certain sub-license rights. Under the License Agreement, we are required to make an upfront payment of an aggregate of up to \$ 6.0 million in installments, and certain payments up to an aggregate of \$ 20.0 million upon the satisfaction of certain development and sales milestones. In addition, Ionis is entitled to royalty payments in the double digits of aggregate annual net sales, subject to minimum sales in certain circumstances, and subject to reduced rates in certain circumstances. The royalty term lasts on a product-by-product and country-by-country basis, until the later of the expiration of the patent rights licensed to us and the expiration of regulatory-based exclusivity for such product in such country. The License Agreement may also be terminated by either party based upon certain uncured material breach by, or insolvency of, the other party, or by us at any time with advanced notice. In connection with the upfront payments and development milestone payments, we also simultaneously entered into a Stock Purchase Agreement with Ionis, pursuant to which we agreed to issue an aggregate of \$ 2.5 million of ordinary shares to satisfy the first installment upfront payment, and the remaining installment of the upfront payment in ordinary shares determined upon the due date of such installment. In addition, the Stock Purchase Agreement provides for the ability for us, at our discretion, to pay the development milestone payments in ordinary shares when such payments are due. We may not issue ordinary shares to Ionis to the extent that such issuance would result in Ionis owning in excess of 18.5% of our issued and outstanding shares, nor may we issue ordinary shares if such issuance, together with previous issuances under the Stock Purchase Agreement, would exceed 19.9% of our outstanding ordinary shares as of the date of the execution of the Stock Purchase Agreement. Under these circumstances, we are required to pay the remainder of the upfront and/or development milestone payments in cash. In addition, in connection with the Stock Purchase Agreement, we also entered into an Investor Agreement with Ionis, pursuant to which we agreed to register for resale the ordinary shares issued by us under the Stock Purchase Agreement, under the circumstances described in the Investor Agreement. The Investor Agreement also contains customary covenants related to our registration of such shares, preparation of filings in connection therewith and indemnification of Ionis. The Investor Agreement also contains lockup provisions prohibiting the disposition of our ordinary shares issued under the Stock Purchase Agreement for a period of 12 months from the applicable issuance date, as well as voting provisions requiring Ionis to vote its ordinary shares in accordance with the recommendations of our board of directors, in each case subject to certain exceptions.

In April 2014 the Company entered into a Patent License Agreement with Radboud University Medical Center, or Radboud in the field of antisense oligonucleotide-based therapy for Leber's Congenital Amaurosis, or LCA. Under the terms of this license agreement, the Company has an exclusive, sublicensable, world-wide royalty-bearing license under certain Radboud patent rights to develop, make, have made, use, sell offer for sale and import of certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of LCA. Pursuant to the terms of the license agreement, the Company is obligated to pay Radboud net-sales-related royalties which shall be determined on a product-by-product and country-by-country basis. If the Company required to pay any third party royalties, it may deduct that amount from that which is owed to Radboud. Radboud shall provide human resources, materials, facilities and equipment that are necessary for preclinical and clinical trials and if the Company does not purchase such trial facilities from Radboud, it is required to pay an increased net-sales-related royalty. In the Company's sole discretion, it may elect to convert the obligation to pay net-sales-related royalties into one of the two lump-sum royalty options depending on whether the Company elects to convert prior to or after regulatory approval has been filed. The license agreement will remain in effect until the date on which all patent applications and all granted patents ensuing from such applications have expired or is terminated earlier in accordance with the agreement. Either party may terminate the agreement if the other party is in default of a material obligation under the agreement which has not been cured within 30 days of notice of such default. Either party may also terminate the agreement if the other party declares bankruptcy, dissolves, liquidates or the like. Radboud may also terminate the agreement if the Company does not pay any amount owed under the agreement and such payment remains overdue for at least 30 days after receiving notice from Radboud of the amount due.

In June 2015, we entered into another license agreement with Radboud. Under the terms of this license agreement, the Company has an exclusive, sublicensable, world-wide royalty-bearing license under certain Radboud patent rights to develop, make, have made, use, sell offer for sale and import of certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of Usher syndrome. Pursuant to the terms of the license agreement, the Company is obligated to pay Radboud net-sales-related royalties which shall be determined on a product-by-product and country-by-country basis. If the Company is required to pay any third party royalties, it may deduct that amount from that which is owed to Radboud. Radboud shall provide human resources, materials, facilities and equipment that are necessary for preclinical and clinical trials and if the Company does not purchase such trial facilities from Radboud, it is required to pay an increased net-sales-related royalty. In the Company's sole discretion, it may elect to convert the obligation to pay net-sales-related royalties into one of the two lump-sum royalty options depending on whether it elects to convert prior to or after regulatory approval has been filed. The license agreement will remain in effect until the date on which all patent applications and all granted patents ensuing from such applications have expired or is terminated earlier in accordance with the agreement. Either party may terminate the agreement if the other party is in default of a material obligation under the agreement which has not been cured within 30 days of notice of such default. Either party may also terminate the agreement if the other party declares bankruptcy, dissolves, liquidates or the like. Radboud may also terminate the agreement if the Company does not pay any amount owed under the agreement and such payment remains overdue for at least 30 days after receiving notice from Radboud of the amount due.

In January 2018, the Company entered into a license agreement with Inserm Transfert SA and Assistance-Publique-Hôpitaux de Paris. Under the terms of the agreement, the Company has a world-wide, exclusive, royalty-bearing license under patent rights belonging to Inserm Transfert SA and other co-owners to develop, have developed, make, have made, use, have used and sell, have sold or otherwise distribute certain licensed products related to antisense oligonucleotides for treating LCA and method of treatment claims relating to modulation of the splicing of the CEP290 gene product. The Company has the right to grant sublicenses to third parties subject to certain limitations such as the sublicensee's activities do not conflict with the public order or ethical obligations of Inserm Transfert SA or any co-owner and do not tarnish the image of Inserm Transfert SA or any co-owner. In partial consideration of the rights and licenses granted by the license agreement, the Company is required to make payments upon the completion of certain milestones: completion of a clinical trial more advanced than First in Man, such as a phase IIb; and the first marketing authorization or any foreign equivalent for a first product. In further consideration of the rights and license granted under the agreement, the Company shall pay to Inserm Transfert SA a running royalty on net sales of products sold by us or our sublicensee. Unless terminated earlier pursuant to termination provisions of Agreement, the license agreement will remain in effect on a country-by-country basis, until the later to occur of the following events (i) the invalidation or expiration of the last to expire or to be invalidated patent rights which covers the manufacture, use or sale of the product

in said country or until the expiration of the exclusive commercialization right granted by a regulatory agency to a product as an orphan drug or (ii) five years after the first commercial sale of a product in the country in which the product is sold. The agreement may be terminated by either party in the event of an uncured breach by the non-breaching party. Inserm Transfert SA may terminate the agreement if we become the subject of voluntary or involuntary winding-up proceedings or judicial recovery, if the Company or its sublicensees interrupt development activities for at least one year, if the Company or its sublicensees interrupt commercialization for more than twelve months after the first commercialization in a country, if the Company does not commercialize a product within two years following our obtaining of marketing approval in a country, or if the Company or our sublicensees do not put a product into commercial use and do not keep products reasonably available to the public within twelve years of the effective date of the agreement.

In January 2016, the Company entered into an agreement with Leiden University Medical Center, or LUMC, which gives us a world-wide, exclusive, royalty-bearing license in the field of amyloid beta related diseases, notably Alzheimer's disease and HCHWA-D, under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to its CNS program. On September 12, 2017, this program was transferred to Amylon Therapeutics B.V., in which the Company maintains a majority ownership.

In January 2017, the Company entered into an agreement with LUMC, which gives us a world-wide, exclusive, royalty-bearing license in the field of Huntington's disease, under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to the HD program.

In 2012, the Company and the General Hospital Corporation (MGH) have entered into a Patent License Agreement for the Company's CF program pursuant to which the Company may have certain royalty and milestone obligations. The Company is also obligated to pay MGH up to \$ 700,000 (€ 623,000) in milestone payments upon the achievement of certain development and regulatory milestones and, beginning after its first commercial sale of a product covered by the licensed patent rights, a \$ 10,000 (€ 9,000) annual license fee which is creditable against royalties due to MGH in the same calendar year. In addition, the Company is obligated to pay MGH 2% of any net sales by the Company, its affiliates or sublicensees on licensed products made or sold in the United States, as well as a low double-digit percentage of any payments the Company may receive from any sublicensee anywhere in the world.

(c) Clinical support agreements

In August 2014, the Company entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, a subsidiary of the Cystic Fibrosis Foundation, pursuant to which CFFT agreed to provide the Company with up to \$ 3 million (€ 2.7 million) to support the clinical development of eluforsen.

Pursuant to the terms of the agreement, the Company is obligated to make a one-time milestone payment to CFFT of up to approximately \$ 16 million (€ 14 million), payable in three equal annual installments following the first commercial sale of eluforsen, the first of which is due within 90 days following the first commercial sale. The Company is also obligated to make a one-time milestone payment to CFFT of up to \$ 3 million (€ 2.7 million) if net sales of eluforsen exceed \$ 500 million (€ 445 million) in a calendar year. Lastly, the Company is obligated to make a payment to CFFT of up to approximately \$ 6 million (€ 5 million) if it transfers, sells or licenses eluforsen other than for certain clinical or development purposes, or if the Company enters into a change of control transaction prior to commercialization. However, the payment in the previous sentence may be set-off against the \$ 16 million milestone payment. Either CFFT or the Company may terminate the agreement for cause, which includes the Company's material failure to achieve certain commercialization and development milestones. The Company's payment obligations survive the termination of the agreement.

On February 9, 2018, the Company entered into an agreement with Foundation Fighting Blindness (FFB), under which FFB will provide funding of \$ 7.5 million (€ 6.7 million) to advance QR-421a into the clinic and will receive future milestone payments.

Pursuant to the terms of the agreement, the Company is obligated to make a one-time milestone payment to FFB of up to \$ 37.5 million (€ 33.4 million), payable in four equal annual installments following the first commercial sale of QR-421a, the first of which is due within 60 days following the first commercial sale. The Company is also obligated to make a payment to FFB of up to \$ 15 million (€ 13.4 million) if it transfers, sells or licenses QR-421a other than for certain clinical or development purposes, or if the Company enters into a change of control transaction. However, the payment in the previous sentence may be set-off against the \$ 37.5 million milestone payment. Either FFB or the Company may terminate the agreement for cause, which includes the Company's material failure to achieve certain commercialization and development milestones. The Company's payment obligations survive the termination of the agreement.

On June 5, 2018, the Company entered into a partnership agreement with EB Research Partnership (EBRP) and EB Medical Research Foundation (EBMRF) under which EBRP and EBMRF have agreed to provide funding of \$ 5.0 million for the clinical development of QR-313 for Dystrophic Epidermolysis Bullosa targeting mutations in exon 73. This agreement was terminated in March 2019 as part of the WINGS Therapeutics Inc. spin-out.

(d) Research and development commitments

The Company has research and development commitments, mainly with CRO's, amounting to € 19,472,000 at December 31, 2019 (2018: € 8,114,000). Of these obligations an amount of € 10,234,000 is due in 2020, the remainder is due in 1 to 5 years.

23. Related-Party Transactions

Details of transactions between the Company and related parties are disclosed below.

(a) Compensation of the Supervisory Board

The remuneration of the supervisory board members in 2019 is set out in the table below:

	2019			Total
	Short term employee benefits	Post-employment benefits	Share-based payment	
		(€ in thousands)		
Mr. Dinko Valerio	74	—	106	180
Mr. Antoine Papiernik	104	—	—	104
Ms. Alison Lawton	41	—	107	148
Mr. Paul Baart	144	—	—	144
Mr. James Shannon	48	—	109	157
Mr. Bart Filius	30	—	26	56
Ms. Theresa Heggie	19	—	18	37
	460	—	366	826

The remuneration of the supervisory board members in 2018 is set out in the table below:

	2018			Total
	Short term employee benefits	Post-employment benefits	Share-based payment	
	(€ in thousands)			
Mr. Dinko Valerio	36	—	69	105
Mr. Antoine Papiernik	72	—	—	72
Ms. Alison Lawton	31	—	75	106
Mr. Paul Baart	80	—	—	80
Mr. James Shannon	33	—	73	106
	252	—	217	469

The 2017 remuneration is set out in the table below:

	2017			Total
	Short term employee benefits	Post-employment benefits	Share-based payment	
	(€ in thousands)			
Mr. Dinko Valerio	36	—	87	123
Mr. Henri Termeer	28	—	160	188
Mr. Antoine Papiernik	76	—	—	76
Ms. Alison Lawton	31	—	99	130
Mr. Paul Baart	84	—	—	84
Mr. James Shannon	33	—	92	125
	288	—	438	726

As at December 31, 2019:

- Mr. Dinko Valerio holds 693,420 ordinary shares in the Company, as well as 130,843 options. These options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant. In 2019, Mr. Valerio was granted 14,918 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 13.78 per option. In 2018, Mr. Valerio was granted 27,500 options at an average exercise price of € 2.74 per option. In 2017, Mr. Valerio was granted 32,164 options at an average exercise price of € 4.65 per option. On September 12, 2017, Mr. Valerio provided a convertible loan to Amylon Therapeutics B.V. This loan is interest-bearing at an average rate of 8% per annum and is convertible into a variable number of ordinary shares within 36 months at the option of the holder or the Company in case financing criteria are met. Any unconverted loans become payable on demand after 24 months in equal quarterly terms.
- Mr. Antoine Papiernik does not hold any shares or options in the Company. As a managing partner of Sofinnova Partners SAS, the management company of Sofinnova Capital VII FCPR, holder of 2,764,194 ordinary shares, Mr. Papiernik may be deemed to have share voting and investment power with respect to such shares.
- Ms. Alison Lawton holds 111,391 options. In 2019, Ms. Lawton was granted 14,918 options under the Option Plan to acquire depositary receipts issued for ordinary shares at with an exercise price of € 13.78 per option. In 2018, Ms. Lawton was granted 27,500 options with an average exercise price of € 2.74 per option. In 2017, Ms. Lawton was granted 32,164 options with an average exercise price of € 4.65 per option. Under these option grants options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant.

- Mr. James Shannon holds 61,538 ordinary shares in the Company and 107,651 options. In 2019, Mr. Shannon was granted 14,918 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 13.78 per option. In 2018, Mr. Shannon was granted 27,500 options at an exercise price of € 2.74 per option. In 2017, Mr. Shannon was granted 32,164 options at an exercise price of € 4.65 per option. Under these option grants options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant.
- Mr. Bart Filius holds 12,755 options. These options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant. In 2019, Mr. Filius was granted 12,755 options under the Option Plan to acquire depositary receipts issued for ordinary shares at with an exercise price of € 10.47 per option.
- Ms. Theresa Heggie holds 13,334 options. These options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant. In 2019, Ms. Heggie was granted 13,334 options under the Option Plan to acquire depositary receipts issued for ordinary shares at with an exercise price of € 8.00 per option.

(b) Compensation of key management

Our management board is supported by our officers, or senior management. The total remuneration of the management board and senior management in 2019 amounted to € 6,117,000 with the details set out in the table below:

	2019			Total
	Short term employee benefits	Post employment benefits	Share-based payment	
	(€ in thousands)			
Mr. D.A. de Boer ¹	722	10	1,533	2,265
Management Board	722	10	1,533	2,265
Senior Management	1,545	48	2,259	3,852
	2,267	58	3,792	6,117

1 Short term employee benefits includes a bonus for Mr. Daniel de Boer, of € 273,000 based on goals realized in 2019.

The total remuneration of the management board and senior management in 2018 amounted to € 5,481,000 with the details set out in the table below:

	2018			Total
	Short term employee benefits	Post employment benefits	Share-based payment	
	(€ in thousands)			
Mr. D.A. de Boer ¹	726	9	668	1,403
Mr. R.K. Beukema ²	809	16	464	1,289
Management Board	1,535	25	1,132	2,692
Senior Management	1,726	64	999	2,789
	3,261	89	2,131	5,481

1 Short term employee benefits includes a bonus for Mr. Daniel de Boer of € 281,000 based on goals realized in 2018.

2 Short term employee benefits includes a bonus for Mr. René Beukema of € 134,000 based on goals realized in 2018.

The total remuneration of the management board and senior management in 2017 amounted to € 5,096,000 with the details set out in the table below:

	2017			Total
	Short term employee benefits	Post employment benefits	Share-based payment	
	(€ in thousands)			
Mr. D.A. de Boer ¹	570	8	622	1,200
Mr. R.K. Beukema ²	411	15	261	687
Management Board	981	23	883	1,887
Senior Management	1,719	66	1,424	3,209
	2,700	89	2,307	5,096

1 Short term employee benefits includes a bonus for Mr. Daniel de Boer of € 217,000 based on goals realised in 2017.

2 Short term employee benefits includes a bonus for Mr. René Beukema of € 113,000 based on goals realised in 2017.

As at December 31, 2019:

- Mr. Daniel de Boer holds 705,309 ordinary shares in the Company as well as 1,081,815 options. In 2019, Mr. de Boer was awarded 253,192 options to acquire ordinary shares at an exercise price of € 13.78 per option. In 2018, Mr. de Boer was awarded 379,285 options at an exercise price of € 2.74 per option. In 2017, Mr. de Boer was awarded 239,717 options at an exercise price of € 4.65 per option. These options vest over four years in equal annual installments and had a remaining weighted-average contractual life of 7.5 years at December 31, 2019.

ProQR does not grant any loans, advance payments and guarantees to members of the Management and Supervisory Board.

24. Auditor fees

The fees for services provided by our external auditor, Deloitte Accountants B.V., are specified below for each of the financial years indicated:

	2019	2018	2017
	(€ in thousands)		
Audit fees	515	181	175
Audit-related fees	57	261	140
Tax fees	—	—	—
All other fees	—	—	—
	572	442	315

Auditor fees consist of aggregate fees for professional services provided in connection with the annual audit of our financial statements, procedures on our quarterly financial statements, consultations on accounting matters directly related to the audit, and comfort letters, consents and review of documents filed with the SEC.

25. Subsequent events

On March 11, 2020, the World Health Organization declared the outbreak of COVID-19 a “pandemic”. The Company expects a delay in patient enrollment of all of its ongoing and scheduled trials, including the pivotal trial of sepfarsen for Leber’s congenital amaurosis 10. The duration and full effects of the COVID-19 outbreak are yet unknown. The Company is implementing mitigation procedures that support a rapid ramp up in enrollment as soon as the disruption resolves, including additional patient identification activities and documentation for additional site activations, while prioritizing the safety of trial participants.

**Lease Agreement
between
Leeds Investment I B.V. and ProQR Therapeutics I B.V.**

**Zernikedreef 9
2333 CK
Leiden**

30 September 2019

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH "[***]". SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

LEASE AGREEMENT FOR OFFICE PREMISES and other business premises within the meaning of Section 7:230a of the Dutch Civil Code

Model established by the Real Estate Council (ROZ) on 30-1-2015 and filed with the Clerk of the District Court at The Hague on 17-2-2015 and registered there under number 15/20. Also published on the website www.roz.nl. This model may only be referred to and utilised if the text that has been filled in, added or modified is clearly recognisable as such. Any additions and amendments should preferably be incorporated under the heading 'Special Provisions'. ROZ accepts no responsibility for adverse consequences arising from the use of the text of the model.

THE UNDERSIGNED

1. The private company with limited liability Leeds Investment I B.V., registered in The Hague and having its offices at Koninginnegracht 12, 2514 AA The Hague, correspondence address: PO Box 82329, 2508 EH The Hague, email address: [***];

hereinafter referred to as the '**Lessor**' or '**Leeds**',

registered in the Trade Register of the Chambers of Commerce under number 68448139,

represented by **Mr R.P.M. van Rossum and Mr R.M. Linders**

AND:

2. the private company with limited liability ProQR Therapeutics I B.V., registered and having its offices at Zernikedreef 9, 2333 CK hereinafter referred to as the '**Lessee**' or '**ProQR**',

registered in the Trade Register of the Chambers of Commerce under number **63634511**

turnover tax number **NL855325811B01** represented by **Mr de Boer, CEO**

The Lessor and the Lessee shall also be collectively referred to as the '**Parties**',

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WHEREAS:

- The Lessee currently leases office and laboratory space together with common areas and 56 parking spaces on the ground, 1st and 2nd floors of the "Gaubius" office building, located at Zernikedreef 9 in Leiden, in each case as recorded in a lease agreement between Leeds's predecessor-in-title and ProQR dated 1 January 2016 and the accompanying addenda 1, 2 and 3;
- The Lessee has invoked the Right of First Refusal granted to it with respect to the lease of additional office and laboratory space, located on the 2nd floor of the "Gaubius" office building;
- In connection with this the Lessor made an offer for lease to the Lessee on 13 June 2019 for the additional lease of approximately 1246.98 m² of lettable floor space, being office space, laboratory space and common areas that will be renovated, located on the 2nd floor (building parts 1 and 3) forming part of the Gaubius office building;
- The Lessor is also prepared to create and renovate, respectively, a new entrance area and canteen with meeting rooms on the ground floor of the "Gaubius" office building and to lease the same to the Lessee exclusively;
- Further to this, the Parties entered into negotiations to agree a lease agreement with respect to the accommodation (including the new accommodation) for ProQR;
- The Parties wish to record in this document their agreement concerning (i) the lease of the office and laboratory space on the 1st and 2nd floor and 70 parking spaces and (ii) the lease of the canteen with meeting rooms and reception on the ground floor for the benefit of ProQR;
- The Parties still need to reach further agreement concerning a number of provisions, for which purpose a revised version of this lease agreement will be signed before the commencement of this Lease.

HAVE AGREED

The Leased Property, purpose

1.1 The Lessor hereby lets to the Lessee and the Lessee hereby rents from the Lessor approx. **4,794.61 m² of lettable floor space**, being office and laboratory space, meeting space/canteen and parking spaces at the property known locally as the Gaubius building, located at Zernikedreef 9, 2333 CK Leiden, recorded in the land register under section X number 4602, consisting of the following parts:

1. approx. 910.94 m² of lettable floor space, being meeting space/canteen, located on the ground floor ("**Leased Property I**");

2. approx. 1,246.98 m² of lettable floor space, being office and laboratory space, located on the 2nd floor ("**Leased Property II**")

3. approx. 2,614.37 m² of lettable floor space, being office and laboratory space, located on the 1st and 2nd floors ("**Leased Property III**");

and:

4. seventy parking spaces located in the parking area belonging to the Leased Property and **22.32 m² of lettable floor space, being storage space in the cellar ("**Leased Property IV**")**.

Leased Properties I, II, III and IV shall be referred to collectively as the "**Leased Property**".

The Leased Property is shown in greater detail in the measurement certificate numbered 190089 complying with NEN 2580 and dated 29 August 2019 attached to this Lease Agreement. The (newly built) condition of Leased Properties I and II shall be recorded in further detail by the parties in a delivery report. The number of m² of lettable floor space of Leased Property I is based on an estimate and will be finally established following renovation and delivery and recorded in a separate addendum to this Lease Agreement.

1.2 The Leased Property shall be designated via or by the Lessee solely for use as

office space, laboratory space, meeting space/canteen, storage and parking spaces for private vehicles.

1.3 The Lessee is not permitted to use the Leased Property for any purposes other than those stated in Article 1.2 without the prior written consent of the Lessor.

1.4 The maximum acceptable loading of the floors of the Leased Property shall be **250 kg/m²**.

1.5 On commencing use of the Leased Property the Lessee shall receive a copy of the energy label, as referred to in the Energy Performance (Buildings) Decree, in respect of the Leased Property.

1.6 Prior to the date of commencement, the Lessee and the Lessor shall recalculate the surface areas stated in Article 1.1. If it turns out that the surface areas stated in Article **1.1** are incorrect, the Parties agree that a difference from the actual size of the Leased Property as determined on the basis of the

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measurement certificate (greater or lesser size) shall result in an adjustment of the (initial) rent. The rent established at that stage shall be recorded in a separate addendum to this Lease Agreement.

Terms and Conditions

2.1 The 'GENERAL TERMS AND CONDITIONS FOR LEASE AGREEMENT FOR OFFICE PREMISES' and other commercial premises in the meaning of Section 7:230a Civil Code', filed with the court registry of the District Court at The Hague on 17-2-2015 and registered there under number 15/21, hereinafter referred to as the 'General Terms and Conditions', form part of this Lease Agreement. The Parties are cognisant of the contents of these General Terms and Conditions. The Lessee and Lessor have received a copy of these General Terms and Conditions.

2.2 The General Terms and Conditions referred to in Article **2.1** shall apply unless and insofar as this Lease expressly deviates from the same or where application of the same is impossible as regards the Leased Property.

Rental period, renewal and notice

3.1 This Lease enters into effect on **1 July 2020** or on such earlier date as **Leased Properties I and II** can be delivered up in accordance with the provisions of Articles 10.2 and 10.7 of the special provisions (hereinafter '**the date of commencement**').

3.2 This Lease has been entered into for a period of **10 (ten) years**, starting on the commencement date to be increased by the period that Leased Property II may be able to be delivered up earlier.

3.3 After the period referred to in Article **3.2** has expired, this Lease shall, subject to notice of termination being given by the **Lessee** only, continue for two consecutive periods of **5 (five) years**.

3.4 This Lease shall subsequently, subject to notice of termination being given by the **Lessor or the Lessee**, continue indefinitely.

3.5 This Lease can be terminated following the expiry of the periods referred to in Articles **3.2 and 3.3** or the expiry of that referred to in Article **3.4**, by notice of termination by the Lessee or by the Lessor and the Lessee, respectively, as at the end of the current rental period, with due observance of a notice period of **12 (twelve) months**.

3.6 Notice of termination must be given by bailiff's writ or by registered letter.

Rent, turnover tax, service costs, rent adjustment, payment obligations, payment period

4.1 The (initial) annual rent of the Leased Property is comprised as follows:

- * the rent for **Leased Property I** shall be **€231,725.44** and is based on a rent of **€254.38 per m² of lettable floor space** (price reference date 1 January 2019). This rent is based on the weighted average of Leased Properties II and III.
- * the rent for **Leased Property II** shall be **€362,650.36** and is based on a rent of **€290.82 per m² of lettable floor space** (price reference date 1 January 2019);
- * the rent for **Leased Property III** shall be **€619,640.31** (price reference date 1 January 2019) and is based on a rent of **€237.00 per m² of lettable floor space** (price reference date 1 January 2019);
- * the rent for **Leased Property IV** shall be **€72,401.70** and is based on a rent of **€1,034.31** per parking space (price reference date 1 January 2019);

4.2 The parties agree that the Lessor **will** charge the Lessee turnover tax on the amounts payable.

4.3 The parties declare, while referring to Section 11 subsection 1 opening words under b. part 5 of the Turnover Tax Act 1968, that they have agreed to a rental subject to turnover tax. Furthermore, turnover tax will be charged on the payment due from the Lessee for goods and services supplied by or on behalf of the Lessor as laid down in Article 5 of this Lease Agreement and Article 18 of the General Terms and Conditions.

By signing this Lease Agreement, the Lessee declares that it intends to use or allow the Leased Property to be used for purposes which render it eligible for a full or substantial deduction of turnover tax further to Section 15 of the Turnover Tax Act 1968, this declaration being made in respect of the current agreement and all future agreements with the Lessor and/or its successors.

4.4 The Lessee's financial year runs from **1 January up to and including 31 December**.

4.5 The rent for Leased Properties **III** and **IV** shall be adjusted annually, for the first time on **1 June 2021**, in accordance with Articles 17.1 to 17.3 of the General Terms and Conditions. The rent per metre for Leased Property I shall be adjusted on the basis of any increase for Leased Property III. The initial rent

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for Leased Property II at the date of commencement shall remain unchanged for a period of 10 years and shall then be adjusted to the rent applicable at that time for Leased Property III.

4.6 The remuneration payable by the Lessee for supplies of goods and services to be provided by or on behalf of the Lessor shall be determined in accordance with Article 18 of the General Terms and Conditions.

A system of advance payments is applied to these payments with a later adjustment, as stated in the General Terms and Conditions.

4.7 The Lessee is no longer required to pay turnover tax on the rent if the Leased Property may no longer be leased with turnover tax, even though the Parties agreed to this. If this is the case, the compensation for turnover tax set out in Article 19.1 of the General Terms and Conditions will be applicable and this payment will be set out in advance in Article

4.8. The Lessee's payment obligations consist of the following components:

The following are payable per payment period of **one calendar month** on the date of entry of the Lease:

- the rental charge;
- the turnover tax due on the rent;
- the advance payment for the remuneration for the supply of goods and services by the Lessor with the turnover tax incurred on the same;
- the advance payment for energy costs with the turnover tax incurred on the same.

4.9 The periodical payments that the Lessee is to make to the Lessor on the basis of this Lease Agreement as set out in Article **4.8** shall be paid in a single amount by means of advance payments in euros and must be received in full by the Lessor before the first day of the period to which the payments relate.

4.10 Unless stated otherwise, all amounts in this Lease Agreement and the General Terms and Conditions forming part of this Lease Agreement are exclusive of turnover tax.

Costs of providing supplies and services

5.1. The following goods and services will be provided by or via the Lessor:

The Parties agree that at the start of the Lease the supplies and services shall include, as applicable and without limitation:

Building maintenance

- Corrective maintenance (daily maintenance of building installations - technical management)
- Preventive maintenance (periodic maintenance and checks of building installations)
- Garden maintenance

Use of energy and water

- Gas
- District heating
- Electricity

Water Risk management

- Security and surveillance
- Prevention / Emergency response procedures / Pest control

Supply of facility and materials

- Supply of tools
- Gases (laboratory materials)

Facility management

- Service coordinator, reception, technical services project manager, handyman

Five per cent administration charge on the cost of supplies and services

The Parties agree that the level of service charges required by the Lessee will be recorded in a separate Service Level Agreement to be entered into at a later stage.

5.2 After due consultation with the Lessor, the Lessee shall be entitled to alter the nature and scope of the supplies and services referred to in Article **5.1** or to let them lapse and to alter or adjust the advance payment payable by the Lessee. The annual advance payment for service charge at the start of this Lease is €105.00 (in words: **one hundred and five euros**) **per m2 of lettable floor space** and

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shall be recalculated and recorded before the commencement date. The advance payment for energy costs at the start of this Lease is €60.00 (in words: **sixty euros**) per m2 of lettable floor space.

Securities

~~6.1 Before the date of commencement the Lessee shall:~~

~~[arrange to provide a bank guarantee for / pay a security deposit*] to the value of €..... (in words:.....).~~

~~6.2 Interest [will/will not*] be paid on the security deposit.~~

Manager

7.1 Until the Lessor advises otherwise, the Manager shall be **the Lessor**.

7.2 Unless agreed otherwise in writing, the Lessee should contact the Manager in writing concerning the content of and all other matters relating to this Lease.

Incentives

8 The Parties declare that no incentives have been agreed between the Parties other than those stated in this Lease Agreement.

Asbestos/Environment

9.1 The Lessor is not aware that asbestos has been incorporated into the Leased Property. The fact that the Lessor is not aware of the presence of asbestos in the Leased Property expressly does not imply any guarantee on the part of the Lessor that no asbestos is present.

9.2 The Lessor is not aware that there is contamination in, on or at the Leased Property to such an extent that it would be necessary to take measures under any applicable legislation at the time of signing the Lease. The fact that the Lessor is not aware of the presence of contamination in, on or at the Leased Property at the time of signing the Lease expressly does not imply any guarantee on the part of the Lessor that no contamination is present.

Special provisions

10. In supplementation and/or variation of the foregoing Articles of this Lease Agreement and the General Terms and Conditions accompanying this Lease Agreement, the Parties agree the following as special provisions.

These special provisions do not in principle alter the matters agreed, but, in the event of any conflict between the special provisions and the foregoing provisions of this Lease Agreement and/or its annexes and/or the General Terms and Conditions, the special provisions shall prevail.

State of delivery at start of Lease Agreement

10.1 After obtaining the necessary permit, the Lessor shall put in place on the 1st floor a roof terrace conforming to the "Gaubius Roof Terrace" design by Centrum Architects dated 13 June 2019, which is attached as an annex to and forms part of this Lease Agreement.

10.2 Before the start of the Lease, Leased Property II shall be renovated by the Lessor at the Lessor's expense, in all aspects in accordance with the provisional design by Van Schie Architects dated 6 June 2019 (prepared in consultation with van Engelen and Krasselt) with accompanying cost estimate, which is attached as an annex to and forms part of this Lease Agreement. With respect to this, the Parties agree as follows:

- all the laboratory areas on the 2nd floor shall be adapted to comply with the current standard requirements for ML1 and ML2;
- the laboratory-related equipment, such as fume cupboards, refrigerators and freezers and lab benches are excluded from the renovations and should therefore be installed at the Lessee's expense;
- industrial gases shall be provided by the Lessor up to the connection points above the suspended ceiling in the laboratories, with 1 connection per gas type for each lab module.

10.3 The state of delivery of Leased Property II shall be recorded in the delivery report prepared and signed by the Parties for that purpose. The delivery report shall also describe the state of the movable property, installations, facilities and/or equipment belonging to the Leased Property. Any defects on delivery shall be described in this delivery report.

10.4 If Leased Property II is not delivered up to the Lessee in accordance with Article 10.2, this shall constitute a defect within the meaning of this term in the legislation and the Lessor shall be obliged to remedy the defect(s) immediately and diligently.

10.5 If no delivery report as described in Article 10.3 is prepared, the Lessee declares that it is familiar with the Leased Property and requires no further description of it. The Lessee also declares that it has accepted the Leased Property at the start of this Lease in good condition and without

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defects.

10.6 If Leased Property II is not delivered up to the Lessee ready for use on 1 July 2020, the Lessor shall owe to the Lessee a penalty payable immediately on demand in the sum of €150,000.00. The term "ready for use" in this Article is understood by the Parties to mean that the Leased Property has been renovated in accordance with the Lessee's provisional design with accompanying cost estimate and the design by Van Schie Architects dated 6 June 2019, which is attached as an annex to this Lease Agreement, and that the Lessee can furnish and start using the Leased Property without any reasonable objection.

The Lessor does not have to pay a penalty:

- if delivery of the Leased Property is delayed as a consequence of the Lessee not having supplied input (on construction matters or otherwise) either at all or satisfactorily (including in good time) for the purposes of the renovation to be carried out by the Lessor, provided that the Lessor has notified the Lessee of this immediately in writing and has appointed a reasonable period for supplying this input after that notification and the Lessee has failed to do so; or
- if the delayed delivery is due to materials required for the renovation not being available either at all or in sufficient quantities or any other force majeure situation applies and the Lessor has notified the Lessee of this immediately in writing.

Extension of the Leased Property to include canteen, meeting rooms and reception

10.7 After obtaining the necessary permit, the Lessor shall create on the ground floor of the "Gaubius" office building, for the exclusive use of the Lessee, a new entrance area and canteen with meeting rooms and reception, in all aspects in accordance with the design by Van Schie Architects dated 21 May 2019 with accompanying components estimate by Heijnenman construction costs agency dated 28 May 2019, which is attached as an annex to and forms part of this Lease Agreement (**'Leased Property I'**). As long as TNO as fellow lessee in the "Gaubius" office building is not yet able to use the new office building that is being created at Sylviusweg 71, TNO shall be entitled to keep using Leased Property I. Prior to the commencement date, the Lessee and the Lessor shall make further arrangements with TNO regarding this and revise the Lease Agreement (including the rent and service charges) on the basis of the shared use by TNO for this limited period.

10.8 The Lessee declares that it is aware of the Municipality of Leiden's plans to create a cycle path alongside the "Gaubius" office building using a strip of land from the plot that is being sold by the Lessor to the Municipality of Leiden for that purpose.

10.9 The state of delivery of Leased Property I shall be recorded in a delivery report prepared and signed by the Parties for that purpose that shall be attached to this Lease Agreement. The delivery report shall also describe the state of the movable property, installations, facilities and/or equipment belonging to the Leased Property. Any defects on delivery shall be described in this delivery report.

10.10 If no delivery report as described in Article 10.9 is prepared, the Lessee declares that it is familiar with Leased Property I and requires no further description of it. The Lessee also declares that it has accepted Leased Property I at the start of this Lease in good condition and without defects.

10.11 The term of the Lease for Leased Property I shall from the time of delivery match that of Leased Properties II, III and IV in terms of end date and including the agreed extension options.

10.12 If Leased Property I is not delivered up to the Lessee ready for use on 31 December 2020, the Lessor shall owe to the Lessee a penalty payable immediately on demand in the sum of €150,000.00. The term "ready for use" in this Article is understood by the Parties to mean that the Leased Property has been renovated in accordance with the Lessee's provisional design with accompanying components estimate by Heijnenman construction costs agency dated 28 May 2019 and the design by Van Schie Architects dated 21 May 2019 with accompanying estimate, which is attached as an annex to this Lease Agreement, and that the Lessee can furnish and start using the Leased Property without any reasonable objection.

The Lessor does not have to pay a penalty:

- if delivery of the Leased Property is delayed as a consequence of the Lessee not having supplied input (on construction matters or otherwise) either at all or satisfactorily (including in good time) for the purposes of the renovation to be carried out by the Lessor, provided that the Lessor has notified the Lessee of this immediately in writing and has appointed a reasonable period for supplying this input after that notification and the Lessee has failed to do so; or
- if the delayed delivery is due to materials required for the renovation not being available either at all or in sufficient quantities or any other force majeure situation applies and the Lessor has notified

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the Lessee of this immediately in writing.

Sub-letting

10.13 Further to Article 6.3 of the General Terms and Conditions, the Lessee is permitted to sub-let to companies/organisations affiliated to ProQR. If the Lessee proceeds to do this, it shall notify the Lessor in writing. No sub-lease may or can be entered into for a longer period than the main Lease. The Lessee warrants that and shall ensure that all other terms of this Lease Agreement and the General Terms and Conditions shall apply equally to the sub-lease situation. If this is not apparent from the draft sub-lease agreement provided by the Lessee to the Lessor, the Lessor shall be entitled to withhold consent to the proposed sub-lease.

10.14 Sub-letting to companies/organisations not affiliated to ProQR is only permitted with the prior written approval of the Lessor. The Lessor may give approval subject to conditions (including financial conditions).

Bank guarantee

10.15 The Parties agree that the Lessee shall not provide a bank guarantee. This varies the requirement for a bank guarantee in Article 24 of the General Terms and Conditions. Instead, ProQR Therapeutics N.V. shall ensure compliance with for the Lessee's obligations under this Lease Agreement as a joint signatory to this Lease Agreement.

Alterations and/or changes to the Leased Property

10.16 With the exception of structural, construction and/or installation alterations and/or changes and alterations and/or changes to the outside of the Leased Property, the Lessee shall be entitled, subject to prior written approval by the Lessor, to make alterations and/or changes in or to the Leased Property during the term of the Lease Agreement, which term shall include any extensions. The Lessor shall not withhold approval on unreasonable grounds. The Lessor may give approval subject to financial and/or other conditions. Any alterations and/or changes approved by the Lessor shall be recorded in writing as an addendum to the delivery report.

10.17 The Lessee is responsible for applying for and obtaining any permits and/or exemptions and/or consents required (under public law or otherwise) for all alterations and/or changes described in this Article.

10.18 The Lessee shall bear the expense and risk of all maintenance, repair and renewal of any alterations and/or changes made by the Lessee under this Article. The Lessee is also obliged to take out and maintain adequate insurance for the aforementioned alterations and/or changes.

10.19 Any alterations and/or changes made by the Lessee in, on or to the Leased Property following the commencement date shall be removed by the Lessee at the end of the Lease, with a simultaneous obligation for the Lessee to deliver the Leased Property up to the Lessor in its original state without any damage, unless the Lessee has at the time of the approval by the Lessor described in this Article agreed with the Lessor, and this agreement is recorded, that it is not necessary to remove the alterations and/or changes at the end of the Lease. The Lessor shall in no circumstances be liable to make any payment for the alterations and/or changes in, on or to the Leased Property made by the Lessee pursuant to this Article.

Utilities

10.20 Further to Article 18.9 of the General Terms and Conditions, the Lessee is aware that the Leased Property does not have its own separate meters (usage meters) for the utilities. The Lessee shall pay its share in the advance payment for energy costs in accordance with the m² apportionment formula, provided that the Lessor reserves the right to measure use with separate meters (usage meters) for the utilities.

10.21 Further to Articles 5.1, 5.2 and 8.2(b) of the General Terms and Conditions, the Lessee shall comply in full with all rules and requirements imposed by the utility companies. The Lessee shall indemnify the Lessor against all penalties, expenses and damage caused by or owed due to the actions of the Lessee or any persons or third parties for whom the Lessee is responsible.

Permits

10.22 Further to Articles 4.3 and 4.4 of the General Terms and Conditions, the Lessee and the Lessor agree that:

- The Lessor does not have authorisation for DM-3 activities as part of its environmental permit (*omgevingsvergunning milieu*);
- The GMO (genetically modified organisms) permits must be applied for by the Lessee;
- The Opium Act exemption (opiate permit) must be applied for by the Lessee;

Lessor's initials
Date: 30 September 2019

Lessee's initials

- The Lessee must apply for its own animal testing permit to carry out animal testing;
- The permits for the use of animal by-products for the purposes of education, research and diagnosis must be applied for by the Lessee;
- Notification must be given to the Inspectorate SZW (Social Affairs and Employment) under Article 4.94 of the Working Conditions Decree before the Lessee commences intentional work with biological agents in class 2 or higher;
- The Lessee is aware of the fact that the permit issued under the Environmental Permits (General Provisions) Act (*wabo-vergunning*) imposes requirements regarding the availability of certain information to the competent authorities.

10.23 The Lessee shall provide to the Lessor the following information (and any changes to the same): Name(s) of Biological Safety Officer(s) (BSO) responsible and Level of BSO responsible. If during the term of this Lease any changes and/or facilities at, in or on the Leased Property or the building of which the Leased Property forms part are required pursuant to requirements and/or guidelines by the government or other bodies such as utility companies or the fire brigade, these changes and/or facilities shall be implemented by and at the expense of the Lessee, unless such changes and/or facilities are necessary as a consequence of the actions or omissions of the Lessor. The Lessor shall cooperate with the implementation of these changes and/or facilities. If the Lessor incurs costs as a result, these shall be payable by the Lessee.

Insurance

10.24 The Lessor is obliged to take out insurance (buildings insurance) for the Leased Property; the provisions of Article 21.1 to of the General Terms and Conditions shall apply in full, with the exception of the words "or Lessee" in Article 21.3.

Access

10.25 The Parties agree that the Lessee shall have access to the Leased Property 24 hours a day, 7 days a week.

Name signage

10.26 The Lessee is not entitled to affix (or arrange for another party to affix) any name or other signage on or at the Leased Property (including the facade of the Leased Property) or to change (or arrange for another party to change) any existing name or other signage on or at the Leased Property (including the facade of the Leased Property). The Lessee shall tolerate existing and/or new name or other signage affixed or to be affixed for the benefit of the Lessee or other users of the Leased Property and cannot derive from this any claims, in any form, against the Lessor or third parties related to the Lessor. The presence of name or other signage on the Leased Property (including the facade of the Leased Property) requires the prior written approval of the competent authorities. The Lessor shall make efforts to remove (or arrange for the removal of) the TNO logo from the Gaubius building prior to the commencement date for Leased Property I.

SIGNATURE PAGE WITH OVERVIEW OF THE ANNEXES ON THE NEXT PAGE

Lessor's initials
Date: 30 September 2019

Lessee's initials

Thus agreed and signed in **duplicate**,

Leiden
place

30 September 2019
date

Leiden
place

30 September 2019
date

ProQR Therapeutics I B.V.
Mr/Mrs

Leeds Investment I B.V.
Mr R.P.M. van Rossum

/s/ Daniel de Boer
(Lessee's signature)

/s/ R.P.M van Rossum
(Lessor's signature)

place

date

In view of the provisions of

Article 10.17 place date

ProQR Therapeutics N.V.
Mr/Mrs

Leeds Investment I B.V.
Mr R.M. Linders

/s/ Daniel de Boer
(Signature)

/s/ R.M. Linders
(Lessor's signature)

Annexes:

- measurement certificate with drawings numbered 190089 complying with NEN 2580 and dated 29 August 2019 on which the areas leased by the Lessee and the areas in common use are marked as such;
- delivery report for Leased Properties I and II (to be added at time of delivery);
- design of "Gaubius Roof Terrace" by Centrum Architects dated 13 June 2019;
- provisional design of renovation of 2nd floor with accompanying cost estimate and the design by Van Schie Architects dated 6 June 2019;
- design by Van Schie Architects dated 21 May 2019 with accompanying elements estimate by Heineman construction costs agency dated 28 May 2019;
- energy label (to be added at time of delivery);
- extract from the Trade Register of the Chamber of Commerce for the Lessee together with identification documents for director(s)

Lessee's separate signature(s) confirming receipt of their own copy of the 'GENERAL TERMS AND CONDITIONS FOR LEASE AGREEMENT FOR OFFICE PREMISES' and other premises in the meaning of Section 7:230a Civil Code' as referred to in Article 2.1.

Lessor's initials
Date: 30 September 2019

Lessee's initials

ASSET PURCHASE AGREEMENT

among

WINGS THERAPEUTICS, INC.,
PROQR THERAPEUTICS I B.V.,
PROQR THERAPEUTICS VII B.V.,
PROQR THERAPEUTICS HOLDING B.V.

and

PROQR THERAPEUTICS, N.V.

Dated as of May 22, 2019

This document is intended solely to facilitate discussions and is subject in all respects to Purchaser's due diligence investigation. Neither this document nor such discussions are intended to create, nor will either or both be deemed to create, a legally binding or enforceable offer or agreement of any type, unless and until a definitive written agreement is executed and delivered by each of the parties hereto.

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH "[***]". SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF DISCLOSED.

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This **ASSET PURCHASE AGREEMENT**, dated as of May 22, 2019, is among WINGS THERAPEUTICS, INC., a Delaware corporation (“Purchaser”), PROQR THERAPEUTICS I B.V., a company organized under the laws of The Netherlands (“ProQR I”), PROQR THERAPEUTICS VII B.V., a company organized under the laws of The Netherlands (“ProQR VII”), PROQR THERAPEUTICS HOLDING B.V., a company organized under the laws of The Netherlands and sole equity owner of ProQR I and PROQR VII (“Holding” and together with ProQR I and PROQR VII, each a “Seller” and together the “Sellers”), and, solely for purposes of Article VI, PROQR THERAPEUTICS N.V., a company organized under the laws of The Netherlands and sole equity owner of Holding (“Parent”). Capitalized terms used herein have the meanings ascribed to them in Section 7.07.

WHEREAS, Sellers desires to sell, and Purchaser desires to purchase, that certain business of Sellers and their Affiliates consisting of the research, development, manufacturing and commercialization activities related to the discovery and development of pharmaceuticals in the Field, including without limitation, exon skipping programs relating to [***], and the program resulting in the compound known as QR-313 (collectively, the “Program”).

NOW, THEREFORE, in consideration of the premises and mutual covenants herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties agree as follows:

ARTICLE I
Purchase and Sale of Acquired Assets

SECTION 1.01 Purchase and Sale. Sellers hereby contribute, sell, convey, assign, transfer and deliver to Purchaser, and shall cause their Affiliates to contribute, sell, convey, assign, transfer and deliver to Purchaser, and Purchaser hereby purchases from Sellers or their Affiliates, as applicable, all of Sellers’ and their Affiliates’ right, title and interest in, to and under the Acquired Assets, for a purchase price (the “Purchase Price”) consisting of (i) [***] shares of Purchaser’s common stock, \$0.001 par value per share, which shares shall be issued by Purchaser to Holding on the Closing Date pursuant to that certain Subscription Agreement, dated as of the date hereof (the “Shares”) and which Shares represent nineteen and nine-tenths percent (19.9%) of the Fully Diluted Shares (as such term is defined in the Subscription Agreement), (ii) the Milestone Payment, payable in accordance with Section 1.02 below, (iii) the Royalty Payments, payable in accordance with Section 1.03 below and (iv) the assumption by Purchaser of the Assumed Liabilities. The purchase and sale of the Acquired Assets, the assumption by Purchaser of the Assumed Liabilities, and the grant of licenses contained herein are referred to in this Agreement collectively as the “Acquisition”. For U.S. federal income tax purposes, the Acquisition, together with the subscription for newly issued preference shares in Purchaser by EB Research Partnership, Inc. and [***] is intended to be treated as a tax deferred contribution under Section 351 of the Internal Revenue Code of 1986, as amended (the “Code”), with the Milestone Payments and the Royalty Payments treated as property that is “boot” for purposes of Section 351(b) and, for all Tax purposes, that such Milestone Payments and Royalty Payments shall be treated as additional purchase price for the Acquired Assets and not a payment of royalties. The parties shall file all applicable Tax Returns in accordance with the foregoing sentence and shall not take any Tax position that is inconsistent with the foregoing sentence, in each case, unless

otherwise required by a final determination, within the meaning of Section 1313 of the Code (or similar provisions of state or local Tax Law).

SECTION 1.02 Milestone Payment.

(a) Net Sales Milestone Event. [***] Dollars (\$[***]) (the “Milestone Event”), Purchaser shall pay to Holding the amount of [***] Dollars (\$[***]) (the “Milestone Payment”) in accordance with Section 1.02(b) below.

(b) Notice and Payment. No later than [***] after the end of the Calendar Quarter in which the Milestone Event occurs, Purchaser shall (A) provide written notice to Holding of the occurrence of the Milestone Event and (B) pay the Milestone Payment.

SECTION 1.03 Royalty Payments. During the Royalty Term, royalty payments (the “Royalty Payments”) shall be paid by Purchaser to Holding in accordance with this Section 1.03.

(a) Royalty Rates. The amount of the Royalty Payments shall equal (i) [***] percent ([***]%) of annual worldwide Net Sales of Patented Products up to \$[***], (ii) [***] percent ([***]%) of annual worldwide Net Sales of Patented Products above \$[***] and up to \$[***], (iii) [***] percent ([***]%) of annual worldwide Net Sales of Patented Products above \$[***] and up to \$[***], and (iv) [***] percent ([***]%) of annual worldwide Net Sales of Patented Products above \$[***].

(b) Royalty Term. The Royalty Payments payable by Purchaser to Sellers shall be paid on a Product-by-Product and country-by-country basis from the date of the first commercial sale of such Product in such country until the expiration in such country of the last to expire Valid Claim of a Transferred Patent claiming such Product (the “Royalty Term”).

(c) Royalty Report and Payment. During the Royalty Term, no later than [***] after the end of each Calendar Quarter, Purchaser or its Affiliates shall pay to Holding the Royalty Payments payable for such Calendar Quarter and provide a royalty report (the “Royalty Report”) showing:

(i) the Net Sales of each Patented Product sold by (A) Purchaser and its Affiliates and (B) Purchaser’s Commercial Licensees, in each case during such Calendar Quarter;

(ii) the Royalty Payments, reflected in Dollars, which shall have accrued hereunder with respect to any Net Sales of each Patented Product;

(iii) withholding Taxes, if any, (x) deducted on a Product-by-Product and country-by-country basis and (y) subject to Section 1.04(b) in connection with the payment of such Royalty Payments; and

(iv) the rate of exchange, if applicable, as calculated using the average of the foreign currency exchange rate for converting the applicable currency into Dollars as published by Bloomberg Business during the Calendar Quarter.

SECTION 1.04 Payments; Records and Audit; Efforts.

(a) Manner of Payment and Exchange Rate. All payments to be made by Purchaser to Holding under Sections 1.02 and 1.03 shall be made in Dollars and shall be paid by wire transfer in immediately available funds to such bank account in the United States as is designated in writing by Holding from time to time. In computing the Dollar amount of Net Sales of a Patented Product outside the United States, after calculating the Net Sales in the currency of sale, the rate of exchange to be used in such computation shall be the average of the rate of exchange published by Bloomberg Business over the course of the Calendar Quarter in which such sales occurred.

(b) Tax Withholding. Purchaser acknowledges that, absent a change in Applicable Law (for the avoidance of doubt, including the Treaty), its interpretation or practice, after the date hereof, and provided that the Seller timely provides all required and properly completed required tax forms necessary to claim the benefits of a complete exemption from withholding tax, including with respect to Seller's eligibility under the Convention between the United States and the Netherlands signed on December 18, 1992 (the "Treaty"), it will not deduct or withhold any United States federal income Taxes from the Milestone Payments and Royalty Payments. Purchaser (or any of its Affiliates or agents, as the case may be) shall be entitled to deduct and withhold any Taxes from any other amounts payable pursuant to this Agreement such amounts, if any, as are required under Applicable Law to be so withheld or deducted. To the extent such amounts are so withheld and remitted to the relevant Governmental Entity, such withheld amounts shall be treated for all purpose of this Agreement as having been paid to the Person in respect of whom such withholding was made, and in a timely manner and as promptly as reasonably practicable Purchaser (or any of its Affiliates) shall transmit to Sellers an official Tax certificate or other reasonable evidence of such Tax obligations and supporting calculations, together with proof of payment from the relevant Governmental Entity or other reasonable documentation in support thereof of all amounts deducted and withheld sufficient to enable Sellers to claim such payment of Taxes with the appropriate Governmental Entity. Purchaser and its Affiliates shall provide Sellers with prior written notice of Purchaser's (or any of its Affiliate's) intention to withhold, the legal basis therefor and a reasonable opportunity to furnish forms, certificates or other items that would reduce or eliminate such withholding Taxes. Each party agrees to use commercially reasonable efforts and to cooperate with the other party to minimize any anticipated withholding Tax required to be paid under any provision of federal, state, local, or foreign Tax law with respect to the payments made by Purchaser to Sellers or their Affiliates under this Agreement.

(c) Records and Audit. Purchaser shall keep, and shall contractually require that its Affiliates and its Commercial Licensees keep, books and records prepared in accordance with their respective standard accounting procedures and in accordance with GAAP, in each case consistently applied, for the purpose of determining and validating (i) the amount of Royalty Payments due to Holding hereunder, including, without limitation, the calculation of Net Sales in each country where Patented Products are sold, and (ii) whether or not the Milestone Event has occurred. Such books and records will be kept at the principal place of business of Purchaser (or its Affiliates or its licenses, as applicable) and maintained for no less than [***] following the end of the Calendar Year to which they pertain. At the request of Sellers, Purchaser and its Affiliates and its Commercial Licensees shall permit an independent certified public accountant appointed by Sellers and reasonably acceptable to Purchaser (or its Affiliates or Commercial Licensees, as applicable), at reasonable times and upon reasonable notice, to examine those records as may be

necessary to determine, with respect to any Calendar Year ending not more than [***] prior to Sellers' request, the correctness or completeness of any report or payment pursuant to Sections 1.02 or 1.03. The foregoing right of review may be exercised only [***] per Calendar Year and only once with respect to each such periodic report and payment. Results of any such examination shall be (A) limited to information relating to Patented Products, (B) made available to both Purchaser and Sellers and (C) subject to the confidentiality provisions set forth below. Prior to commencing any examination, the independent certified public accountant shall have agreed in writing to maintain all information learned in confidence, except as necessary to disclose to Purchaser and Sellers the results of such examination, and shall have executed all customary release letters reasonably requested by Purchaser's independent auditors. Sellers shall bear the full cost of the performance of any such audit, unless such audit discloses a variance to the detriment of Sellers of more than [***] percent ([***]%) from the amount of the original report or Royalty Payment calculation. In such case, Purchaser shall bear the full cost of the performance of such audit. Any underpayments of Royalty Payments or the Milestone Payment shall be paid by Purchaser within [***] of notification of the results of such audit, together with interest at a rate of [***] percent ([***]%) [***] period since the payment due date. Any overpayments of Royalty Payments or Milestone Payment shall be fully creditable by Purchaser against any amounts subsequently payable by Purchaser pursuant to this Agreement or, if no such amounts become payable within [***] after notification of such results, shall be refunded by Sellers to Purchaser or its designee. Purchaser shall contractually require that its Affiliates and their respective Commercial Licensees submit to the exercise of Sellers' right of audit hereunder.

SECTION 1.05 Transfer of Assets.

(a) Sellers hereby sell, convey, assign, transfer and deliver to Purchaser, and hereby cause their Affiliates to sell, convey, assign, transfer and deliver to Purchaser, and Purchaser hereby purchases from Sellers and their Affiliates, all of Sellers' and such Affiliates' right, title and interest in, to and under the assets described or identified below (other than Excluded Assets), used in, or otherwise related to, the Program (collectively, the "Acquired Assets"):

(i) the Intellectual Property listed in Schedule 1.05(a)(i) hereto, and all copies and tangible embodiments or descriptions thereof (in whatever form or medium) and all goodwill associated therewith, and all rights related to or otherwise associated with, any of the foregoing in any jurisdiction in the world (including all rights to collect royalties, products and proceeds in connection with any of the foregoing, and to sue and bring other claims for past, present and future infringement, misappropriation or other violation of any of the foregoing, and to recover damages (including attorneys' fees and expenses) in connection therewith) (collectively, the "Transferred Intellectual Property");

(ii) all Supplies;

(iii) [intentionally omitted];

(iv) the Contracts identified in Schedule 1.05(a)(iv) hereto (collectively, the "Transferred Contracts");

(v) all Regulatory Materials, including without limitation those identified in Schedule 1.05(a)(v) hereto;

(vi) all books and records (or portions of books and records), including laboratory notebooks and other records, pre-clinical and clinical studies lists, files (including patent prosecution files), documents, correspondence, creative and promotional materials, studies, reports, data (including all pharmacological, pre-clinical, clinical, analytical, quality control and manufacturing data (including batch records and technical reports)) and other printed, written or electronic materials (in all cases, in any form or medium);

(vii) all goodwill of, or associated with, the Program and the use of its Trademarks; and

(viii) Except as described on Schedule 1.05(a)(viii), all proprietary rights to the information, materials, data and work product in respect of research and development activities and pre-clinical trials conducted or being conducted as part of the Program or otherwise for use in connection with the research or development of any Product.

(b) Notwithstanding anything to the contrary contained in Section 1.05(a) or elsewhere in this Agreement, the following (collectively, the "Excluded Assets") shall not be part of the sale and purchase contemplated hereunder, are excluded from the Acquired Assets, and shall remain the property of Sellers or their Affiliate after the Closing:

(i) all cash and cash equivalents of Sellers and their Affiliates;

(ii) all assets of Sellers and their Affiliates that are not Acquired Assets;

(iii) the general ledgers, accounting records, minute books, statutory books and corporate seals;

(iv) the personnel records and any other records that the Seller or any subsidiary of Seller is required by Law to retain in its possession

(v) all bank accounts;

(vi) the capital stock, or partnership or limited liability company interests, as applicable, of all subsidiaries of the Seller;

(vii) all rights and claims of Sellers or any of their Affiliates to the extent relating to any Excluded Asset or any Excluded Liability, including any such items arising under insurance policies and all guarantees, warranties, indemnities and similar rights in favor of Sellers and their Affiliates in respect of any Excluded Asset or any Excluded Liability; and

(viii) all rights of Sellers and their Affiliates under this Agreement, the Other Transaction Documents and the other agreements and instruments executed and delivered in connection with this Agreement.

SECTION 1.06 Assumed Liabilities.

(a) Upon the terms and subject to the conditions of this Agreement, Purchaser shall assume, effective as of the Closing, all of the following liabilities, obligations and commitments (“Liabilities”) of Sellers, other than any Excluded Liability (the “Assumed Liabilities”):

(i) any and all Liabilities arising from Purchaser’s ownership of, and activities related to, each of the Acquired Assets and the Program, including its development, use, marketing and exploitation of any Products from and after the Closing; and

(ii) all Liabilities of Sellers under the Transferred Contracts, each as related to the period from and after the Closing (other than liabilities and obligations attributable to any failure by any Seller or their Affiliates to comply with the terms thereof).

(b) Notwithstanding any other provision of this Agreement, Purchaser shall not assume any Excluded Liability. The term “Excluded Liability” means:

(i) any and all Liabilities to the extent arising out of or relating to the Excluded Assets; and

(ii) any and all Liabilities arising prior to the Closing Date from Sellers’ or their Affiliates’ ownership of, and activities related to, the Program, including the development, use, marketing and exploitation of any Products prior to the Closing, but excluding the payment of any operational cost for the Program incurred as of April 1, 2019 that Purchaser agreed to pay, which payment will be settled after Closing.

SECTION 1.07 Further Assurances. If, at any time after the Closing, any further action is necessary or desirable to carry out the purposes of this Agreement, at any party’s reasonable request and, subject to Section 5.03, at such party’s sole cost and expense, each party shall take such further action (including the execution and delivery to the other party of such other reasonable instruments of sale, transfer, conveyance, assignment, assumption and confirmation, providing materials and information) as shall reasonably be deemed necessary to transfer, convey and assign to Purchaser all of the Acquired Assets and to confirm Purchaser’s assumption of the Assumed Liabilities.

SECTION 1.08 Allocation of Payments. Purchaser and Sellers will make reasonable efforts to agree on an allocation of the payments made pursuant to Section 1 among the Acquired Assets in a manner that is consistent with the principles of Section 1060 of the Internal Revenue Code of 1986, as amended (or any successor provision of any future Tax law, or any comparable provision of state, local or foreign Tax law), within [***] after the Closing Date; *provided, however*, the Parties agree to use any explicit allocations that are set forth in this Agreement. If the Parties are able to agree to an allocation of the payments hereunder pursuant to the preceding sentence, Purchaser and Sellers will (a) act in accordance with such allocation in the preparation and filing of all Tax returns (including the preparation and filing of IRS Form 8594, if applicable) and (b) take no position inconsistent with the allocation for any Tax purposes unless required by Applicable Laws. In the event that such allocation is disputed by any Tax authority, the party receiving notice of the dispute shall promptly notify the other party hereto and shall forward to such other party copies of all correspondence with such Tax authority in respect of such disputed

allocation. If Purchaser and Sellers are unable to agree as to the allocation of the payments hereunder, then Purchaser and Sellers may each prepare their own allocation and each of Purchaser and Sellers will have no liability to the other for any additional Taxes that may be imposed by any Tax authority as a result of the inconsistencies between the respective allocations of the Purchase Price by Purchaser and Sellers.

SECTION 1.09 Transition Plan. In order to transfer the Program responsibility to Purchaser as contemplated hereunder, the Parties shall use commercially reasonable efforts to comply with the transition plans set forth as Schedule 1.9 hereto (collectively the "Transition Plan"), which, for clarity, shall consist of those plans for Sellers and their Affiliates to transfer to Purchaser: (a) regulatory obligations in respect of the Regulatory Materials; (b) the inventory of Seller Product; (c) results and data from all pre-clinical studies relating to Seller Products conducted prior to the Closing; and (d) all Know-How included within the Transferred Intellectual Property. In furtherance thereof, Sellers and their Affiliates shall make available to Purchaser appropriately qualified personnel to provide consulting and technical scientific support to Purchaser with respect to the transfer of the Know-How included within the Transferred Intellectual Property (collectively, the "Transfer Activities"). Sellers and Purchaser will initiate the Transfer Activities promptly after the Closing in accordance with a time plan as specified in the Transition Plan. Within [***] after Closing, Sellers and/or their Affiliates shall execute and deliver a letter to the applicable Regulatory Authority authorizing Purchaser and its designees to cross-reference the existing INDs and other Regulatory Materials covering the Seller Products. Sellers and Purchaser shall use commercially reasonable efforts to perform the Transfer Activities and complete such Transfer Activities within the time periods specified in the Transition Plan.

ARTICLE II Closing

SECTION 2.01 Closing. The closing of the Acquisition (the "Closing") shall take place on the date hereof (the "Closing Date") either (a) electronically or (b) at such other place and in such other manner as is mutually agreeable to Purchaser and Seller. The Closing and will be effective as of 12:01 AM New York local time on the Closing Date.

(a) In connection with the execution and delivery of this Agreement, Purchaser has delivered to Sellers:

(i) an executed counterpart of the Assignment and Assumption Agreement with respect to the Assumed Liabilities;

(ii) an executed counterpart of the IP Assignment Documents with respect to the Transferred Intellectual Property; and

(iii) executed counterparts of the Subscription Agreement and the Stockholder Agreements.

(b) In connection with the execution and delivery of this Agreement, Sellers have delivered to Purchaser:

- (i) the Bill of Sale and such other instruments and documents as Purchaser may reasonably request to effect or evidence the transfer to Purchaser of the Acquired Assets;
- (ii) an executed counterpart of the Assignment and Assumption Agreement with respect to the Assumed Liabilities;
- (iii) an executed counterpart of the IP Assignment Documents with respect to the Transferred Intellectual Property; and
- (iv) executed counterparts of the Subscription Agreement and the Stockholder Agreements.

ARTICLE III
Representations and Warranties of Seller

Except as set forth in the Seller Disclosure Schedule attached hereto (the “Seller Disclosure Schedule”), Sellers hereby represent and warrant to Purchaser as of the Closing Date as follows:

SECTION 3.01 Authority. Sellers and each of their Affiliates that is transferring Acquired Assets to Purchaser hereunder is a legal entity, duly organized, validly existing and in good standing (with respect to jurisdictions that recognize such concept) under the laws of the jurisdiction of its organization. Sellers have all requisite corporate power and authority to enter into this Agreement, and Sellers and each of their Affiliates have all requisite corporate power and authority to enter into the Other Transaction Documents to which it is, or is specified to be, a party and to consummate the transactions contemplated hereby and thereby. All corporate acts and other proceedings required to be taken by Sellers and each of their Affiliates to authorize the execution, delivery and performance of this Agreement and the Other Transaction Documents to which it is, or is specified to be, a party and to consummate the transactions contemplated hereby and thereby have been duly and properly taken. This Agreement and the Other Transaction Documents have been duly executed and delivered by Sellers and, assuming this Agreement and the Other Transaction Documents have been duly authorized, executed and delivered by Purchaser and, if applicable, its Affiliates, constitute a legal, valid and binding obligation of Sellers, enforceable against Sellers in accordance with their terms, subject, as to enforcement, to applicable bankruptcy, insolvency, moratorium, reorganization or similar laws affecting creditors’ rights generally and to general equitable principles.

SECTION 3.02 No Conflicts; Consents.

(a) The execution and delivery of this Agreement and the Other Transaction Documents by Sellers and their Affiliates, as applicable, and the consummation of the transactions contemplated hereby and thereby, and compliance with the terms and conditions hereof and thereof will not, conflict with, or result in any violation of or default (with or without notice or lapse of time, or both) under, or give rise to a right of termination, cancellation or acceleration of any obligation or loss of a material benefit under, or result in the creation of any liens, claims, encumbrances, security interests, licenses, covenants not to use, options, charges or restrictions of any kind (“Liens”) upon any of the Acquired Assets under any provision of (i) the certificate of incorporation or by-laws (or the comparable governing instruments) of Sellers or any of their

Affiliates, (ii) any contract, to which either Seller or such Affiliate is a party or by which any of their respective properties or assets are bound, or (iii) any judgment, order or decree, or, subject to the matters referred to in clauses (i) and (ii) of paragraph (b) below, Applicable Laws; except in the case of clauses (ii) and (iii) as would not have a material adverse effect on the ability of Sellers to consummate the transactions contemplated hereby or under the Other Transaction Documents and to perform their obligations under this Agreement or under each of the Other Transaction Documents. No vote or approval of the stockholders of either Seller or any of their Affiliates is required in order to consummate the transactions contemplated by this Agreement or the Other Transaction Documents.

(b) The execution, delivery and performance of this Agreement and the Other Transaction Documents, and the consummation of the transactions contemplated hereby or thereby, do not, and will not, require any consent, approval, license, permit, order or authorization of, or registration, declaration or filing with, any Governmental Entity except as may be required solely by reason of Purchaser's or any Affiliate of Purchaser's (as opposed to any third party's) participation in the transactions contemplated hereby or thereby, including recordation of suitable patent assignment documents in the U.S. Patent and Trademark Office and comparable foreign patent offices and assignments of Regulatory Materials with Governmental Entities.

SECTION 3.03 Assets and Properties. Schedule 1.05 hereto lists all of the Acquired Assets. Except as set forth on Section 3.03 of the Seller Disclosure Schedule, the Acquired Assets are the assets used or necessary to conduct the Program as currently conducted by Sellers. Sellers or their Affiliates have good and valid title to all Acquired Assets, in each case free and clear of all Liens. Neither Seller nor any of their Affiliates has any indebtedness that would create a Lien on the Acquired Assets or prevent the sale, transfer and assignment of the Acquired Assets as contemplated by this Agreement. At the Closing, Sellers or their Affiliates, as applicable, will transfer to Purchaser good record (where applicable) and marketable title to all of the Acquired Assets, in each case free and clear of all Liens. All of the Supplies included within the Acquired Assets conform to the specifications annexed to Section 3.03 of the Seller Disclosure Schedule.

SECTION 3.04 Intentionally Omitted.

SECTION 3.05 Intellectual Property.

(a) Schedule 1.05(i) hereto sets forth, for each Transferred Patent, the name of the current owner(s) (including any co-owner) thereof (and, if the owner is not a Seller or any of their Affiliates, the corresponding license agreement pursuant to which Sellers and/or any of their Affiliates have the right to use such Intellectual Property) and the jurisdiction of each such issued or pending Patent. The Transferred Patents are (A) valid, enforceable, subsisting and in full force and effect and/or, as applicable, have been filed in accordance with all Applicable Laws, (B) are not the subject of any opposition, cancellation, interference, reissue, reexamination or other similar proceeding, (C) owned, held and recorded solely in the name of a Seller or its Affiliate as record and beneficial owner and (D) in compliance with all formal legal requirements. All annuity and maintenance fees that are necessary in order to keep the Transferred Patents in force have been paid by the Sellers and Section 3.05(a) of the Seller Disclosure Schedule lists all maintenance fees or actions falling due within [***] after the date hereof.

(b) Either Sellers or their Affiliates solely and exclusively owns all right, title and interest in and to the Transferred Intellectual Property, free and clear of all Liens, including any restrictions, limitations and obligations (including any royalty payment or other obligations or contractual limitations), and the consummation of the transactions contemplated hereby does not conflict with, alter or impair any such rights of Sellers and/or their Affiliates in or to any of the Transferred Intellectual Property and the Transferred Intellectual Property shall be solely and exclusively owned or available for use by Purchaser immediately after the Closing on terms and conditions substantially identical to those under which Sellers or any of their Affiliates owned and/or used the Transferred Intellectual Property immediately prior to the Closing. No Transferred Intellectual Property is subject to any outstanding consent, settlement, decree, order, injunction, judgment or ruling, or any contract restricting or otherwise limiting the use, ownership, validity, enforceability, disposition or exploitation thereof.

(c) No academic institution, research center or Governmental Entity (or any person working for or on behalf of any of the foregoing) or any other person (other than Sellers and/or any of their Affiliates) has, or will be entitled to have, any right, title or interest (including any "march in" or co-ownership rights) in or to any Transferred Intellectual Property (including any claim or option to any of the foregoing). Except as set forth in Section 3.05(c) of the Seller Disclosure Schedule, neither Seller nor any of their Affiliates has granted any license (including any sublicense), option, assignment or other agreement (including any covenants not to sue) or any other right, title or interest with respect to any Transferred Intellectual Property.

(d) To the Knowledge of the Sellers, the conduct of the Program and the research and development of Products by Sellers and their Affiliates has not infringed, misappropriated or otherwise violated the Intellectual Property rights of any other person. Neither Seller nor any of their Affiliates has received any written charge, complaint, claim, demand, communication or other notice, or is or has been a party to any lawsuit, claim, action or proceeding, where any person has (i) alleged, with respect to the Program or any Product, that Sellers or any of their Affiliates has infringed, misappropriated or otherwise violated, or will violate through the Program or the exploitation of any such Product, any Intellectual Property rights of any other person (including pursuant to any notice or demand that a Seller or any of its Affiliates must license or refrain from using any Intellectual Property of any other person), or (ii) challenged the validity, use, ownership, enforceability of, or has claimed any right, title or interest in or to, any Transferred Intellectual Property, and, with respect to each of clauses (i) and (ii) no such claim has been asserted or threatened, and to the Knowledge of Sellers there is no reasonable basis for any such claim. To the Knowledge of Sellers, no person has infringed, misappropriated or otherwise violated any Transferred Intellectual Property.

(e) Sellers and their Affiliates have taken commercially reasonable steps to protect, and to maintain and enforce all rights under, the Transferred Intellectual Property, including the secrecy, confidentiality and value of trade secrets and other confidential information. To the extent permissible under Applicable Law, Sellers and each of their Affiliates require each of their current and former employees and consultants to enter into valid and enforceable agreements with Sellers or such Affiliate pursuant to which such person agrees and is bound to maintain and protect the confidential information of Sellers and their Affiliates and assigns to Sellers or such Affiliate all Intellectual Property authored, developed or otherwise created by such person in the course of such person's employment or other engagement with Sellers or any of their

Affiliates, all in accordance with all Applicable Laws, and uses commercially reasonable efforts to ensure that any entity conducting any research, develop or other activities on behalf of Sellers or their Affiliates does the same.

(f) The listed inventors in the Transferred Patents are the only inventors of such Patents, including as the term “inventor” is defined and interpreted under United States patent law or patent laws of other relevant jurisdictions, and all inventors of any inventions claimed or covered by any Transferred Patent or other Transferred Intellectual Property have each assigned such person’s entire right, title and interest in and to any and all intellectual property rights in and to such inventions to a Seller or their Affiliates, or, if a Seller or its Affiliates acquired any such Patents or other Intellectual Property, then to the person who employed or otherwise engaged such inventor, and such person has assigned the same to a Seller or its Affiliate. To the Knowledge of Sellers, no claims have been asserted challenging the inventorship of any of the Transferred Patents.

SECTION 3.06 Compliance with Applicable Laws. Sellers and their Affiliates are, and have been, in compliance with all applicable federal, state, local or foreign statutes, laws, principles of common law, ordinances, rules, orders, regulations and any other provisions having the force or effect of law, including the United States Foreign Corrupt Practices Act of 1977, as amended (15 U.S.C. § 78dd-1 et seq.), the United Kingdom Bribery Act 2010, or any Applicable Law prohibiting similar conduct of any applicable jurisdiction, except for instances of noncompliance that, individually or in the aggregate, would not be material to the Acquired Assets, the Program or the Products. Neither Seller nor any of their Affiliates has received during the [***] prior to the date hereof any written communication from a Governmental Entity that alleges that Sellers or any of their Affiliates is in violation of any Applicable Laws except for any such violations that, individually or in the aggregate, would not be material to the Acquired Assets, the Program or the Products.

SECTION 3.07 Absence of Undisclosed Liabilities. Neither Seller nor any of their Affiliates has any liabilities, obligations or commitments of any nature, whether accrued, absolute, contingent, or otherwise (including liabilities, as guarantor or otherwise, in respect of obligations of others) that would (a) create a Lien on any of the Acquired Assets or (b) become, by Applicable Law or otherwise, a liability or obligation of Purchaser upon the execution of this Agreement and/or the taking of the actions contemplated by this Agreement, or (c) prevent the sale, transfer and assignment of the Acquired Assets as contemplated by this Agreement.

SECTION 3.08 Litigation. No litigation, arbitration, action, suit, proceeding or investigation (whether conducted by any judicial or regulatory body, arbitrator, or other Person) affecting the Program or the Acquired Assets is pending, or threatened in writing, against any Seller or any of their Affiliates. To the Knowledge of Sellers, there is no basis for any litigation, arbitration, action, suit, proceeding or investigation relating to the Program or affecting the sale, transfer and assignment of the Acquired Assets.

SECTION 3.09 Taxes. There are no Liens for Taxes on the Acquired Assets.

SECTION 3.10 Transferred Contracts. All of the Transferred Contracts are in full force and effect. Sellers and their Affiliates have performed all material obligations required to be

performed by it and is not in material default under or in material breach of nor in receipt of any written claim of default or breach under any Transferred Contract and no event has occurred which (with or without the passage of time or the giving of notice or both) would, or would reasonably be expected to, (i) result in a material default, breach or event of noncompliance by any Seller or its Affiliate under any Transferred Contract, (ii) give any Person the right to declare a material default or exercise any remedy under any Transferred Contract, (iii) give any Person the right to materially accelerate the maturity or performance of any Transferred Contract, or (iv) give any Person the right to cancel, terminate or modify any Transferred Contract. Seller: (i) has not received any written notice regarding any actual or possible material violation or breach of, or default under, any Transferred Contract; and (ii) has not waived any of its rights under any Transferred Contract. Sellers have provided to Purchaser a true, correct and complete copy of each of the Transferred Contracts, together with all written amendments, waivers or other changes thereto.

SECTION 3.11 Regulatory Compliance.

(a) All Seller Products that are subject to the jurisdiction of the FDA, the EMA or comparable Governmental Entities are being and have been manufactured, labeled, stored and tested in compliance in all material respects with all applicable rules and regulations of the FDA, EMA and all other requirements of applicable Governmental Entities. The Seller Products are not, and have never been, commercially distributed. Seller has not received any written or oral notice from the FDA, EMA or any other Governmental Entity or third Person alleging that its manufacturing, labeling, storing, testing, distributing, or other practices are unlawful or threatening to revoke, suspend, cancel, withdraw, curtail, or seek damages related to any existing certification, license, or approval necessary to the operation of Seller's business. None of the Seller Products have been the subject of any voluntary or involuntary recall, third party action or governmental investigation other than routine inspections of Sellers' facilities, and all U.S. and international regulatory approvals, licenses, and certifications are owned by and registered in the name of Sellers and are in full force and effect.

(b) All human clinical trials conducted in relation to Seller Products by or on behalf of Sellers have been, and are being, conducted in all material respects in compliance with the applicable requirements of Good Clinical Practices and all applicable requirements relating to protection of human subjects contained in 21 CFR Parts 50, 54, and 56 and all similar Applicable Laws. Section 3.11(b) of the Seller Disclosure Schedule contains a complete and accurate list of all Phase I and Phase II clinical trials that have been or are being conducted by or on behalf of Sellers or their Affiliates relating to the Program.

(c) Sellers and their Affiliates have, in relation to the Seller Products, not made any untrue statement of fact or fraudulent statement to the FDA, the EMA or any other Governmental Entities, nor have they failed to disclose any fact required to be disclosed to the FDA, the EMA or any other Governmental Entity, and to the Knowledge of Sellers, no officer, employee, agent, or subcontractor of Sellers has made any untrue statement of fact or fraudulent statement to the FDA, the EMA or any other Governmental Entity relating to the Seller Products, nor has any officer, employee, agent, or subcontractor of Sellers failed to disclose any facts required to be disclosed to the FDA, the EMA, or any other Governmental Entity relating to the Sellers, their Affiliates, or Seller Products.

(d) All Manufacturing operations conducted by, or for the benefit of, Sellers or their Affiliates with respect to Seller Products have been and are being conducted in accordance, in all material respects, with Good Manufacturing Practices where required by FDA or EU Applicable Laws for drug substances or drug products. Sellers and their Affiliates are in compliance in all material respects with all applicable registration and listing requirements set forth in 21 U.S.C. Section 360 and 21 CFR Part 207 and all similar Applicable Laws. No Seller Product, whether or not distributed is or has been adulterated or misbranded. All labeling of Seller Products is in compliance in all material respects with requirements of the FDA and any other applicable Governmental Entity.

(e) Neither Sellers nor their Affiliates nor, to the Knowledge of Sellers, any of their representatives, agents, or subcontractors (including any clinical research organization or investigator utilized by Sellers), has been convicted of any crime or engaged in any conduct which could result in criminal liability or debarment or disqualification by the FDA, EMA or any other Governmental Entity; or to the Knowledge of Sellers debarred or disqualified by the FDA, EMA or other Governmental Entity. To the Knowledge of Sellers, no Seller nor any Affiliates of Seller is employing or utilizing the services of any individual or organization that has been debarred or disqualified by the FDA, EMA or any other Governmental Entity.

(f) Neither Seller, nor their Affiliates, nor any of their representatives, nor any of their licensees or assignees of material Intellectual Property, has received any written notice that the FDA, EMA or any other comparable Governmental Entity has initiated, or threatened to initiate, any action to issue a clinical hold, suspend any clinical trial, suspend or terminate any IND sponsored by Sellers or otherwise restrict the preclinical research on or clinical study of any Seller Product or to recall, suspend or otherwise restrict the manufacture of any Seller Product.

(g) All animal studies or other preclinical tests performed as the basis for any regulatory approval required for the Seller Products have been conducted, where required, in accordance, in all material respects, with applicable Good Laboratory Practice requirements contained in 21 CFR Part 58 and all similar Applicable Laws and regulations.

(h) With respect to Seller Products, Sellers have made available to Purchaser or its representatives accurate and complete copies of any and all notices of inspectional observations, establishment inspection reports and any other material documents received by Seller from the FDA, EMA or other similar Governmental Entity, that state or describe a lack of compliance with the regulatory requirements of the FDA, EMA or other similar Governmental Entity. Sellers have made available to Purchaser for review all material correspondence to or from the FDA, EMA or other similar Governmental Entity, minutes of meetings, written reports of phone conversations, visits or other contact with the FDA, EMA or other similar Governmental Entity, and all other documents concerning material communications to or from the FDA, EMA or other similar Governmental Entity, or prepared by or which bear in any material way on Sellers' compliance with regulatory requirements of the FDA, EMA or other similar Governmental Entity, or on the likelihood or timing of approval of any Seller Products. Section 3.11(h) of the Seller Disclosure Schedule sets forth a complete and accurate list of all documents described in this Section 3.11(h) of the Seller Disclosure Schedule, each of which has been made available to Purchaser.

(i) There are no proceedings pending or, to the Knowledge of Sellers, threatened in writing with respect to a violation or alleged violation by Sellers or their Affiliates of the FDCA, the PHSA or any other applicable law or regulation promulgated by any other comparable Governmental Entity.

(j) Sellers possess, and have included in the Acquired Assets, quantities of Phase I drug product of QR-313 that Sellers believe are sufficient to perform those Phase I or Phase II clinical trials described in Section 3.11(b) of the Seller Disclosure Schedule in compliance with all Applicable Laws, and (ii) the capabilities to manufacture clinical trial materials in compliance with all Applicable Laws.

(k) Sellers have in their possession, or have access to, all material documentation of the chemistry, manufacturing and controls activities undertaken in the development of the Seller Products to date. Sellers have in their possession, or have access to, all documentation related to tests and studies, including, for example, case report forms and data analyses, undertaken in the development of the Seller Products to date.

SECTION 3.12 Potential Conflicts of Interest. Except as set forth in Section 3.12 of the Seller Disclosure Schedule, no officer, director, stockholder, or other Affiliate of a Seller (a) owns, directly or indirectly, in whole or in part, any tangible or intangible property that the Sellers are using or the use of which is necessary for the business of the Sellers as it relates to the Program; (b) has any cause of action or other claim whatsoever against the Sellers relating to the Program; or (c) is party to, or entitled to any benefit under, a Transferred Contract.

SECTION 3.13 Brokers' and Finders' Fees. Sellers and their Affiliates have not incurred, nor will they incur, directly or indirectly, any liability for brokerage or finders' fees or agents' commissions or any similar charges in connection with this Agreement or any Other Transaction Document to which Sellers are a party or any transaction contemplated hereby or thereby.

ARTICLE IV Representations and Warranties of Purchaser

Purchaser hereby represents and warrants to Sellers as follows:

SECTION 4.01 Authority. Purchaser is a legal entity, duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization. Purchaser has all requisite corporate power and authority to own and operate its properties and assets and carry on its business as currently conducted, and to enter into this Agreement and the Other Transaction Documents to which it is, or is specified to be, a party and to consummate the transactions contemplated hereby and thereby. All corporate acts and other proceedings required to be taken by Purchaser to authorize the execution, delivery and performance of this Agreement and the Other Transaction Documents to which it is, or is specified to be, a party and to consummate the transactions contemplated hereby and thereby have been duly and properly taken. This Agreement and the Other Transaction Documents have been duly executed and delivered by Purchaser and, assuming this Agreement and the Other Transaction Documents have been duly authorized, executed and delivered by Sellers, constitute a legal, valid and binding obligation of Purchaser,

enforceable against Purchaser in accordance with their terms, subject, as to enforcement, to applicable bankruptcy, insolvency, moratorium, reorganization or similar laws affecting creditors' rights generally and to general equitable principles.

SECTION 4.02 No Conflicts; Consents.

(a) The execution and delivery of this Agreement and each Other Transaction Document by Purchaser does not, and will not, and the consummation of the transactions contemplated hereby and thereby and compliance with the terms hereof and thereof will not, conflict with, or result in any violation of or default (with or without notice or lapse of time, or both) under, or give rise to a right of termination, cancellation or acceleration of any obligation or to loss of a material benefit under, or result in the creation of any Lien upon any of the properties or assets of Purchaser under, any provision of (i) its certificate of incorporation or by-laws, (ii) the provisions of any of Purchaser's preferred shares or convertible securities, (iii) any contract to which Purchaser is a party or by which any of its properties or assets are bound or (iv) any judgment, order, or decree, or, subject to the matters referred to in paragraph (b) below, Applicable Laws, except, in the case of clauses (iii) and (iv), as would not have a material adverse effect on the ability of Purchaser to consummate the transactions contemplated hereby or under any of the Other Transaction Documents and to perform its obligations under this Agreement and under each of the Other Transaction Document. No vote or approval of the stockholders of Purchaser or any of its Affiliates is required in order to consummate the transactions contemplated by this Agreement or the Other Transaction Documents.

(b) No consent, approval, license, permit, order or authorization of, or registration, declaration or filing with, any Governmental Entity is required to be obtained or made by or with respect to Purchaser or any of its Affiliates in connection with the execution, delivery and performance of this Agreement, the Other Transaction Documents or the consummation of the transactions contemplated hereby or thereby.

SECTION 4.03 Actions and Proceedings. There are no (a) outstanding judgments, orders, injunctions or decrees of any Governmental Entity against Purchaser, (b) lawsuits, actions or proceedings pending or, to the knowledge of Purchaser, threatened against Purchaser, or (c) investigations by any Governmental Entity which are pending or, to the knowledge of Purchaser, threatened against Purchaser.

ARTICLE V
Covenants

SECTION 5.01 Publicity. Sellers and Purchaser agree that no public release or announcement shall be issued or any communications made to any news media concerning the transactions contemplated hereby or under the Other Transaction Documents by either party or its Affiliates without the prior written consent of the other party (which consent shall not be unreasonably withheld or delayed), except as such release or announcement may be required by Applicable Laws or the rules or regulations of any United States or foreign securities exchange to which such party is subject.

SECTION 5.02 Bulk Transfer Laws. The parties hereby waive compliance with the provisions of any so-called “bulk transfer law” of any jurisdiction in connection with the sale of the Acquired Assets to Purchaser.

SECTION 5.03 Tax Matters. Sellers will pay all federal, state, local and foreign taxes imposed on it by Applicable Law arising out of the sale and transfer of the Acquired Assets (“Transfer Taxes”). Purchaser and the Sellers shall use reasonable efforts to minimize the amount of all such Transfer Taxes and shall cooperate in providing each other with any appropriate resale exemption certifications and other similar documentation. The Party that is required by applicable law to make the filings, reports or returns and to handle any audits or controversies with respect to any applicable Transfer Taxes shall do so, and the other Party shall cooperate with respect thereto as necessary.

SECTION 5.04 Books and Records.

(a) In order to facilitate the resolution of any claims made against or incurred by Sellers prior to the Closing, or for any other reasonable purpose, for a period of [***] after Closing, Purchaser shall:

(i) retain the books and records relating to periods prior to the Closing in a manner reasonably consistent with the prior practices of Sellers; and

(ii) upon reasonable notice afford the Sellers’ representatives access (including the right to make, at Sellers’s expense, photocopies), during normal business hours, to such books and records.

(b) In order to facilitate the resolution of any claims made by or against or incurred by Purchaser after Closing, or for any other reasonable purpose, for a period of [***] after Closing, Sellers shall:

(i) retain the books and records of Sellers which relate to the Acquired Assets and its operations for periods prior to Closing; and

(ii) upon reasonable notice, afford Purchaser’s representatives reasonable access, during normal business hours, to such books and records.

(c) Neither Purchaser nor Sellers shall be obligated to provide the other party with access to any books or records pursuant to this Section 5.04 where such access would violate any Applicable Law.

SECTION 5.05 Recordation of Transfer of Intellectual Property. Purchaser shall be responsible, at its sole cost and expense, for all applicable recordations of the assignment of the Transferred Intellectual Property.

SECTION 5.06 Non-Competition. For a period of [***] following the Closing Date (the “Restricted Period”), Sellers shall not, and shall cause their Affiliates not to, directly or indirectly, engage or participate, anywhere in the world, in the development, product design, manufacturing, production, distribution, marketing, sale, commercialization or other similar

activities relating to the discovery and development of Restricted Products, in each case including by owning, managing, operating, controlling or otherwise participating in the ownership, management, operation or control of any entity engaged in any such activities, whether as an employer, proprietor, partner, equityholder, consultant, agent, lender or guarantor or otherwise. If a court of competent jurisdiction determines in a final, non-appealable judgment that the Sellers have breached the terms of this Section 5.06, then the Restricted Period shall be extended by a period of time equal to the duration of such breach.

SECTION 5.07 Confidential Information. The Sellers shall keep confidential, and shall cause their Affiliates and instruct their officers, directors, employees and advisors to keep confidential, all non-public information relating to the Program, the Acquired Assets and the Assumed Liabilities, except as required by law or with Purchaser's written consent and except for information that becomes public other than as a result of a breach of this Section 5.07.

SECTION 5.08 Non-Assertion Clause. The Parties hereto hereby acknowledge that Purchaser has acquired the Transferred Intellectual Property under this Agreement with the intention to Develop and Commercialize the Program. As a result, while this Agreement is still in effect, in the event that any activities of Purchaser or any licensee of Purchaser with respect to the Development, Manufacturing, Commercialization or other efforts to Exploit the Program infringe any Intellectual Property of Sellers or their Affiliates (a "Blocking Claim"), Sellers covenant and agree for themselves and their Affiliates that they will not directly or indirectly enforce such Blocking Claim against Purchaser or any licensee of Purchaser with respect to such activities.

SECTION 5.09 Transition Support. Sellers will, and will cause their Affiliates to, continue to perform their best efforts to reasonably support the Purchaser's conduct of the Program following the Closing, provided that Sellers and their Affiliates resources are reasonably available and such use would not have a material negative impact on Sellers' and their Affiliates' other businesses. Sellers agree to, and to cause their Affiliates to, continue to reasonably cooperate with the Purchaser at cost price on the development of Seller Product QR-313, by making individuals available for the Purchaser's scientific advisory board and Board of Directors.

ARTICLE VI Indemnification

SECTION 6.01 Indemnification by Sellers and Parent. From and after the Closing, Sellers and Parent, jointly and severally, shall indemnify Purchaser and its Affiliates and each of their respective officers, directors, employees, agents, representatives, partners, shareholders and members against and hold them harmless from any loss, liability, claim of any kind, damage, diminution, obligation, interest or expenses (including reasonable and documented legal fees and expenses and the cost of enforcing any right to indemnification hereunder) (collectively, "Losses") suffered or incurred by any such indemnified party to the extent arising from (a) any breach of any representation or warranty of Sellers contained in this Agreement or in any of the Other Transaction Documents, or in any certificate or instrument delivered pursuant hereto or thereto, (b) any breach of any covenant of Sellers contained in this Agreement or any of the Other Transaction Documents, or in any certificate or instrument delivered pursuant hereto or thereto, or (c) any Excluded Liability.

SECTION 6.02 Indemnification by Purchaser. From and after the Closing, Purchaser shall indemnify Sellers and their Affiliates and each of their respective officers, directors, employees, agents, representatives, partners, shareholders and members against and hold them harmless from any Losses suffered or incurred by any such indemnified party to the extent arising from (a) any breach of any representation or warranty of Purchaser contained in this Agreement or any of the Other Transaction Documents, or in any certificate or instrument delivered pursuant hereto or thereto, (b) any breach of any covenant of Purchaser contained in this Agreement or any of the Other Transaction Documents, or in any certificate or instrument delivered pursuant hereto or thereto, or (c) any Assumed Liability.

SECTION 6.03 Indemnification Payments; Limitations on Liability. The amount of any Losses for which indemnification is provided under this Article VI shall be net of any amounts actually received by the indemnified party under insurance policies with respect to such Losses.

(a) Notwithstanding anything to the contrary contained in this Agreement, any “materiality” or other similar qualification contained in a representation or warranty shall not be given any effect solely for purposes of determining the amount of Losses arising from any breach of any such representation or warranty.

(b) If Purchaser asserts a claim pursuant to this Agreement for indemnification against Losses and (i) Sellers agree in writing that Purchaser is entitled to indemnification with respect to such Losses or (ii) a court of competent jurisdiction determines in a final, non-appealable judgment that Purchaser is entitled to indemnification with respect to such Losses, then Purchaser shall have the right to withhold from any unpaid Milestone Payments and/or any unpaid Royalty Payments the amount of such Losses.

(c) Notwithstanding any provision herein, neither Sellers, Parent nor Purchaser, nor any of their respective Affiliates, shall in any event be liable for any punitive damages in connection with any claims arising hereunder, except on account of any indemnity obligation set forth in Section 6.01 or Section 6.02 to the extent punitive damages are actually awarded to a third party in connection with a Third Party Claim.

(d) Payments by an indemnifying party pursuant to Sections 6.01 or 6.02 in respect of any Losses shall be limited to the amount of any liability or damage that results after deducting therefrom any insurance proceeds and any indemnity, contribution or other similar payment received by the indemnified party in respect of any such claim. The indemnifying party shall use its commercially reasonable efforts to recover under insurance policies or indemnity, contribution or other similar agreements for any Losses prior to seeking indemnification under this Agreement.

(e) Sellers and Purchaser shall each take, and shall cause their respective Affiliates to take, all reasonable steps to mitigate any Losses upon becoming aware of any event or circumstance that would reasonably be expected to, or does, give rise to Losses, including incurring costs only to the extent reasonably necessary to remedy the breach that gives rise to such Losses.

(f) Other than claims of, or causes of action arising from, intentional breach or fraud, recovery by indemnified parties of their indemnifiable Losses in the aggregate will be subject to the following limitations:

(i) The Sellers and the Purchaser may not recover Losses for any claim pursuant to Section 6.01(a) and Section 6.02(a), as applicable, unless and until the aggregate amount of all such Losses exceeds [***] Dollars (\$[***]) (the “Deductible”), after which, such indemnified parties shall be entitled to recover all Losses in excess of the Deductible; and

(ii) Except to the extent indemnifiable Losses arise out of an inaccuracy or breach of any Fundamental Representation, the maximum amount of Losses that an indemnified party may recover under Section 6.01(a) or Section 6.02(a), as applicable, shall be [***] Dollars (\$[***]); and

(iii) The maximum amount of Losses that a Purchaser indemnified party may recover under Section 6.01 pursuant to an inaccuracy or breach of any Fundamental Representation, shall be [***] Dollars (\$[***]).

(g) The parties acknowledge and agree that each party’s sole and exclusive remedy with respect to claims arising from the breach of any representation or warranty contained in this Agreement or in any of the any Other Transaction Documents, or in any certificate or instrument delivered pursuant hereto or thereto (other than claims of, or causes of action arising from, intentional breach or fraud), shall be pursuant to the indemnification provisions set forth in this Article VI.

SECTION 6.04 Termination of Indemnification.

(a) The obligations to indemnify and hold harmless a party hereto pursuant to (i) Sections 6.01(a) and 6.02(a) shall terminate when the applicable representation or warranty terminates pursuant to paragraph (b) below and (ii) the other clauses of Sections 6.01 and 6.02 shall not terminate; *provided, however*, that as to clause (i) of this sentence such obligations to indemnify and hold harmless shall not terminate with respect to any item as to which the person to be indemnified or the related party thereto shall have, before the expiration of the applicable period, previously made a claim by delivering a notice of such claim (stating in reasonable detail the basis of such claim) to the indemnifying party, in which case any such claim and such obligations to indemnify and hold harmless shall survive the expiration of the applicable period until final resolution of such claim.

(b) The representations and warranties contained in this Agreement or in any Other Transaction Document, or in any certificate or instrument delivered pursuant hereto or thereto, shall survive the Closing for a period of [***] after the Closing Date, *provided, however*, that the Fundamental Representations shall survive the Closing indefinitely. Each indemnified party must give written notice to the indemnifying party of any claim for indemnification under this Article VI in accordance with Section 6.05 or 6.06, as applicable. Any claim for indemnification made in writing by the indemnified party on or prior to the expiration of the applicable survival period shall survive, and may continue to be asserted and indemnified against, until such claim is finally and fully resolved. The covenants and agreements contained in this

Agreement or in any Other Transaction Document, or in any certificate or instrument delivered pursuant hereto or thereto, shall survive the Closing until fully performed or satisfied.

SECTION 6.05 Procedures Relating to Indemnification for Third Party Claims.

(a) In order for a party (the “indemnified party”) to be entitled to any indemnification provided for under this Agreement in respect of, arising out of or involving a claim or demand made by any person who is not a party to this Agreement or an Affiliate, agent or representative of the foregoing against the indemnified party (a “Third Party Claim”), such indemnified party shall, as promptly as reasonably practicable, notify the indemnifying party in writing, and in reasonable detail, of the Third Party Claim for which indemnity may be sought hereunder; *provided, however*, that failure to give such notification shall not affect the indemnification provided hereunder except and only to the extent the indemnifying party forfeits rights or defenses by reason of such failure or shall have been materially prejudiced as a result of such failure. Such notice by the indemnified party shall describe the Third Party Claim in reasonable detail, shall include copies of all material written evidence thereof and shall include the estimated amount (if it is reasonably possible to calculate such amount) of the Losses that have been or may be sustained by the indemnified party. Thereafter, the indemnified party shall deliver to the indemnifying party, promptly after the indemnified party’s receipt thereof, copies of all notices and documents (including court papers) received by the indemnified party relating to the Third Party Claim.

(b) If a Third Party Claim is made against an indemnified party, the indemnifying party shall be entitled to participate in the defense thereof and, if it so chooses, to assume the defense thereof with counsel selected by the indemnifying party (not reasonably objected to by the indemnified party) and the indemnified party shall cooperate in good faith in such defense; *provided, however*, that the indemnifying party shall not be entitled to assume the defense of any Third Party Claim that (A) involves criminal liability or any admission of wrongdoing, (B) seeks equitable relief or any other non-monetary remedy against the indemnified party or (C) involves any Governmental Entity as a party thereto. If the indemnifying party elects to assume the defense of a Third Party Claim in accordance with this Section 6.05(b), the indemnifying party shall not be liable to the indemnified party for legal expenses subsequently incurred by the indemnified party in connection with the defense thereof; *provided, however*, that if in the reasonable opinion of outside counsel to the indemnified party (1) a conflict or potential conflict exists between the indemnified party and the indemnifying party that would make separate representation advisable or (2) the indemnified party has legal defenses available to it which are different from or in addition to the defenses available to the indemnifying party, then the indemnified party may retain its own counsel at the expense of the indemnifying party; *provided, further*, that that indemnifying party shall not be required to pay for more than one such counsel for all indemnified parties in connection with any such Third Party Claim. If the indemnifying party elects to assume the defense of a Third Party Claim in accordance with this Section 6.05(b), the indemnified party shall have the right to participate in the defense thereof and, without limiting the preceding sentence, to employ counsel, at its own cost and expense, separate from the counsel employed by the indemnifying party. The indemnifying party shall be liable for the fees and expenses of counsel employed by the indemnified party for any period during which the indemnifying party has failed to assume the defense thereof in accordance with this Section 6.05(b).

(c) If the indemnifying party so elects to assume the defense of a Third Party Claim in accordance with Section 6.05(b), the indemnified party shall cooperate with the indemnifying party in the defense or prosecution thereof. Such cooperation shall include the retention and (upon the indemnifying party's request) the provision to the indemnifying party of records and information which are reasonably relevant to such Third Party Claim, and making employees available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder. If the indemnified party is conducting the defense of any Third Party Claim, the indemnifying party shall cooperate with the indemnified party in the defense or prosecution thereof. Such cooperation shall include the retention and (upon the indemnified party's request) the provision to the indemnified party of records and information which are reasonably relevant to such Third Party Claim, and making employees available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder. The indemnifying party shall not admit any liability with respect to, or settle, compromise or discharge, any Third Party Claim without the indemnified party's prior written consent, unless (i) the proposed settlement or disposition involves only the payment of money damages by the indemnifying party for which the indemnified party shall have no liability, (ii) the proposed settlement or disposition does not impose an injunction or other equitable relief upon the indemnified party, (iii) the proposed settlement or disposition does not include any admission of wrongdoing or misconduct and (iv) the indemnified party is fully and unconditionally released from any liability relating to such Third Party Claim. The indemnified party shall not admit any liability with respect to, or settle, compromise or discharge, any Third Party Claim without the indemnifying party's prior written consent. In the event that a settlement offer solely for monetary damages is made by the applicable Third Party claimant, and the indemnifying party notifies the indemnified party of its willingness to accept the offer and, subject to the applicable limitations of Section 6.02, pay the amount called for by such offer, and the indemnified party declines to accept such offer, the indemnified party may continue to contest such Third Party claim, free of any participation from the indemnifying party, and the amount of any ultimate liability with respect to such Third Party Claim that the indemnifying party has an obligation to pay hereunder shall be limited to the lesser of (x) the amount of the settlement offer that the indemnified party declined to accept or (y) the aggregate Losses of the indemnified party with respect to such Third Party Claim.

SECTION 6.06 Procedures Related to Indemnification for Other Claims. In the event any indemnified party should have a claim against any indemnifying party under Section 6.01 or 6.02 that does not involve a Third Party Claim being asserted against or sought to be collected from such indemnified party, the indemnified party shall promptly deliver written notice of such claim, in reasonable detail, to the indemnifying party; *provided, however,* that failure by any indemnified party to so notify the indemnifying party shall not relieve the indemnifying party from any liability which it may have to such indemnified party under Section 6.01 or 6.02, except and only to the extent that the indemnifying party forfeits rights or defenses by reason of such failure or shall have been materially prejudiced as a result of such failure. If the indemnifying party disputes its liability with respect to such claim, the indemnifying party and the indemnified party shall proceed in good faith to negotiate a resolution of such dispute and, if not resolved through negotiations, such dispute shall be resolved by litigation in an appropriate court of competent jurisdiction.

SECTION 6.07 Tax Treatment of Indemnification Payments. For all United States Tax purposes, Purchaser, Sellers and each of their respective Affiliates agree to treat any indemnity payment under this Agreement as an adjustment to the Purchase Price received by Sellers for the transactions contemplated by this Agreement unless a final determination (as defined in Section 1313 of the Code) provides otherwise.

ARTICLE VII

Miscellaneous

SECTION 7.01 Assignment. This Agreement and the rights and obligations hereunder shall not be assignable or transferable by Purchaser, Sellers or Parent (including by operation of law in connection with a merger, consolidation or sale of substantially all the assets of Purchaser, Sellers or Parent) without the prior written consent of the other party hereto; *provided, however*, that Purchaser may assign its rights and obligations hereunder, without such consent, to any direct or indirect wholly owned subsidiary of Purchaser or to an acquirer of all or substantially all of the stock or assets of Purchaser, whether pursuant to a merger, sale of assets, or sale of stock or other ownership interests; *provided, further*, that Sellers may assign their rights and obligations hereunder, without such consent, to Parent or any direct or indirect wholly owned subsidiary of Sellers; *provided, further*, that no assignment shall relieve any party of its obligations hereunder. Any attempted assignment in violation of this Section 7.01 shall be void.

SECTION 7.02 Terms. As used throughout this agreement, references to Purchaser or Purchaser's Affiliates shall be read to include any of their respective successors in interest.

SECTION 7.03 No Third-Party Beneficiaries. This Agreement is for the sole benefit of the parties hereto and their permitted assigns and nothing herein expressed or implied shall give or be construed to give to any person, other than the parties hereto and such assigns, any legal or equitable rights hereunder.

SECTION 7.04 Expenses. Whether or not the transactions contemplated hereby are consummated, and except as otherwise specifically provided in this Agreement, all costs and expenses incurred in connection with this Agreement and the transactions contemplated hereby shall be paid by the party incurring such costs or expenses.

SECTION 7.05 Amendments. This Agreement may not be amended except by an instrument in writing signed on behalf of each of the parties hereto. By an instrument in writing Purchaser, on the one hand, or Sellers, on the other hand, may waive compliance by the other with any term or provision of this Agreement that such other party was or is obligated to comply with or perform. Any such waiver will only be effective in the specific instance and for the specific and limited purpose for which it was given and will not be deemed a waiver of any other provision of this Agreement or of the same breach or default upon any recurrence thereof. No failure on the part of any party to exercise any power, right, privilege or remedy under this Agreement, and no delay on the part of any party in exercising any power, right, privilege or remedy under this Agreement, shall operate as a waiver of such power, right, privilege or remedy, and no single or partial exercise of any such power, right, privilege or remedy shall preclude any other or further exercise thereof or of any other power, right, privilege or remedy.

SECTION 7.06 Notices. All notices, requests, claims, demands or other communications required or permitted to be given hereunder shall be in writing and shall be deemed to have been duly given when delivered in person, or upon confirmation of receipt when transmitted by electronic mail, or if mailed, [***] after mailing ([***] in the case of overnight mail or overnight courier service), as follows:

(a) if to Purchaser, to:

Wings Therapeutics, Inc.
2600 Tenth Street, #435
Berkeley, CA 94710
Attention: Mark P. de Souza, President
E-mail:

with a copy (which shall not constitute notice) to:

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
One Financial Center
Boston, MA 02111
Attention: Daniel H. Follansbee, Esq.
E-mail: [***]

(b) if to Sellers or Parent, to:

ProQR Therapeutics, N.V.
Zernikedreef 9
2333 CK Leiden
The Netherlands
Attention: Nico Bunnik
E-mail: [***]

with a copy (which shall not constitute notice) to:

Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210
Attention: Danielle M. Lauzon, Esq.
E-mail: [***]

SECTION 7.07 Interpretation; Definitions.

(a) The definitions of the terms herein shall apply equally to the singular and plural forms of the terms defined. Whenever the context may require, any pronoun shall include the corresponding masculine, feminine and neuter forms. The words “include”, “includes” and “including” shall be deemed to be followed by the phrase “without limitation”. The word “will” shall be construed to have the same meaning and effect as the word “shall”. Unless the context requires otherwise, (i) any definition of or reference to any agreement, instrument or other document herein shall be construed as referring to such agreement, instrument or other document

as from time to time amended, supplemented or otherwise modified, (ii) the words “herein”, “hereof” and “hereunder”, and words of similar import, shall be construed to refer to this Agreement in its entirety and not to any particular provision hereof, (iii) all references herein to Articles, Sections, Exhibits or Schedules shall be construed to refer to Articles, Sections, Exhibits and Schedules of or to this Agreement, as the case may be, and (iv) the headings contained in this Agreement or any Exhibit or Schedule hereto and in the table of contents to this Agreement are for reference purposes only and shall not affect in any way the meaning or interpretation of this Agreement. Any capitalized terms used in any Exhibit or Schedule hereto but not otherwise defined therein shall have the meanings as defined in this Agreement. Whenever this Agreement refers to a number of days, such number shall refer to calendar days unless business days are specified. In the event of an ambiguity or a question of intent or interpretation, this Agreement shall be construed as if drafted jointly by the parties and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Agreement.

(b) For all purposes hereof:

“Acquired Assets” has the meaning ascribed to such term in Section 1.05(a).

“Affiliate” means, with respect to any specified person, any other person directly or indirectly controlling or controlled by or under direct or indirect common control with such specified person; and for the purposes of this definition, “control” when used with respect to any specified person means the power to direct the management and policies of such person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise; and the terms “controlling” and “controlled” have meanings correlative to the foregoing.

“Applicable Laws” means, with respect to each party hereto, all laws, statutes, constitutions, treaties, directives, rules, regulations, principles of common law, resolutions, codes, ordinances, requirements, judgments, orders, decrees, injunctions, and writs of any Governmental Entity which has, or such party believes is reasonably likely to have, jurisdiction over such party or the businesses, operations or assets of such party, as they may be in effect on or prior to the Closing.

“Approval” or “Approved” means, with respect to a Product in any regulatory jurisdiction, approval from the applicable Regulatory Authority sufficient to manufacture, distribute, use (including in clinical trials) and sale of a Product in such regulatory jurisdiction in accordance with Applicable Laws including receipt of pricing and reimbursement approvals, where applicable.

“Asset” means any interest in any property of any kind, including money, wherever located, whether personal, real or mixed, whether tangible or intangible and whether or not reflected or of a nature that would be reflected in a balance sheet.

“Assignment and Assumption Agreement” means an assignment and assumption agreement with respect to the Transferred Contracts.

“Assumed Liabilities” has the meaning ascribed to such term in Section 1.06(a).

“Bill of Sale” means a bill of sale and assignment with respect to the Acquired Assets.

“business day” means any day, other than a Saturday or Sunday, on which commercial banks are not required or authorized to close in New York, New York.

“Calendar Quarter” means the respective periods of three (3) consecutive calendar months ending March 31, June 30, September 30 and December 31.

“Calendar Year” means each successive period of twelve (12) calendar months commencing on January 1 and ending on December 31.

“Code” means the U.S. Internal Revenue Code of 1986, as amended.

“Combination Product” means a product that includes a Product and at least one additional active ingredient (whether co-formulated or co-packaged) other than a Product. [***].

“Commercial License” means the contract pursuant to which Purchaser or any of its Affiliates grants a Commercial Licensee the right to co-develop, co-promote, co-market or otherwise has a license or other right to develop, promote, market, distribute, offer for sale, sell or import or to otherwise commercialize a Product.

“Commercial Licensee” means any third party that is a party to a contract with Purchaser or any of its Affiliates pursuant to which such third party obtains rights to co-develop, co-promote, co-market or otherwise has a license or other right to develop, promote, market, distribute, offer for sale, sell or import or to otherwise commercialize a Product.

“Commercialize” means activities directed to the marketing, promotion, use, selling, or offering for sale of a product, including pre-marketing, advertising, educating, planning, marketing, promoting, distributing, importing, exporting and post-marketing safety surveillance and reporting. For clarity, Commercialization shall not include any activities related to the Manufacturing or Development of Products.

“Contract” means any agreement, contract, lease, license, promissory note, conditional sales contract, indenture, mortgage, deed of trust, commitment, undertaking, instrument or arrangement of any kind, whether or not in writing, under which (in each case) any obligation is legally enforceable against any Person, Asset or right. Without limiting the generality of the foregoing, any agreement, commitment, undertaking or arrangement of any kind with a Governmental Entity shall constitute a “Contract” whether it was entered into voluntarily or pursuant to applicable law or in settlement of a claim or possible claim by such Governmental Entity, or otherwise.

“Develop” means non-clinical and clinical research and biological product development activities, including toxicology, test method development and stability testing, process development, formulation development, delivery system development, quality assurance and quality control development, statistical analysis, clinical studies (including pre- and post-approval studies), regulatory affairs, and product approval and clinical study regulatory activities.

“Dollars” or “\$” means lawful money of the United States of America.

“Excluded Assets” has the meaning ascribed to such term in Section 1.05(b).

“Excluded Liability” has the meaning ascribed to such term in Section 1.06(b).

“EMA” means the European Medicines Agency.

“EU” means the European Union.

“Exploit” means to make, have made, import, use, sell or offer for sale, including to research, Develop, Commercialize, register, Manufacture, have Manufactured, hold or keep (whether for disposal or otherwise), have used, export, transport, distribute, promote, market or have sold or otherwise dispose of.

“Field” means all uses for the prevention, treatment, mitigation, palliation or diagnosis of epidermolysis bullosa.

“FDA” means the United States Food and Drug Administration.

“First Commercial Sale” means, with respect to a Product, the first sale for use or consumption by the general public of a Product in any country after Approval of a Product has been granted, or such marketing and sale is otherwise permitted, by the applicable Regulatory Authority of such country.

“Fundamental Representation” means the representations and warranties of the Sellers set forth in Sections 3.01 (*Authority*), 3.02 (*No Conflict; Consents*), and 3.03 (*Assets and Properties*) excluding the last sentence thereof.

“GAAP” means generally accepted accounting principles in the United States.

“Good Clinical Practices” means, with respect to Sellers, the then current standards for clinical trials for pharmaceuticals (including all applicable requirements relating to protection of human subjects), as set forth in the FDCA and applicable regulations promulgated thereunder (including, for example, 21 C.F.R. Parts 50, 54, and 56), as amended from time to time, and such standards of good clinical practice (including all applicable requirements relating to protection of human subjects) as are required by other organizations and Governmental Entities in any other countries, including applicable regulations or guidelines from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, in which a Product of Sellers or their Affiliates is sold or intended to be sold, to the extent such standards are not less stringent than in the United States.

“Good Laboratory Practices” mean, with respect to Sellers, the then current standards for pharmaceutical laboratories, as set forth in the FDCA and applicable regulations promulgated thereunder, as amended from time to time, and such standards of good laboratory practices as are required by other organizations and Governmental Entities in any other countries, including applicable regulations or guidelines from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use in which a Product of Sellers or their Affiliates is sold or intended to be sold, to the extent such standards are not less stringent than in the United States.

“Good Manufacturing Practices” mean, with respect to Sellers, the then current standards for the manufacture, processing, packaging, testing, transportation, handling and holding of drug products, as set forth in the FDCA and applicable regulations promulgated thereunder, as amended from time to time, and such standards of good manufacturing practices as are required by other organizations and Governmental Entities in any other countries, including applicable regulations or guidelines from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use in which a Product of Sellers or their Affiliates are sold or intended to be sold, to the extent such standards are not less stringent than in the United States.

“Governmental Entity” means any federal, state, local or foreign government or any political subdivision thereof or any department, commission, board, bureau, agency, court, panel or other instrumentality of any kind of any of the foregoing, including without limitation any Regulatory Authority.

“Health Laws” means any law of any Governmental Entity (including multi-country organizations) the purpose of which is to ensure the safety, efficacy and quality of medicines or pharmaceuticals by regulating the research, development, manufacturing and distribution of these products, including laws relating to Good Laboratory Practices, Good Clinical Practices, investigational use, product marketing authorization, manufacturing facilities compliance and approval, Good Manufacturing Practices, labeling, advertising, promotional practices, safety surveillance, record keeping and filing of required reports such as the U.S. Federal Food, Drug, and Cosmetic Act of 1938, as amended (the “FDCA”), and the Public Health Service Act, as amended (the “PHSA”), in each case including the associated rules and regulations promulgated thereunder and all of their foreign equivalents.

“IND” means an Investigational New Drug Application filed with the FDA pursuant to Part 312 of Title 21 of the U.S. Code of Federal Regulations (or its successor regulation) with respect to a Product, or the equivalent application or filing filed with any equivalent agency or Governmental Entity outside the United States of America (including any supra-national agency such as the EMA), and all supplements, amendments, variations, extensions and renewals thereof that may be filed with respect to the foregoing.

“Intellectual Property” means all Patents, Trademarks, Internet Domain Name Registrations, Copyrights and Know-How and all other intellectual property and all copies and tangible embodiments or descriptions of any of the foregoing (in whatever form or medium) and all goodwill associated with, and all rights related to or otherwise associated with, any of the foregoing in any jurisdiction in the world (including all rights to collect royalties, products and proceeds in connection with any of the foregoing, and to sue and bring other claims for past, present and future infringement, misappropriation or other violation of any of the foregoing, and to recover damages (including attorneys’ fees and expenses) and lost profits in connection therewith).

“IP Assignment Documents” means with respect to any Transferred Intellectual Property, intellectual property (patent, trademark, copyright and domain name assignments, as applicable) assignments of such Transferred Intellectual Property.

“Knowledge of Sellers” means the actual knowledge of [***], after due and reasonable investigation.

“Know-How” means any data, results, and information of any type whatsoever, whether tangible or intangible and regardless of the form or medium, including any know-how, trade secrets, expertise, knowledge, practices, techniques, concepts, methodologies, methods, processes, protocols, designs, ideas, inventions (whether or not patentable or reduced to practice), improvements, industrial designs and models, discoveries, developments, unpublished patent applications, specifications, formulations, formulae, materials or compositions of matter of any type or kind (patentable or otherwise), assays, screens, software, algorithms, models, data, databases, database rights, chemistry, manufacturing and control (CMC) information and data, lab notebooks, Patent data, stability, technology, test data and results (including pharmacological, biological, chemical, biochemical, toxicological, pre-clinical and clinical test data), analytical and quality control data, results or descriptions, studies and procedures, development, manufacturing and distribution costs, information contained in submissions to and information from regulatory authorities, and marketing and other reports.

“Liability” or “Liabilities” has the meaning ascribed to such term in Section 1.06(a).

“Liens” has the meaning ascribed to such term in Section 3.02.

“Losses” has the meaning ascribed to such term in Section 6.01.

“MAA” means an EU marketing authorization application.

“Manufacture” means making and having made, including all operations in the acquisition of materials and the production, testing, warehousing, packaging, labeling and, as applicable, release to the market, importing and having imported.

“Milestone Event” has the meaning ascribed to such term in Section 1.02.

“Milestone Payment” has the meaning ascribed to such term in Section 1.02.

“NDA” means a new drug application for a drug submitted in accordance with 21 C.F.R. Part 314, and all supplements submitted pursuant to the requirements of the FDA, including all documents, data and other information concerning the applicable drug which are necessary for FDA approval to market such drug in the United States, and any equivalent application submitted to any other health authority.

“Net Sales” [***]

“Non-Disclosure Agreement” means the Confidential Disclosure Agreement, dated as of March 26, 2019, between Parent and Purchaser.

“Other Transaction Documents” means (i) the Bill of Sale, (iii) the Assignment and Assumption Agreement and (iii) the IP Assignment Documents.

“Patented Product” means a Product, the manufacture, use, sale, offer for sale or importation of which in or into a particular country would infringe a Valid Claim within the Transferred Patents, as determined on a Product-by-Product and country-by-country basis.

“Patents” means all issued patents, pending patent applications, statutory invention registrations and patent disclosures, and all reissues, continuations, continuations-in-part, divisional applications, substitutions, extensions, supplementary protection certificates, reexaminations, extensions and all foreign equivalents of any of the foregoing.

“person” means any individual, firm, corporation, partnership, limited liability company, trust, joint venture, Governmental Entity or other entity.

“Product” means a pharmaceutical preparation based on an exon skipping approach for dystrophic epidermolysis bullosa.

“Program” has the meaning ascribed to such term in the preamble.

“Purchase Price” has the meaning ascribed to such term in Section 1.01.

“Regulatory Authority” means any national or supranational Governmental Entity, including the FDA or the EMA, with responsibility for granting any license, registrations or Approvals with respect to a Product.

“Regulatory Materials” means all U.S. and non-U.S. regulatory applications, filings, submissions and approvals (including all INDs and NDAs, and foreign counterparts thereof, including MAAs, and all Approvals) for a Product or otherwise related to the Program (including manufacturing approvals, technical, medical, and scientific licenses, and pre-clinical, clinical and non-clinical study authorization applications or notifications), all amendments, supplements, supporting files, data, results, outcomes, studies, and reports relating thereto (in hard and electronic form) and all technical and other information contained therein, and all correspondence with Regulatory Authorities and other Governmental Entities relating to the foregoing, that, in each case, are in the possession of or controlled by, or held by or for Sellers or their Affiliates, whether generated, filed or held by or for Sellers or their Affiliates.

“Restricted Products” means programs involving exon skipping for dystrophic epidermolysis bullosa (including without limitation programs for [***]).

“Royalty Term” has the meaning ascribed to such term in Section 1.03(b).

“Royalty Report” has the meaning ascribed to such term in Section 1.03(c).

“Seller Products” means Products included within the Acquired Assets.

“Shares” has the meaning ascribed to such term in Section 1.01 “subsidiary” of any person means another person, an amount of the voting securities, other voting ownership or voting partnership interests of which is sufficient to elect at least a majority of its Board of Directors or other governing body (or, if there are no such voting interests, fifty percent (50%) or more of the

equity interests of which) is owned directly or indirectly by such first person or by another subsidiary of such person.

“Supplies” means any and all raw materials, compounds, base chemicals, work in process, finished goods, supplies, parts and other supplies of any kind of the Sellers or their Affiliates of or relating to the Program, whether located on any of the Sellers’ premises, suppliers’ premises, in transit or elsewhere and all rights of the Sellers and their Affiliates with respect thereto.

“Tax” or “Taxes” means any and all taxes, charges, fees, duties, contributions, levies or other similar assessments or liabilities, including income, gross receipts, corporation, ad valorem, premium, value-added, consumption, net worth, capital stock, capital gains, documentary, recapture, alternative or add-on minimum, registration, recording, excise, real property, personal property, sales, use, license, lease, service, service use, transfer, withholding, business license, business organization, environmental, profits, severance, stamp, occupation, windfall profits, escheat, customs duties, import, export, franchise, estimated and other taxes of any kind whatsoever imposed by the United States federal government or any state, local or foreign government, or any agency or political subdivision thereof (whether payable directly or by withholding), together with any interest, fines, penalties, assessments, additions to tax or additional amounts imposed with respect to such items, including any liability for payment of taxes as a transferee or successor by contract or otherwise.

“Transferred Intellectual Property” has the meaning ascribed to such term in Section 1.05(a).

“Transferred Patents” means the Patents included within the Transferred Intellectual Property.

“U.S.” or “United States” means the United States of America, including its territories and possessions (excluding all military bases and other military installations outside of the continental United States, Alaska, Hawaii and Washington, D.C.).

“Valid Claim” means a claim of an issued and unexpired patent which has not been held permanently revoked, unenforceable or invalid by a decision of a court or other Governmental Entity of competent jurisdiction, unappealable or unappealed within the time allowed for appeal and that is not admitted to be invalid or unenforceable through reissue, disclaimer or otherwise (*i.e.*, only to the extent the subject matter is disclaimed or is sought to be deleted or amended through reissue).

“VAT” means value added tax imposed in any member state of the EU pursuant to Council Directive (EC) 2006/112 on the common system of value added tax and national legislation implementing that Directive or any predecessor to it, or supplemental to that Directive, or any similar tax which may be substituted for or levied in addition to it or any value added, sales turnover, goods and services or similar Tax imposed in a country which is not a member of the EU.

SECTION 7.08 Counterparts. This Agreement may be executed in one or more counterparts (including by facsimile or other means of electronic transmission, such as by electronic mail in “pdf” form), all of which shall be considered one and the same agreement, and

shall become effective when one or more such counterparts have been signed by each of the parties and delivered to the other party.

SECTION 7.09 Entire Agreement. This Agreement, the Other Transaction Documents and the Non-Disclosure Agreement contain the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersede all prior agreements, drafts, understandings, promises, undertakings or implications relating to such subject matter, whether written or oral, including without limitation the Legally Binding Heads of Terms, dated March 25, 2019, between ProQR, Purchaser and Holding. No provision of this Agreement shall be interpreted in favor of, or against, any party by reason of the fact that any such provision is inconsistent with any prior draft hereof.

SECTION 7.10 Severability. If any provision of this Agreement (or any portion thereof) or the application of any such provision (or any portion thereof) to any person or circumstance shall be held invalid, illegal or unenforceable in any respect by a court of competent jurisdiction, such invalidity, illegality or unenforceability shall not affect the validity or enforceability of any other provision hereof (or the remaining portion thereof) or the application of such provision (or the remaining portion thereof) to any other persons or circumstances. In the event that any provision of this Agreement shall be held by a court of competent jurisdiction to be invalid, illegal or unenforceable, such provision shall be limited or eliminated, but only to the minimum extent necessary so that this Agreement shall otherwise remain in full force and effect.

SECTION 7.11 Governing Law. This Agreement shall be governed by and construed in accordance with the internal laws of the State of New York applicable to agreements made and to be performed entirely within such state, without regard to the conflicts of law principles of such state.

SECTION 7.12 Representations and Warranties, Indemnities. The representations and warranties made in this Agreement or made in writing pursuant hereto shall survive the Closing and be enforceable notwithstanding any investigation of or knowledge with respect to the matters covered thereby by or on behalf of any Party to whom they are made. The Sellers and Purchaser acknowledge that the other is entering into this Agreement, and will consummate the transactions contemplated hereby, in reliance upon the express representations and warranties of the other Party made in this Agreement or made in a writing delivered pursuant hereto. The indemnifications set forth in Article VI are intended to transfer the risk of the matters covered to the indemnifying party, irrespective of any knowledge that the indemnified party has with respect to the matters covered.

SECTION 7.13 Dispute Resolution.

(a) All disputes or claims arising under or in any way relating to this Agreement or to the acquisition of the Acquired Assets by Purchaser or Purchaser's use or enjoyment of any of the Acquired Assets shall be settled by arbitration before a panel of three (3) neutral arbitrators (selected from a panel of persons who are attorneys having experience with and knowledge of the pharmaceutical industry), in New York, New York and administered by the American Arbitration Association in accordance with its Commercial Arbitration Rules as then in effect. Any provisional or equitable remedy which would be available from a court of law shall be available

from the arbitrator. Judgment upon the award of the arbitrators may be enforced in any court having jurisdiction thereof. Any award rendered by the arbitrators shall be conclusive and binding upon the Parties hereto; *provided, however*, that any such award shall be accompanied by a written opinion of the arbitrators giving the reasons for the award. In making such award, the arbitrators shall be authorized to award interest on any amount awarded. This provision for arbitration shall be specifically enforceable by the Sellers and Purchaser and the decision of the arbitrators in accordance herewith shall be final and binding and there shall be no right of appeal therefrom.

(b) To the extent that arbitration may not be legally permitted and the Sellers and Purchaser do not at the time of such dispute or claim mutually agree to submit such dispute or claim to arbitration the Sellers or Purchaser may commence a civil action in a court of appropriate jurisdiction to solve disputes or claims hereunder. Nothing contained in this Section 7.13 shall prevent the Sellers and Purchaser from settling any dispute or claim by mutual agreement at any time.

(c) Neither Party shall be precluded by this Section 7.13 from seeking, from the courts of any jurisdiction, provisional or equitable remedies of a type not available in arbitration, including temporary restraining orders and preliminary or permanent injunctions, nor shall the pursuit of such provisional or equitable relief constitute a waiver or modification of such Party's right and obligation to arbitrate any related or unrelated dispute that is otherwise subject to arbitration under this Agreement, unless such waiver is expressed in writing and signed by such Party. In the event any Person not a Party to this Agreement shall commence any interpleader or similar action that either directly or indirectly raises issues that are subject to arbitration, the Sellers and Purchaser shall seek a stay of such proceedings pending arbitration in accordance with this Agreement.

(d) The Parties hereto acknowledge that a breach of this Section 7.13 would result in irreparable injury to the non-breaching Party, and the non-breaching Party will be entitled to seek equitable relief, including specific performance, to enforce the provisions of this Section 7.13.

(e) In the event of any Third Party Claim where the Indemnifying Party does not assume the defense of such Third Party Claim, nothing in this Section 7.13 shall prevent the Indemnified Party from impleading the Indemnifying Party or otherwise joining the Indemnifying Party to any litigation relating to such Third Party Claim.

SECTION 7.14 Consent to Jurisdiction; Service of Process. The Parties consent to the nonexclusive jurisdiction of the state courts of New York located in New York City in connection with any action arising out of or relating to this Agreement or, at the option of the Party bringing the action or proceeding, the federal courts located in New York City in the State of New York. The Parties agree that venue is proper in and waive any objection that they may now or in the future have to any action being brought in any of these courts, and agree not to plead or claim that any action brought in any of these courts has been brought in an inconvenient forum. The Parties further waive personal service of any summons, complaint or other process in connection with such action and agree that service may be made by any means permitted or prescribed in this Agreement for delivery of notices or by any means permitted by applicable law. Nothing contained in this Section 7.14 is intended to limit the applicability of Section 7.13. In the event of any conflict

between the provisions of this Section 7.14 and the provisions of Section 7.13, the provisions of Section 7.13 shall control.

[Remainder of page intentionally left blank; signature page follows.]

IN WITNESS WHEREOF, Purchaser and Sellers have duly executed this Agreement as of the date first written above.

PURCHASER:

WINGS THERAPEUTICS, INC.

By: /s/ Mark P. de Souza

Name: Mark P. de Souza

Title: President

SELLERS:

PROQR THERAPEUTICS I B.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: Managing Director, on behalf of ProQR
Therapeutics N.V.

PROQR THERAPEUTICS VII B.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: Managing Director, on behalf of ProQR
Therapeutics N.V.

PROQR THERAPEUTICS HOLDING B.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: Managing Director, on behalf of ProQR
Therapeutics N.V.

PARENT:

SOLELY FOR PURPOSES OF ARTICLE VI:

PROQR THERAPEUTICS N.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: CEO

Schedule 1.05(a)

[***]

Schedule 1.9

[***]

Disclosure Schedules

[***]

SUBSCRIPTION AGREEMENT

This **SUBSCRIPTION AGREEMENT** (this “Agreement”), dated as of May 22, 2019 (the “Effective Date”), is made by and between Wings Therapeutics, Inc., a Delaware corporation (the “Company”), and ProQR Therapeutics Holding B.V., a company organized under the laws of The Netherlands (“ProQR”).

RECITALS

WHEREAS, the Company desires to issue and sell to ProQR, and ProQR desires to acquire from the Company, [***] shares (the “Shares”) of the Company’s common stock, \$0.001 par value per share (“Common Stock”), which represent nineteen and nine-tenths percent (19.9%) of the Fully Diluted Shares (as defined below) as of the Effective Date.

NOW, THEREFORE, in consideration of the foregoing, the agreements set forth in this Agreement, and other good and valuable consideration, the adequacy and receipt of which are hereby acknowledged, the parties hereto hereby agree as follows:

1. Purchase and Sale of Shares; Anti-Dilution; Definitions.

a. Purchase and Sale of Shares. Subject to the terms and conditions hereof, the Company hereby issues and sells to ProQR, and ProQR hereby subscribes for and agrees to purchase from the Company, the Shares as partial consideration for the “Acquired Assets,” as defined in and contemplated by that certain Asset Purchase Agreement between the Company, ProQR and certain affiliates of ProQR, dated as of the date hereof (the “Asset Purchase Agreement”). Concurrently with, and as a condition precedent to, the execution of this Agreement the Company, ProQR, and certain stockholders of the Company shall enter into a Voting Agreement and a Right of First Refusal and Co-Sale Agreement (together, the “Shareholders Agreements”).

b. Anti-Dilution. In the event that the Company conducts one or more financings that involve a sale of any equity securities of the Company (such financing, a “Financing,” and such securities, the “Offered Securities”), then the Company shall issue to ProQR, for no additional consideration, that number of additional shares of Common Stock as is required for ProQR’s ownership of shares of Common Stock to be equal to nineteen and nine-tenths percent (19.9%) of the Fully Diluted Shares; provided, however, that no additional shares shall be issued to ProQR pursuant to this Section 1.b. once the Company has achieved the Financing Threshold (as defined below). For avoidance of doubt, if the Company achieves the Financing Threshold as a result of receiving proceeds in a particular Financing (whether such Financing is the first Financing or a subsequent Financing), then the Company shall issue to ProQR, for no additional consideration, that number of additional shares of Common Stock as is required for ProQR’s ownership of shares of Common Stock to be equal to nineteen and nine-tenths percent (19.9%) of the Fully Diluted Shares, which percentage shall be calculated as if such Financing resulted in the Company having raised in gross proceeds only the amount that is necessary to achieve

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH “[***]”. SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF DISCLOSED.

the Financing Threshold. All shares of Common Stock issued to ProQR pursuant to this Section 1.b. shall be duly authorized and validly issued and considered fully paid and nonassessable. All such shares of Common Stock shall be free and clear of all encumbrances created, imposed or suffered to be imposed by the Company.

c. The term “Financing Threshold” means the receipt by the Company of gross proceeds in the aggregate amount of [***] Dollars (\$[***] USD) through (A) the issuance and sale by the Company of any equity securities of the Company in one or more Financings; (B) the receipt of non-dilutive grant funding from any administrative agency of any country, state or locality; or (C) any combination of the foregoing.

d. The term “Fully Diluted Shares” means the sum of: (A) all of the issued and outstanding shares of Common Stock, preferred stock (calculated on an as-converted to Common Stock basis) and other capital stock or equity security of the Company (calculated on an as-converted to Common Stock basis); (B) any issued and outstanding security which is convertible, with or without consideration, into any Common Stock, preferred stock or other equity security of the Company; and (C) any issued and outstanding options and warrants to purchase Common Stock, preferred stock or other capital stock or equity security of the Company (calculated on an as-exercised, as- converted to Common Stock basis).

2. Representations.

a. Company Representations.

i. The Company is duly formed and validly existing under the laws of Delaware, with full power and authority to conduct its business as it is currently being conducted and to own its assets; and has secured any other authorizations, approvals, permits and orders required by law for the conduct by the Company of its business as it is currently being conducted.

ii. All corporate action required to be taken by the Company’s Board of Directors and stockholders in order to authorize the Company to enter into this Agreement and to issue the Shares has been taken. This Agreement constitutes a valid and legally binding obligation of the Company, enforceable against the Company in accordance with its terms except (i) as limited by applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, or other laws of general application relating to or affecting the enforcement of creditors’ rights generally, or (ii) as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies.

iii. The Shares have been duly authorized and, when issued, sold, and delivered in accordance with the terms of and for the consideration set forth in this Agreement, will be validly issued, fully paid and nonassessable.

iv. The Shares represent not less than nineteen and nine-tenths percent (19.9%) of the Fully-Diluted Shares.

b. ProQR Representations.

i. ProQR has full power and authority to enter into this Agreement. When executed and delivered by ProQR, this Agreement will constitute a valid and legally binding obligation of ProQR, enforceable in accordance with its terms, except (i) as limited by applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, or other laws of general application relating to or affecting the enforcement of creditors' rights generally, or (ii) as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies.

ii. ProQR does not presently have any contract, undertaking, agreement or arrangement with any person to sell, transfer or grant participations to such person or to any third person, with respect to any of the Shares, and ProQR has not been formed for the specific purpose of acquiring the Shares.

iii. ProQR has satisfied itself as to the full observance of the laws of its jurisdiction in connection with any invitation to subscribe for the Shares or any use of this Agreement, including (i) the legal requirements within its jurisdiction for the purchase of the Shares, (ii) any foreign exchange restrictions applicable to such purchase, (iii) any governmental or other consents that may need to be obtained, and (iv) the income tax and other tax consequences, if any, that may be relevant to the purchase, holding, redemption, sale, or transfer of the Shares. ProQR's subscription and payment for and continued beneficial ownership of the Shares will not violate any applicable securities or other laws of its jurisdiction.

iv. ProQR has been furnished with or has had access to all information it has requested from the Company and has had an opportunity to review the books and records of the Company and to discuss with management of the Company its business and financial affairs and has generally such knowledge and experience in business and financial matters and with respect to investments in securities of privately held development-stage companies so as to enable it to understand and evaluate the risks of such investment and form an investment decision with respect thereto.

v. ProQR has been advised and acknowledges that (i) the Shares have not been registered under the Securities Act of 1933, as amended (the "Securities Act", the securities laws of any state of the United States or the securities laws of any other country; (ii) in issuing and selling the Shares to ProQR pursuant hereto, the Company is relying upon the "safe harbor" provided by Regulation S promulgated under the Securities Act by the U.S. Securities and Exchange Commission ("SEC") for offers and sales of securities occurring outside the United States ("Regulation S"); (iii) it is a condition to the availability of the Regulation S safe harbor that the Shares not be offered, sold, assigned, transferred, pledged, encumbered or otherwise disposed of in the United States or to a U.S. Person or for the account or benefit of any U.S. Person until the expiration of a period of one year following the date hereof; and (iv) notwithstanding the foregoing, prior to the expiration of one year after the date hereof (the "Restricted Period"), the Shares may be offered and sold by the holder thereof only: (x) if the offer or sale is within the United States or to or for the account of a U.S. Person (as such terms are defined in Regulation S), the securities are

offered and sold pursuant to an effective registration statement or pursuant to Rule 144 under the Securities Act; (y) pursuant to an exemption from registration under the Securities Act; or (z) the offer and sale is outside the United States and to other than a U.S. Person as an offshore transaction in compliance with Regulation S. The foregoing restrictions are binding upon subsequent transferees of the Shares, except for transferees pursuant to an effective registration statement. As used in this Section, the term "United States" means and includes the United States of America, its territories and possessions, any State of the United States, and the term "U.S. Person" means: (i) a natural person (regardless of citizenship) resident in the United States; (ii) any partnership or corporation organized or incorporated under the laws of the United States; (iii) any estate or trust of which any executor, administrator or trustee is a U.S. Person; (iv) any agency or branch of a foreign entity located in the United States; (v) any nondiscretionary or similar account (other than an estate or trust) held by a dealer or other fiduciary for the benefit or account of a U.S. Person (whether or not the dealer or other fiduciary is a U.S. Person); (vi) any discretionary or similar account (other than an estate or trust) held by a dealer or other fiduciary organized, incorporated and (if an individual) resident in the United States; and (vii) a corporation or partnership organized under the laws of any jurisdiction other than the United States by a U.S. Person principally for the purpose of investing in securities that have not been registered under the Securities Act.

vi. ProQR (i) is domiciled and has its principal place of business outside the United States; and (ii) certifies it is not a U.S. Person and is not acquiring the Shares for the account or benefit of any U.S. Person. At the time of ProQR's execution of this Agreement, ProQR or persons acting on ProQR's behalf in connection herewith are located outside the United States; are not acquiring the Shares for the benefit of a U.S. Person nor with a view to the offer, sale or delivery, directly or indirectly, of such Shares within the United States or to a U.S. Person; did not receive the offer to purchase the Shares while it was in the United States; was not in the United States at the time such offer was accepted; and for the entire Restricted Period will continue to have full investment discretion with respect to the purchase, holding and disposition of the Shares. ProQR understands and agrees that all certificates evidencing any of the Shares whether upon initial issuance or upon any permitted transfer thereof, shall bear a legend, prominently stamped or printed thereon, reading substantially as follows:

"THE SHARES OF CAPITAL STOCK REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), OR ANY APPLICABLE STATE SECURITIES LAWS AND MAY NOT BE SOLD OR OTHERWISE TRANSFERRED BY ANY PERSON, INCLUDING A PLEDGEE, UNLESS (1) EITHER (A) A REGISTRATION WITH RESPECT THERETO SHALL BE EFFECTIVE UNDER THE SECURITIES ACT, OR (B) THE ISSUER SHALL HAVE RECEIVED AN OPINION OF COUNSEL SATISFACTORY TO THE ISSUER THAT AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT IS AVAILABLE, AND (2) THERE SHALL HAVE BEEN COMPLIANCE WITH ALL APPLICABLE STATE SECURITIES OR "BLUE SKY" LAWS."

vii. ProQR agrees that with respect to the Shares, until the expiration of the Restricted Period: (i) ProQR (including any agent or representative of the Purchaser) has not and will not solicit offers to buy, offer for sale or sell any of the Shares or any beneficial interest therein in the United States or to or for the account of a U.S. Person. ProQR has not engaged, nor is it aware that any party has engaged, and ProQR will not engage or cause any third party to engage in any directed selling efforts (as such term is defined in Regulation S) in the United States with respect to the Shares. ProQR is not a “distributor” (as defined in Regulation S) or a “dealer” (as defined in the Securities Act).

3. Miscellaneous.

a. Notices. All notices and other communications provided for herein shall be in writing and shall be deemed to have been duly given if delivered personally or sent by registered or certified mail, return receipt requested, postage prepaid to the following addresses (or such other address as either party shall have specified by notice in writing to the other):

If to the Company:

Wings Therapeutics, Inc.
2600 Tenth Street, #435
Berkeley, CA 94710
Attention: Mark P. de Souza, President
E-mail:

With a copy to:

Mintz Levin
One Financial Center
Boston, MA 02111
Attention: Lewis J. Geffen, Esq.
Email: [***]

If to ProQR:

ProQR Therapeutics Holding, B.V.
Zernikedreef 9
2333 CK Leiden
The Netherlands
Attention: Nico Bunnik
E-mail: [***]

With a copy (which shall not constitute notice) to:

Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210

Attn: Danielle M. Lauzon, Esq.
Email: [***]

b. Amendment. Neither this Agreement nor any provision hereof may be changed, waived, discharged or terminated orally or by course of dealing, but only by a statement in writing signed by the party against which enforcement of the change, waiver, discharge or termination is sought.

c. Parties in Interest. All the terms and provisions of this Agreement shall be binding upon and inure to the benefit of and be enforceable by the respective successors and assigns of the parties hereto, whether so expressed or not.

d. Headings. The headings of the sections and paragraphs of this Agreement have been inserted for convenience of reference only and shall not affect the meaning or interpretation of this Agreement.

e. Choice of Law. It is the intention of the parties that the internal laws, and not the laws of conflicts, of the State of Delaware should govern the enforceability and validity of this Agreement, the construction of its terms and the interpretation of the rights and duties of the parties hereto.

f. Counterparts. This Agreement may be executed in any number of counterparts, including by facsimile transmission, and by different parties hereto in separate counterparts, with the same effect as if all parties had signed the same document. All such counterparts shall be deemed an original, shall be construed together and shall constitute one and the same instrument.

g. Dispute Resolution. The parties (a) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of New York and to the jurisdiction of the United States District Court for the Southern District of New York for the purpose of any suit, action or other proceeding arising out of or based upon this Agreement, (b) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement except in the state courts of New York or the United States District Court for the Southern District of New York, and (c) hereby waive, and agree not to assert, by way of motion, as a defense, or otherwise, in any such suit, action or proceeding, any claim that it is not subject personally to the jurisdiction of the abovenamed courts, that its property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient forum, that the venue of the suit, action or proceeding is improper or that this Agreement or the subject matter hereof may not be enforced in or by such court.

h. Severability. If any term or provision of this Agreement is invalid, illegal or unenforceable in any jurisdiction, such invalidity, illegality or unenforceability shall not affect any other term or provision of this Agreement or invalidate or render unenforceable such term or provision in any other jurisdiction.

i. Entire Agreement. This Agreement, together with the Asset Purchase Agreement and the Shareholders Agreements, constitutes the entire agreement between the

Company and ProQR with respect to the subject matter hereof and supersedes all prior agreements and understandings related to such subject matter.

* * * * *

IN WITNESS WHEREOF, the parties hereto have duly executed this Subscription Agreement as of the date first written above.

COMPANY:

WINGS THERAPEUTICS, INC.

By: /s/ Mark de Souza

Name: Mark de Souza

Title: Chief Executive Officer

PROQR:

PROQR THERAPEUTICS HOLDING B.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer, o.b.o.

ProQR Therapeutics N.V.

Title: Managing Director

SIGNATURE PAGE TO SUBSCRIPTION AGREEMENT

SUPPLY AND SERVICES AGREEMENT

THIS SUPPLY AND SERVICES AGREEMENT is effective as of July 12th, 2019 (the “Effective Date”) and is made by and between ProQR Therapeutics IV B.V., having an office at Zernikedreef 9, 2333 CK Leiden, The Netherlands (“CUSTOMER”) and Nitto Denko AVECIA Inc. (“AVECIA”), having an office at 125 Fortune Boulevard, Milford, MA 01757. CUSTOMER and AVECIA are sometimes referred to herein individually as a “Party” and collectively as “Parties”.

Recital

CUSTOMER wishes to engage AVECIA as a manufacturer and supplier to CUSTOMER of clinical and commercial quantities of its product known by ProQR as internal product code QR-110, INN: sepofarsen, (“Product”), and AVECIA, having the requisite expertise, capability, experience, facilities and permits and authorizations, wishes to manufacture and sell Product, and provide related services, to CUSTOMER, all on the terms and conditions as set forth herein.

NOW, INTENDING TO BE LEGALLY BOUND, IT IS HEREBY AGREED as follows:

1. DEFINITIONS

The terms in this Agreement with initial letters capitalized or all letters capitalized, as applicable, whether used in the singular or plural, shall have the meaning set forth or cross referenced in this Section 1 below (and derivative forms of such terms shall be interpreted accordingly):

- 1.1 “Affiliate” means any person, corporation or other entity which Controls, is Controlled by or is under common Control with, a Party to this Agreement.
- 1.2 “Agreement” means this Supply Agreement with all attachments, as may be amended from time to time.
- 1.3 “Product Requirements” means the requirements established by or set forth in (a) GMP, (b) the Specifications, (c) this Agreement and (d) the Quality Agreement.
- 1.4 “Applicable Laws” means applicable laws and regulations of the (i) United States, (ii) the European Union and (iii) any other jurisdiction agreed to by AVECIA in the applicable Scope of Work.
- 1.5 “Applicable Price(s)” shall have the meaning set forth in Section 5.1.
- 1.6 “AVECIA” shall have the meaning set forth in the preamble to this Agreement.
- 1.7 “AVECIA Delivery Forecast” shall have the meaning set forth in Section 6.1.

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH “[***]”. SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF DISCLOSED.

- 1.8 “Batch” means a specific quantity of Product, as defined in the applicable Scope of Work that is intended to be of uniform character and quality and is produced during the same cycle of manufacture as defined by the applicable batch record.
- 1.9 “Capacity Limitation” means the manufacture of not more than [***] Batches of Product during any period of [***].
- 1.10 “Certificate of Analysis” or “CoA” means a document identified as such, that (a) is provided by AVECIA and signed by an employee designated by AVECIA as having responsibility for the issuance of such certificate certifying that the Specifications for Product have been met and that the testing methods applied to Product provide accurate results (i.e., a Certificate of Compliance) and (b) sets forth the analytical test results obtained from testing of a representative sample against the Specifications for the batch to be delivered. The CoA shall include, but not be limited to: Product name, lot number, Specifications, test results for the specific batch, a reference to the test method, date of manufacture, date of release and date for retesting.
- 1.11 “Confidential Information” means any technical, business, financial and other information disclosed (whether disclosed in writing, orally, by way of sample or by any other means and whether directly or indirectly) by either Party or any of its Representatives (the “Disclosing Party”) to the other Party or any of its Representatives (the “Receiving Party”).
- 1.12 “Control” means the power to vote more than 50% of the voting shares or other voting interests of a person.
- 1.13 “Contract Standard” shall have the meaning set forth in Section 3.4.
- 1.14 “CUSTOMER” shall have the meaning set forth in the preamble to this Agreement.
- 1.15 “CUSTOMER Demand Forecast” shall have the meaning set forth in Section 6.1.
- 1.16 “CUSTOMER Product Licensee” means any person or entity that is not an Affiliate of CUSTOMER and that is granted, directly or indirectly, a license or similar right to market or sell the Product.
- 1.17 “CUSTOMER’S Purchase Obligations” shall have the meaning set forth in Section 4.1.
- 1.18 “Delivery” shall have the meaning set forth in Section 7.2.
- 1.19 “Documentation” means the documents to be provided by AVECIA to CUSTOMER with each shipment of Product, including the Certificate of Analysis and Certificate of Compliance for such Product.
- 1.20 “Effective Date” shall have the meaning set forth in the preamble to this Agreement.
- 1.21 “Extended Term” shall have the meaning set forth in Section 2.1.
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- 1.22 “Facility” means AVECIA’s GMP manufacturing facility located in Milford, MA or Cincinnati, Ohio, as the case may be.
- 1.23 “FDA” means the U.S. Food and Drug Administration, or any successor entity thereto.
- 1.24 “Firm Take or Pay Obligation(s)” shall have the meaning set forth in Section 6.3.
- 1.25 “GMP” or “cGMP” means current good manufacturing practice and standards as defined by ICH Q7 and the current Good Manufacturing Practices as established in the United States Code of Federal Regulations (the “CFR”), EudraLex Volume 4, PIC’S, the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines), and with the agreement of AVECIA, other comparable laws and regulations of any competent regulatory authority applicable to Product and its manufacture.
- 1.26 “Independent Intellectual Property” shall have the meaning set forth in Section 16.1.
- 1.27 “Intellectual Property” means patents, patent applications, all provisional, divisional, continuations, renewals, continuations-in-part, re-examinations, patents of additions, supplementary protection certificates, extensions, letters of patent, registration or confirmation patents and reissues with respect to any patents described in the foregoing clauses, any Know- How, data, technology, copyrights, industrial property and technical information.
- 1.28 “Know-How” means non-patented proprietary information, inventions, discoveries, designs, developments, techniques, materials, processes, manufactures, compositions of matter or methods of use and trade secrets, whether or not patentable or copyrightable.
- 1.29 “Latent Defect” shall have the meaning set forth in Section 8.2.
- 1.30 “Launch Date” means the date of the first commercial sale of Product after approval of the FDA.
- 1.31 “Party” shall have the meaning set forth in the preamble to this Agreement.
- 1.32 “Permits” shall have the meaning set forth in Section 10.1.
- 1.33 “PPI” and “PPI Adjustment” shall have the meanings set forth in Section 5.2.
- 1.34 “PPQ-Activities” shall have the meaning set forth in Section 3.4.
- 1.35 “Pre-PPQ Activities” shall have the meaning set forth in Section 3.3.
- 1.36 Pre-PPQ Scope of Work shall have the meaning set forth in Section 3.3
- 1.37 “Product” shall mean CUSTOMER’S product known as QR-110.
- 1.38 “Quality Agreement” means the Quality Agreement between AVECIA and CUSTOMER dated on or around the Effective Date and relating to Product.
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- 1.39 “Regulatory Authority” means the FDA and/or the EMA and, if applicable and agreed to in writing by CUSTOMER and AVECIA, any other instrumentality of any country or region outside the U.S.A, that performs a function for such country or region similar to the function of the FDA with regard, among other things, to the approval, licensing, registration or authorization to manufacture, promote, market, distribute, use, store, import, transport or sell a drug product in a defined territory or political or economic subdivision.
- 1.40 “Representative” means, with respect to each Party, each of such Party’s Affiliates, and each of the directors, officers, managers, employees, agents or other authorized representatives of such Party and its Affiliates.
- 1.41 “Retention Samples” shall have the meaning set forth in Section 7.3.
- 1.42 “Scope of Work” means any document referred to as a Scope of Work in Section 3.
- 1.43 “Services” means those services, including, without limitation, the manufacture of Product, set forth in the Scope of Work.
- 1.44 “Specifications” means the specifications for Product set forth in the applicable Scope of Work and/or Quality Agreement, as such may be modified in writing from time to time by CUSTOMER.
- 1.45 “Term” shall have the meaning set forth in Section 2.1 and “Initial Term” shall have the meaning set forth in Section 2.1.
- 1.46 “Territory” means worldwide.
- 1.47 “Third Party Infringement Claim” shall have the meaning set forth in Section 16.3.
- 1.48 “Transfer Taxes” shall have the meaning set forth in Section 5.3.
- 1.49 “Volume Requirements” means all requirements in the Territory for Product of CUSTOMER and, if applicable, its Affiliates and CUSTOMER Product Licensees during the Term.
2. TERM
- 2.1 This Agreement is effective as of the Effective Date and shall remain in effect for a period of ten (10) years from the Launch Date (the “Initial Term”), unless terminated earlier in accordance with Sections 8.7, 13.3 or 14 hereof. [***].
3. SCOPE OF WORK
- 3.1 The Parties have developed and agreed to the Scopes of Work attached hereto as Attachment 2, and may develop and agree to further Scope(s) of Work relating to Product that may be attached hereto. Pricing for the Services shall be set forth in each Scope of Work. Any changes to any Scope of Work will be accomplished through Change Orders
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(as defined below) or a new Scope of Work, as agreed to by the Parties. AVECIA shall meet the schedule of deliverables in each Scope of Work. If any of the project assumptions in the Scope of Work are incorrect, the timing, required resources, price and deliverables may have to be adjusted as mutually agreed to be the Parties.

- 3.2 Either Party may recommend changes to the Scope of Work for consideration of the other Party (a “Change”). In the event of a Change, AVECIA shall be responsible for providing a written assessment of (i) estimated costs that would be incurred resulting from the Change, (ii) the estimated time of implementing such Change and (iii) any resulting change in timing and delivery of Product, Services or other deliverables under the Scope of Work (each such assessment (a “Change Order”). Upon CUSTOMER’S written approval of the Change Order, AVECIA shall implement the Change Order.
- 3.3 Prior to the execution of this Agreement by the Parties, the Parties entered into that certain Proposal entitled “Pre-PPQ Activities to Support QR-110 PPQ Program”, a copy of which is attached hereto as Attachment 1 (the “Pre-PPQ Scope of Work”), whereby AVECIA performs for Client the pre-PPQ activities set forth therein (the “Pre-PPQ Activities”). For purposes of clarity, the Pre-PPQ Activities performed before and after the Effective Date shall be solely governed by the terms of this Agreement.
- 3.4 AVECIA acknowledges that time is of essence for the Pre-PPQ Activities as well as the PPQ activities set forth in the Scope of Work entitled “QR-110 PPQ activities and Process Performance Qualification Batches” (all such activities, together with the Pre-PPQ Activities (the “PPQ Activities”). AVECIA, therefore, shall use reasonable best commercial efforts (the “Contract Standard”) to perform the PPQ Activities substantially in line with the GANTT chart contained in the Pre-PPQ Scope of Work, as it may be amended by the Parties from time to time. More specifically, AVECIA shall use reasonable best commercial efforts to meet the following Pre-PPQ Scope of Work Timelines:

- Pre-PPQ manufacturing (under GMP): start batch record preparation on [***] and deliver certificate of analysis on or before [***]
- PPQ batch release: deliver certificate of analysis on or before [***]
- Process Qualification report is made available to ProQR on or before [***]

If, at any time, ProQR believes that AVECIA is not using its reasonable best commercial efforts in the performance of the PPQ Activities, AVECIA, at ProQR’s request and as early as mutually possible, shall meet with representatives of ProQR to address any concerns that ProQR may have with respect to AVECIA’s efforts, and if applicable, AVECIA shall take any steps reasonably appropriate to ensure that AVECIA’s performance is at the Contract Standard.

- 3.5 [***].
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- 3.6 For the avoidance of doubt, Batches of Product manufactured as “Commercial Validation Batches” pursuant to Scopes of Work under this Agreement, shall be considered Products sold under this Agreement and shall in all aspects be subject to the applicable standards of this Agreement.
- 3.7 With respect to clinical supply of the Product and other compounds, the parties acknowledge that prior to the Effective Date, CUSTOMER has been purchasing from AVECIA and AVECIA has been supplying to CUSTOMER on an ad hoc basis via individual quotations and purchase orders certain quantities of such products for clinical purposes. The parties hereby agree that CUSTOMER may continue to purchase such clinical materials and AVECIA will continue to supply to CUSTOMER such clinical materials through the same mechanism of ad hoc proposals requested by CUSTOMER and provided by AVECIA (with previously negotiated terms and conditions as set forth in the master service agreement or referenced therein) and at comparable, reasonable pricing levels.
- 3.8 Attachment 3 to this Agreement contains the Collaboration Manual which shall govern the interactions and communication between Parties in relation to all aspects of this Agreement. Parties shall adhere to the provisions of the Collaboration Manual. In case of any conflict between the Collaboration Manual and this Agreement, the terms of this Agreement shall prevail.
- 3.9 all adhere to the provisions of the Collaboration Manual. In case of any conflict between the Addendum A and this Agreement, the terms of this Agreement shall prevail.
4. PURCHASE OF VOLUME REQUIREMENTS; AFFILIATES AND CUSTOMER PRODUCT LICENSEES; CAPACITY ALLOCATION
- 4.1 Subject to the terms and conditions of this Agreement and the Capacity Limitation, CUSTOMER shall, and shall require its Affiliate(s) and any CUSTOMER Product Licensee(s) to, purchase from AVECIA (i) during the first five years of the Initial Term, all of their respective Volume Requirements, and (ii) during the remainder of the Initial Term and during any Extended Term, at least fifty percent (50)% of their respective Volume Requirements (iii) (the quantity of Product required to be purchased by CUSTOMER under clauses (i) and (ii) called “CUSTOMER’S Purchase Obligations”). CUSTOMER, its Affiliates and CUSTOMER Product Licensees may purchase Product in excess of CUSTOMER’S Purchase Obligations from third parties.
- 4.2 [***].
- 4.3 [***].
- 4.4 [***].
- 4.5 [***].
5. PRICE
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- 5.1 The price to be paid to AVECIA for Services, including the price for quantities of Product that are Delivered in accordance with all applicable terms and conditions of this Agreement, shall be as set forth in the Scope of Work (the “Applicable Prices”) The Applicable Prices for Product shall be adjusted as set forth in Section 5.2.
- 5.2 [***].
- 5.3 The prices chargeable to CUSTOMER, its Affiliate(s) and CUSTOMER Product Licensee(s) exclude any applicable sales, use, consumption, value added or excise taxes duties, tariffs and other similar assessments which may be imposed by any governmental authority on the sale to CUSTOMER (other than with respect to any income, corporate or similar taxation on AVECIA) (“Transfer Taxes”); provided, however, that the Parties shall cooperate and take any reasonable steps necessary to reduce or eliminate any Transfer Taxes.
6. FORECASTS AND ORDERS FOR POST LAUNCH PRODUCT
- 6.1 Subject to the Capacity Limitation and beginning on the first day of the calendar quarter during which the Launch Date occurs, and within [***] after the end of each subsequent six (6) month period during the Term or on the next business day if such [***] is on a holiday or weekend, CUSTOMER shall provide to AVECIA a written forecast of CUSTOMER’S Delivery requirements for Product during the thirty-six (36) months beginning as of calendar quarter following the calendar quarter in which such forecast is submitted (each, a “CUSTOMER Demand Forecast”). (For example, the CUSTOMER Demand Forecast which would be issued between [***] would be for the period that starts [***].) Within [***] of AVECIA’s receipt of a CUSTOMER Demand Forecast, AVECIA will provide to CUSTOMER a forecast showing AVECIA’s Delivery of the API for at least the first twelve (12) months of such CUSTOMER Demand Forecast (each, an “AVECIA Delivery Forecast”).
- 6.2 The forecasted quantities with respect to each of the first twelve (12) months of the CUSTOMER Demand Forecast shall constitute a firm commitment by CUSTOMER to purchase (a “Firm Take or Pay Obligation”, as defined in Section 6.3 below) and a firm commitment of AVECIA to Deliver at least 100% of such forecasted amount during such twelve-month period. [***].
- 6.3 [***].
- 6.4 [***].
7. RELEASE; DELIVERY; STORAGE; TITLE
- 7.1 In accordance with the Quality Agreement, AVECIA shall test and release or cause to be tested and released by third party testing facilities specified in the Quality Agreement and audited by AVECIA, the Product manufactured pursuant to this Agreement. AVECIA shall deliver to CUSTOMER a Certificate of Analysis for Product in accordance with the Quality Agreement.
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- 7.2 Product will be delivered Ex Works (INCOTERMS 2010) AVECIA's facilities at Cincinnati, Ohio ("Delivery"). Title and risk of loss in Product shall pass to CUSTOMER, its Affiliate or CUSTOMER Product License, as the case may be, at the time at which the applicable Product is made available for CUSTOMER'S, its Affiliate's or CUSTOMER Product Licensee's designated carrier at the Facility, or at the time the Product is taken into storage by AVECIA in accordance with, and as specified in, any applicable Scope of Work for storage services.
- 7.3 AVECIA shall properly store and retain appropriate samples (identified by batch number) of the API that its supplies under this Agreement in conditions and for times consistent with all Product Requirements and to permit appropriate or required internal regulatory checks and references (collectively, the "Retention Samples").
- 7.4 CUSTOMER understands and agrees that the Product supplied to CUSTOMER shall be packaged in standard sized containers as agreed to by the Parties in the applicable Scope of Work and/or the Quality Agreement, and that, as such, the quantity of Product supplied in response to any order may vary marginally from the quantity of Product so ordered by reason of the package size.
8. INVOICING; ACCEPTANCE AND PAYMENT:
- 8.1 Invoices for Services shall be provided by AVECIA to CUSTOMER in accordance with the applicable provisions of the Scope of Work. Each invoice for Services shall be provided by email (with confirmation of receipt) to [***] and, absent a then existing good faith dispute, shall be due and payable within [***] of CUSTOMER'S, its Affiliates' or its CUSTOMER Product Licensees', as applicable, receipt thereof. Invoices for Product supplied under this agreement will be [***]% due [***] before the manufacturing start date for a batch and [***]% on Acceptance of such Product in accordance with Sections 8.2 and 8.3.
- 8.2 Commencing upon the receipt of delivery of any Product to CUSTOMER and CUSTOMER'S receipt of the applicable Certificate of Analysis and the applicable compliance certificates, CUSTOMER shall have [***] to determine if (i) the quantity of Product so delivered is less than the quantity required to be delivered to CUSTOMER or (ii) the corresponding Product fails to conform to the Product Requirements in any ways that are reasonably detectable through the performance of standard testing and inspections protocols and an additional [***] after the discovery of any Latent Defects in such Product. For the purposes of this Section 8.2, a "Latent Defect" means an impurity or other characteristic of the applicable Product which is unknown and not reasonably apparent to CUSTOMER and not reasonably discoverable through the performance of standard testing and inspection protocols and whose introduction is attributable to AVECIA.
- 8.3 If CUSTOMER fails to notify AVECIA within the [***] time period specified in Section 8.2 that such Product does not conform to the Product Requirements, then CUSTOMER shall be deemed to have accepted such Product ("Product Acceptance") and waived its right to revoke acceptance, except for Latent Defects. In case of a Latent Defect, if
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CUSTOMER fails to notify AVECIA within the [***] day time period specified in Section 8.2 that such Product does not conform to the Product Requirements, then CUSTOMER shall be deemed to have waived its right to revoke acceptance in relation to such Latent Defect.

- 8.4 If CUSTOMER believes that (i) the quantity of Product so delivered is less than the quantity required to be delivered to CUSTOMER or (ii) Product does not conform to the Product Requirements, CUSTOMER (a) shall give written notice to AVECIA either documenting such shortage or specifying the manner in which such Product does not conform to the Product Requirements and (b), shall have the right to withhold payment of the applicable Delivery Invoice. In the event AVECIA accepts such determination, AVECIA shall (i) in case of a shortage, process free of charge sufficient Product to make up such shortage or (ii) in case of non-conformance with the Product Requirements, either, at CUSTOMER'S discretion, (a) replace the defective Product and dispose of the defective Product at AVECIA's own cost, or (b) refund any amounts paid in relation to the Product concerned.
 - 8.5 If a dispute arises between the Parties as to any failure of Product to meet the Product Requirements which cannot be resolved by the Parties within [***] of CUSTOMER notifying AVECIA of pursuant to Section 8.2, either CUSTOMER or AVECIA shall be entitled to require that the matter in dispute be referred to an independent laboratory nominated by agreement of the Parties. Such referral shall be solely for the purpose of establishing whether or not there is any failure of the relevant Product delivered by AVECIA to CUSTOMER to meet the Product Requirements. The decision of such independent laboratory shall be binding upon the Parties and the Party against which the decision is made shall be responsible for the costs of the independent laboratory. If the decision of such independent laboratory shows that AVECIA failed to supply Product in accordance with the Product Requirements, then AVECIA shall process free of charge sufficient Product to make up such shortage or replace the defective Product and shall dispose of the defective Product at its own cost.
 - 8.6 In the event of the sale of Product to an Affiliate or CUSTOMER Product Licensee as provided in this Agreement, the provisions of this Section 8.2 through Section 8.5 shall be applicable to any such Affiliate or CUSTOMER Product Licensee.
 - 8.7 CUSTOMER will promptly notify AVECIA of any relevant new or changed specifications or requirements for Product or the manufacture thereof, whether required by a Regulatory Authority or otherwise. Subject to the remaining sentences of this Section 8.7, AVECIA will implement such new or changed specifications or requirements as soon as practicable. In the event that the implementation of any such new or changed specifications or requirements results in additional costs to AVECIA, either on a one-time or ongoing basis, CUSTOMER will reimburse AVECIA for such reasonable additional costs by a reasonable and appropriate adjustment to the Applicable Price or as otherwise agreed to by the Parties. If AVECIA is unwilling to agree to any such change in specifications, then CUSTOMER may immediately begin a technology transfer with a third-party supplier of CUSTOMER'S choice, and CUSTOMER will be
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immediately relieved of [***] hereunder and may immediately terminate this Agreement upon written notice to AVECIA.

- 8.8 In the event AVECIA believes a recall, field alert, Product withdrawal or field correction (“Recall”) may be necessary with respect to any Product provided under this Agreement, AVECIA shall immediately notify CUSTOMER in writing. AVECIA will not act to initiate a Recall without the express prior written approval of CUSTOMER, unless otherwise required by Applicable Laws. In the event CUSTOMER believes a Recall may be necessary with respect to any Product provided under this Agreement, CUSTOMER shall immediately notify AVECIA in writing and AVECIA shall provide all necessary cooperation and assistance to CUSTOMER. The cost of any Recall shall be borne by CUSTOMER and CUSTOMER shall compensate for expenses incurred with any Recall, in each case unless such Recall is due to a breach of any warranty of AVECIA under this Agreement, in which case AVECIA, subject to the limitation of liability provisions of Section 11.4, shall bear the full costs of the Recall as well as the costs for replacement of the Product concerned or a refund in accordance with section 8.4 as applicable to a Latent Defect.
9. QUALITY AGREEMENT
- 9.1 The Quality Agreement in support of this Agreement is attached hereto as Attachment 4 and incorporated herein by reference. In case this Agreement is executed, and activities hereunder are commencing, before the execution of the Quality Agreement, the most recent quality agreement executed between AVECIA and CUSTOMER or any of its Affiliates shall govern such activities until the Quality Agreement is executed.
10. REPRESENTATIONS AND WARRANTIES
- 10.1 AVECIA represents and warrants to CUSTOMER as follows: (i) all Product sold hereunder conforms to, and has been produced in accordance with, the Product Requirements; (ii) AVECIA is in material compliance with during the Term of this Agreement, all Applicable Laws, including, without limitation, all permits, licenses and other authorizations with respect thereto (the “Permits”), (iii) AVECIA shall conduct all Services in accordance with all Applicable Laws and the Product Requirements; (iv) no person performing services on behalf of AVECIA under this Agreement has been debarred under Section 306 of the United States Federal Food, Drug and Cosmetic Act or convicted of a crime for which a person can be debarred under Section 306 of the United States Federal Food, Drug and Cosmetic Act; (v) manufacture of Product will be performed consistent with standards then customary in the oligonucleotide industry, and, in any event, with at least the degree of care and quality that AVECIA uses to perform similar activities for other parties; (vi) AVECIA has freedom to operate with respect to the manufacturing process for the Product, and AVECIA’s use of its Intellectual Property in the performance of this Agreement and the manufacturing process applied will not infringe the Intellectual Property or other rights of any third party; and (vii) AVECIA has in place an information security program (including physical security of physical items) that is reasonably designed to ensure the security of confidentiality of, and to protect against any anticipated hazards to the security or integrity of any CUSTOMER’S
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Confidential Information, and to protect against unauthorized access to or use of such CUSTOMER'S Confidential Information. This representation shall not be read to limit AVECIA's obligation to indemnify CUSTOMER under clause (ii) of Section 11.1.

- 10.2 CUSTOMER represents and warrants to AVECIA that, to the best of CUSTOMER'S knowledge, AVECIA's use of CUSTOMER'S Intellectual Property in the performance of this Agreement will not infringe the Intellectual Property or other rights of any third party. This representation shall not be read to limit CUSTOMER'S obligation to indemnify AVECIA under clause (ii) of Section 11.2.
- 10.3 EXCEPT AS EXPRESSLY PROVIDED HEREIN, NEITHER PARTY MAKES ANY WARRANTY OF ANY KIND, EXPRESS, IMPLIED, STATUTORY OR OTHERWISE, WITH RESPECT TO THE SUBJECT MATTER OF THIS AGREEMENT.
11. INDEMNIFICATION; LIABILITY; INSURANCE
 - 11.1 [***].
 - 11.2 [***].
 - 11.3 Each Party's agreement to indemnify, defend and hold harmless the other is conditioned on the indemnified Party (i) providing written notice to the indemnifying Party of any claim, demand or action arising out of the indemnified activities within [***] after the indemnified Party has knowledge of such claim, demand or action, provided that the failure to so notify the indemnifying Party will not relieve the indemnifying Party of its obligations hereunder except to the extent such failure shall have actually materially prejudiced the indemnifying Party; (ii) permitting the indemnifying Party to assume full responsibility to investigate, prepare for and defend against any such claim, demand or action; (iii) assisting the indemnifying Party, at the indemnifying Party's reasonable expense, in the investigation, preparation, and defense of any such claim, demand or action; (iv) undertaking reasonable steps to mitigate any loss, damage or expense with respect to the applicable claim, demand or action; and (v) not settling such claim, demand or action without the indemnifying Party's prior written consent.
 - 11.4 Notwithstanding anything to the contrary set forth herein and except for (i) any liability for bodily injury or death caused by AVECIA's gross negligence or willful misconduct, (ii) AVECIA's breach of the representation and warranty set forth in Section 10.1(vi), (iii) breaches of Section 15 or Section 16 of this Agreement, (iv) liability arising in connection with AVECIA's indemnification obligations hereunder, or (v) any equitable or injunctive relief granted to CUSTOMER, CUSTOMER'S exclusive remedy under this Agreement shall be for damages and AVECIA's per-claim liability for any such damages, shall in no event exceed [***] percent ([***]%) of the aggregate amount paid or payable by CUSTOMER for the Product and Services under the applicable Scope of Work at the time of such claim. In no event shall either Party be liable to the other for special, incidental, punitive or consequential damages, whether the claim is in contract, negligence, strict liability or otherwise, except (a) as and to the extent that such special,

incidental, punitive or consequential damages are imposed on either Party as part of the damages covered by indemnification hereunder, in which case the indemnification obligation will cover and include such damages as and to the extent provided; (b) for any liability for bodily injury or death caused by a Party's gross negligence or willful misconduct; or (c) for a breach by a Party of Section 15 (Confidentiality) of this Agreement.

- 11.5 Each Party will, at its own expense, maintain throughout the Term and for a minimum period of [***] thereafter (a) product liability and general liability insurance with limits of \$[***] per occurrence and in the annual aggregate and (b) workers' compensation insurance with not less than the minimum coverage required by applicable law. Each Party shall provide to the other Party, upon request, evidence that such insurance coverage is in effect by providing a duly signed certificate of insurance issued by the applicable insurance company or companies. The Parties shall have purchased such insurance from an insurance company or companies with an A.M. Best rating of A- or better.
12. REGULATORY; FACILITY ACCESS; AUDITS
- 12.1 AVECIA shall be responsible for obtaining at its own expense all permissions, licenses and approvals necessary to discharge its obligations under this Agreement, and shall ensure compliance with any applicable Environment, Health and Safety requirements. AVECIA shall comply with all Applicable Laws and GMP relating to the manufacture of Product and shall keep all documentation and records as required by such Applicable Laws or GMP. AVECIA shall promptly furnish to CUSTOMER such information and documentation as CUSTOMER may reasonably request relating to any regulatory filings or submissions for Product. CUSTOMER shall provide to AVECIA a copy of all proposed submissions to any regulatory agency that directly relate to the manufacture of Product hereunder for AVECIA's review and verification.
- 12.2 Subject to reasonable obligations of confidentiality, CUSTOMER has the right to have one or more Representatives at the Facility during manufacturing of Product and related activities, including, without limitation, access to the review of all batch records and any other relevant documents.
- 12.3 CUSTOMER shall have the rights to conduct, upon reasonable notice and at its own expense, periodic technical, quality, IT, data management, and environmental health and safety audits. AVECIA shall give reasonable access (under normal circumstances, considered to be [***) to CUSTOMER for purposes of auditing the Facility and any records that AVECIA is required to keep under this Agreement. Generally, [***)' notice shall be reasonable, but immediate access shall be permitted in case of rejections or emergency conditions. Notwithstanding the above, AVECIA shall permit CUSTOMER to have such access at additional times with AVECIA's approval, upon the giving of [***)' notice, to accommodate actual or potential licensees or collaborators of CUSTOMER. All visitations of the Facility by CUSTOMER, its representatives, potential licensees or collaborators shall be subject to reasonable obligations of confidentiality and any reasonable requirements of AVECIA relating to health and safety.
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- 12.4 AVECIA will promptly advise CUSTOMER if any regulatory agency intends to inspect the Facility and the nature of the inspection. CUSTOMER shall have the right to have up to two of its Representatives on site during any such inspection relating to the manufacture of Product. AVECIA shall promptly provide a report to CUSTOMER of any Product-related results of such inspection, as well as of any major findings (including at the minimum any finding that would trigger issuance of a FDA 483 or any equivalent thereof) in relation to the Facility. AVECIA, in its sole discretion, will determine the extent of CUSTOMER'S participation in any such inspection, provided that AVECIA shall not withhold reasonable participation of CUSTOMER insofar the inspection relates to the manufacture of the Product. In addition, AVECIA shall also promptly notify CUSTOMER of any notice of any deficiencies by any regulatory agency, and provide to CUSTOMER unredacted copies (except as provided below) of any FDA 483(s) and Establishment Inspection Reports or their equivalents issued as a result of said inspection and any follow-up written communications between AVECIA and the relevant regulatory agency; provided however, before providing such reports or FDA 483(s) to CUSTOMER, AVECIA may redact any confidential information of a third party from such reports or FDA 483(s). AVECIA will promptly and diligently and use best efforts to take appropriate actions to rectify and correct any deficiencies or non-compliance identified by any inspection or audit by any governmental authority or CUSTOMER, in a timely manner. AVECIA shall implement any procedures necessary to avoid repetition of such deficiencies or non-compliance.
- 12.5 AVECIA shall cooperate with CUSTOMER, free of charge, except for out-of-pocket expenses, to satisfy regulatory requirements regarding the Product within the jurisdictions of the United States of America and the European Union. AVECIA shall cooperate with CUSTOMER to satisfy regulatory requirements regarding the Product in any other jurisdictions and the Parties will agree on a plan and budget for such other jurisdictions. CUSTOMER will reimburse AVECIA based on such plan and budget. Such cooperation shall include the providing of reasonable regulatory support, including, but not be limited to, AVECIA providing to CUSTOMER all data and information reasonably necessary for preparation of CMC/CTD documents and assistance in the review of such documents
- 12.6 All approvals arising out of the matters addressed in Section 12.5 shall be in the name of CUSTOMER, and all related documentation and materials shall be the sole property of CUSTOMER; provided, however, that, subject to the confidentiality obligations of Section 14 and the terms and conditions of this Agreement, AVECIA shall have the right to retain copies of any such documentation which relate to the API provided to CUSTOMER pursuant to this Agreement.
13. FORCE MAJEURE
- 13.1 Neither Party is liable for any failure to perform or delay in performing any obligations under this Agreement, if such failure or delay is due to causes beyond the reasonable control of such defaulting Party, which may include fire, flood, war, embargo, legal prohibition, terrorism, insurrection, regulatory delay or any other cause beyond the reasonable control of such defaulting Party. The Party so affected will, upon giving notice thereof to the other party, be excused from such performance to the extent of such
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prevention, restriction or delay. The affected Party is obligated to use its commercially reasonable efforts to avoid or to remove such causes of non-performance and to continue performance with the utmost dispatch whenever such causes are removed.

- 13.2 For clarity, CUSTOMER shall not be entitled to relief under this Section 13 with respect to any Firm Take or Pay Obligations existing immediately prior to the time of any event covered by Section 13.1. Neither Party shall be entitled to relief under this Section 13 for any delay or failure in performing any of its payment obligations under this Agreement.
 - 13.3 Notwithstanding the foregoing, if CUSTOMER fails to maintain, through no fault of its own, the requisite regulatory approval for commercial sale of Product in the United States of America, and (if such regulatory approval previously has been obtained by CUSTOMER) the European Union, (i) CUSTOMER may terminate this Agreement upon written notice to AVECIA and (ii) and, in such case, CUSTOMER shall pay to AVECIA, within thirty (30) days of such termination, an amount equal to the aggregate Applicable Prices of Product which is included within the Firm Take or Pay Obligation as of the date of such termination. Further, if CUSTOMER fails to maintain, through no fault of its own, the requisite regulatory approval previously obtained by CUSTOMER for commercial sale of Product in any one of the jurisdictions of (x) the United States of America, (y) the European Union and (z) any other jurisdiction within the Territory, CUSTOMER may adjust the then applicable CUSTOMER Demand Forecast to reflect the demonstrable reduction in Volume Requirements by reason of such failure to maintain such regulatory approval within any such jurisdiction.
 14. TERMINATION; CONSEQUENCES OF TERMINATION
 - 14.1 Without prejudice to any other rights or remedies which may be available to a Party, this Agreement may be terminated at any time by mutual agreement of both Parties in writing.
 - 14.2 Without prejudice to any other rights or remedies which may be available to them, either Party may terminate this Agreement upon written notice of termination to the other Party if the other commits a material breach of any of the provisions of this Agreement; and, in the case of a breach capable of being remedied, fails to remedy that breach within [***] of receiving written notice specifying that breach and requiring the same to be remedied.
 - 14.3 CUSTOMER may terminate this Agreement upon written notice:
 - (i) if CUSTOMER no longer continues the development or commercialization programs relating to the Product; or
 - (ii) in the event of a Supply Failure;
 - 14.4 Except in the case that CUSTOMER terminates this Agreement pursuant to Sections 8.7 or 14.2, CUSTOMER shall be liable to AVECIA for all Firm Take or Pay Obligations in effect as of the date of termination of this Agreement.
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- 14.5 Without prejudice to any other rights or remedies which a Party may have, upon the termination of this Agreement, howsoever the same occurs, each Party shall (i) promptly pay to the other all sums which at the date of termination are due and payable to the other hereunder, including ; (ii) except as stated to the contrary in Section 16 regarding each Party's rights to Intellectual Property, immediately cease all use of any property of the other, including without limitation any Intellectual Property of the other; and (iii) at the expense of the requesting Party, promptly return to the other Party, or certify to the other Party the destruction of, any property or Confidential Information of the other in its possession, custody or control, provided however (x) each Party may retain one (1) copy of the other Party's Confidential Information in its secure files solely for the purpose of monitoring compliance with the terms of this Agreement and (y) CUSTOMER shall have the right to retain and use such Confidential Information of AVECIA which is reasonably required for the continued exercise of any rights or licenses granted to CUSTOMER which survive the termination or expiration of this Agreement. The terms of Section 15 (Confidentiality) of this Agreement will apply to such post-termination retention or use of Confidential Information.
- 14.6 Subject to the other Sections of this Article 14 and except in the event that CUSTOMER terminates this Agreement pursuant to Section 14.2, upon termination of this Agreement, CUSTOMER (x) shall purchase from AVECIA all amounts of API which have been manufactured in accordance with all Product Requirements and other applicable terms of this Agreement but not yet delivered and (y) shall pay to AVECIA for any remaining inventory of raw materials and supplies relating to manufacture of Product, and AVECIA shall promptly deliver to CUSTOMER or destroy all such inventory, at CUSTOMER'S expense as directed by CUSTOMER in writing.
- 14.7 All terms of this Agreement applicable to Product required to be supplied under this Agreement or Delivery thereof remain applicable after termination of this Agreement whether the actual Delivery occurs before or after termination of this Agreement.
- 14.8 In case of termination of this Agreement, other than termination by AVECIA pursuant to Section 14.2, and at any moment between the applicable notice of termination and the termination effective date, CUSTOMER shall have the right, exercisable by written request to AVECIA, to a technology transfer to CUSTOMER or a contract manufacturer of CUSTOMER'S choice, of any technology, information and data as CUSTOMER or its designee may reasonably require in order to manufacture the Product, and AVECIA will cooperate in good faith with such a technology transfer without undue delay, subject, except in the case of termination by CUSTOMER pursuant to Section 14.2, to CUSTOMER'S reimbursement of AVECIA of its reasonable costs incurred for such technology transfer.
15. CONFIDENTIALITY
- 15.1 In consideration of the Disclosing Party (either AVECIA or CUSTOMER or their respective Representative, as the case may be) disclosing Confidential Information to the Receiving Party (either AVECIA or CUSTOMER or their respective Representative, as the case may be), the Receiving Party agrees to maintain confidential all such
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Confidential Information and it will accordingly not use or disclose any of the Confidential Information in whole or in part except for the purposes exercising its rights and performing its obligations under this Agreement. If the Confidential Information disclosed is personal data (including sensitive personal data) as defined by applicable privacy or data protection laws (“Personal Data”), the Disclosing Party consents to the Receiving Party processing such Personal Data for purposes of its activities under this Agreement and, to the extent the Personal Data relates to third parties, confirms that it has the consent of each such third parties to provide such Personal Data to the Recipient to process for such purposes. The Receiving Party shall handle all Personal Data in accordance with the Applicable Laws.

15.2 Confidential Information does not include information that:

15.2.1 the Receiving Party can prove with competent written evidence was already in its possession and at its free disposal, without burden of confidentiality, before the disclosure to it by the Disclosing Party;

15.2.2 is hereafter disclosed to, purchased or otherwise legally acquired by the Receiving Party by or from a third party who has not derived it directly or indirectly from the Disclosing Party;

15.2.3 is or becomes available to the public whether in printed publications or otherwise through no act or default on the part of the Receiving Party or its agents or employees; or

15.2.4 the Receiving Party can prove through competent written evidence has been developed independently of the Disclosing Party by any employee of the Receiving Party without reference to any of the Confidential Information disclosed by the Disclosing Party, as shown by contemporaneous written records.

15.2.5 Was the subject of a written permission to disclose provided by the Disclosing Party.

15.3 In order to secure the obligations set out in this Section 15, the Receiving Party agrees to exercise reasonable precaution to prevent and restrain the unauthorized disclosure and use of Confidential Information I, and not to disclose the Confidential Information of the Disclosing Party to any party, provided that Receiving Party may disclose such Confidential Information I to such of its Representatives who are bound by the term of this Agreement or other written obligations of confidentiality similarly restrictive to those contained herein to keep such information confidential, and who need to have such access for the purpose of exercising rights or performing obligations pursuant to this Agreement. Each Party will be liable for the breach of this Section 15 by any of its Representatives.

15.4 The confidentiality obligations under this Section 15 shall not apply to the extent that a Party is required to disclose information by applicable law, regulation or order of a governmental agency or a court of competent jurisdiction, including without limitation SEC and/or stock-exchange regulations; provided, however, that such Party shall provide prior written notice thereof to the other Party, consult with the other Party with respect to

such disclosure and provide the other Party sufficient opportunity to object prior to any such disclosure or to request confidential treatment thereof.

- 15.5 The provisions of this Section 15 shall survive termination or expiry of this Agreement and shall continue for a period of [***] from the date of that termination or expiry, except with respect to trade secret information, which shall survive termination or expiry of this Agreement and shall continue thereafter as long as such information remains a trade secret to the Party making such claim.
- 15.6 All Customer-Owned Project IP and all information, results, data, and other deliverables developed or generated pursuant to this Agreement relating solely to Product shall be the exclusive property of CUSTOMER and are deemed CUSTOMER'S Confidential Information and for the purposes of this Agreement, CUSTOMER shall be deemed the Disclosing Party with respect thereto. AVECIA shall keep complete and accurate records of the foregoing information and data.
- 15.7 Except as required by AVECIA to perform its obligations under this Agreement or as required by applicable law, regulation or order, on a written request from CUSTOMER, AVECIA shall promptly, at CUSTOMER'S option, either return to CUSTOMER or destroy (and provide written certification of such destruction) all documents and materials that embody or set forth CUSTOMER'S Confidential Information, provided that AVECIA may retain one (1) copy of CUSTOMER'S Confidential Information in its secure files solely for the purpose of monitoring compliance with the terms of this Agreement.
16. INTELLECTUAL PROPERTY; LICENSES
- 16.1 Nothing in this Agreement shall affect the ownership by either Party of (i) any Intellectual Property or process owned or controlled by that Party at the Effective Date or (ii) Intellectual Property developed after the Effective Date independently of the work undertaken under this Agreement without reference to any of the Confidential Information disclosed by the other Party ((i) and (ii) together being referred to as "Independent Intellectual Property"). Other than giving AVECIA the right to manufacture Product for the CUSTOMER, nothing in this Agreement shall give AVECIA the right to use the CUSTOMER'S Independent Intellectual Property. Other than as expressly set forth in this Agreement, nothing in this Agreement shall give CUSTOMER the right to use Independent Intellectual Property of AVECIA. All Intellectual Property generated, developed, discovered or invented by AVECIA in connection with work conducted pursuant to this Agreement relating to the composition of matter of, or specifically to the making or manufacturing of, Product or derived from AVECIA's access to CUSTOMER'S Confidential Information shall be owned by CUSTOMER ("CUSTOMER-Owned Project IP"). Any other Intellectual Property generated, developed, discovered or invented by AVECIA in connection with work conducted pursuant to this Agreement shall be owned by AVECIA ("AVECIA-Owned Project IP"). AVECIA hereby assigns and transfers to CUSTOMER all right, title and interest in and to CUSTOMER-Owned Project IP and agrees to take all reasonable acts
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necessary to evidence such Assignment and transfer to CUSTOMER, at CUSTOMER'S expense.

16.2 License

During the Term, CUSTOMER grants to AVECIA a royalty-free, worldwide, non-exclusive license to Independent Intellectual Property of CUSTOMER, solely for the purposes of and to the extent reasonably useful for, manufacturing Product under this Agreement, and any such license shall immediately terminate upon expiration or termination of this Agreement. AVECIA grants to CUSTOMER a non-exclusive, irrevocable, worldwide, royalty-free license, with the right to grant sublicenses, under AVECIA's interest in any AVECIA-Owned Project IP to the extent that such AVECIA-Owned Project IP is necessary or useful for the manufacture, marketing, promoting, using, selling, offering for sale, importing or distributing of Product.

- 16.3 AVECIA will notify CUSTOMER within [***] of receipt of any third-party claims alleging that any CUSTOMER Independent Intellectual Property, or the use thereof, infringes or misappropriates the Intellectual Property rights of such third party (a "Third-Party Infringement Claim") and shall include any information in its possession to enable CUSTOMER to assess the merits of such Third-Party Infringement Claim. CUSTOMER will have the sole right (but not the obligation) to defend, negotiate, and settle Third Party Infringement Claims and will have final decision-making authority regarding all aspects of the defense of any such Third-Party Infringement Claims. AVECIA will cooperate fully with CUSTOMER in the defense of all such Third-Party Infringement Claims and will provide CUSTOMER with such information and assistance as CUSTOMER may reasonably request, at the expense of CUSTOMER. AVECIA shall not agree to settle any Third-Party Infringement Claim without the express written permission of CUSTOMER.

17. INDEPENDENT CONTRACTOR

- 17.1 Nothing in this Agreement shall create, or be deemed to create, a partnership or the relationship of principal and agent or employer and employee between the Parties. Each Party agrees to perform under this Agreement solely as an independent contractor.

18. ENTIRE AGREEMENT

- 18.1 This Agreement, including the Attachments, Schedules, Appendices, and Exhibits attached hereto, and the Quality Agreement, contains the entire agreement between the Parties regarding the subject matter hereof and supersedes any previous agreements relating to the subject matter hereof and any understandings between the Parties with respect thereto, and may not be modified except by an instrument in writing signed by the duly authorized representatives of the Parties. In case of any conflict between the terms of this Agreement and any Scope of Work, the terms of this Agreement shall prevail, unless the Parties explicitly indicate in any such Scope of Work that the terms of the Scope of Work shall prevail with respect to such conflict. In case of any conflict between
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the terms of this Agreement and the Quality Agreement, the terms of this Agreement shall prevail.

19. ANNOUNCEMENTS; PUBLICITY

19.1 Subject to Section 19.2, the Parties agree that they will not make any official press release, announcement or other formal publicity relating to the transactions which are the subject of this Agreement, without first obtaining in each case the prior written consent of the other Party (which consent will not be unreasonably withheld); provided, however, that such consent obligation will not apply to communications required by law or SEC and/or stock-exchange regulation, disclosures of information for which consent has previously been obtained, or information that has been previously disclosed publicly.

19.2 If during the Term of this Agreement or the period of confidentiality specified in Section 15, a Party or any of its employees should wish to make any publication or file a patent application incorporating any of the results arising from the work undertaken under this Agreement or which incorporates any Confidential Information, that Party shall provide the other Party with at least [***]' notice and provide a copy thereof prior to its submission for publication.

20. ASSIGNMENT; SUBCONTRACTING

20.1 This Agreement shall be binding upon and inure to the benefit of the Parties hereto and their respective legal successors and permitted assigns. Neither Party may assign this Agreement without the prior written consent of the other Party, which consent will not be unreasonably withheld, conditioned or delayed, provided that CUSTOMER may assign this Agreement to an Affiliate, to the purchaser of all or substantially all of its assets related to this Agreement or to its successor entity or acquirer in the event of a merger, consolidation or change in control, without prior written notice.

20.2 AVECIA shall not subcontract any of its obligations under this agreement without prior written approval of CUSTOMER.

21. ILLEGALITY

21.1 If any provision of this Agreement is agreed by the Parties to be illegal, void or unenforceable under any law that is applicable hereto or if any court of competent jurisdiction in a final decision so determines, this Agreement shall continue in force save that the parties shall modify such provision so as to preserve the original intent of the provision concerned.

22. WAIVER

22.1 A failure by either Party hereto to exercise or enforce any rights conferred upon it by this Agreement shall not be deemed to be a waiver of any such rights or operate so as to bar the exercise or enforcement thereof at any subsequent time or times.

23. NOTICES

- 23.1 All notices and other communications given or made in relation to this Agreement shall be in English and in writing and delivered by hand, registered post or by electronic mail (with confirmation of receipt) to the appropriate address of the party shown in Section 23.2.
- 23.2 If to AVECIA:
- Nitto Denko Avecia Inc.
125 Fortune Boulevard
Milford, MA 01757
Attention: President
E-mail address: [***]
- If to CUSTOMER:
ProQR Therapeutics IV B.V,
Zernikedreef 9
2333 CK Leiden
The Netherlands
Attention: General Counsel
E-mail address: [***]
24. DUTY TO MITIGATE
- 24.1 Each of the Parties shall use all reasonable endeavors to mitigate any costs, losses or expenses due to be incurred or suffered by the other Party in connection with the performance or nonperformance of this Agreement.
25. LAW; JURISDICTION
- 25.1 The laws of the commonwealth of Massachusetts (without giving effect to its conflicts of law principles) govern all matters arising out of or relating to this Agreement.
- 25.2 In the event of the actual or threatened breach by a Party of any of the terms of Section 14 or Section 15 hereof, the aggrieved Party shall have the right to seek specific performance and injunctive relief. The rights granted by this Section 25.2 are in addition to all other remedies and rights available at law or in equity.
- 25.3 The Parties will seek to settle amicably any and all disputes, controversies or claims arising under, out of or relating to this Agreement and any subsequent amendments of this Agreement. Any such dispute between the Parties will be promptly presented to the Chief Executive Officer of ProQR and the President of AVECIA (the "Senior Representatives"), or their respective designees, for resolution. Such Senior Representatives, or their respective designees, will meet in person or by teleconference as soon as reasonably possible thereafter, and use their good faith efforts to agree upon the resolution of the dispute. If a dispute between the Parties arising out of or relating to the validity or interpretation of, compliance with, breach or alleged breach of or termination of this Agreement cannot be resolved within [***] of presentation to the Senior
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Representatives, or their respective designees, for resolution, then the dispute will be referred to binding arbitration to be conducted as set forth below in Section 25.4.

25.4 If a dispute subject to Section 25.3 is not resolved pursuant to Section 25.3 such dispute will be resolved through binding arbitration in accordance with this Section 25.4 and under the Commercial Arbitration Rules of the American Arbitration Association (“AAA”) then in effect, including application of the “Expedited Procedures” of the Commercial Arbitration Rules of the AAA. The proceedings and decisions of the arbitrators will be confidential, final and binding on the Parties, and judgment upon the award of such arbitrators may be entered in any court having jurisdiction thereof. The arbitration will take place in Boston, M.A., U.S. and will be conducted by three arbitrators. Each of CUSTOMER and AVECIA will appoint one arbitrator within 30 days after the notice that initiated the arbitration. These two arbitrators will in turn appoint a third arbitrator who will be reasonably acceptable to the Parties and who will be appointed in accordance with AAA rules. Each arbitrator chosen hereunder will have educational training and industry experience sufficient to demonstrate a reasonable level of scientific, financial, medical and industry knowledge relevant to the particular dispute.

26. SURVIVAL

26.1 Sections 1,7.3, 8, 10, 11, 12, 14.7, 14.8, 15, 16, 18, 19, 21, 22, 23, 24, 25, and the representations and warranties hereunder will survive the expiration or any earlier termination of this Agreement. This provision will not be construed to limit the survival of any other provisions that also survive the termination or expiration of this Agreement by the express or implied terms of such provisions.

27. COUNTERPARTS

27.1 This Agreement may be executed in two or more counterparts, each of which will be deemed an original, but all of which together will constitute one and the same instrument. This Agreement may be executed and delivered electronically or by facsimile, and upon such delivery, the electronic or facsimile signature will be deemed to have the same effect as if the original signature had been delivered to the other Party.

[Signatures follow on next page]

IN WITNESS WHEREOF, this Agreement has been entered into the day and year first above written.

NITTO DENKO AVECIA INC.

PROQR THERAPEUTICS IV B.V.

By: /s/ Tammy Cooper

By: /s/ D.A. de Boer

Name: Tammy Cooper

Name: D.A. de Boer

Title: V.P. of Business Development

Title: CEO

ATTACHMENTS:

1. Pre-PPQ Activities to Support QR-110 PPQ Program
 2. QR-110 PPQ Activities and Process Performance Qualification Batches
 3. Collaboration Manual (will be added after execution of the Agreement)
 4. Quality Agreement
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PROQR THERAPEUTICS N.V.

Ordinary Shares
(nominal value €0.04 per share)

Sales Agreement

March 31, 2020

Citigroup Global Markets Inc.
388 Greenwich Street
New York, New York, 10013

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022

Ladies and Gentlemen:

ProQR Therapeutics N.V., a Dutch public company with limited liability (the “**Company**”), confirms its agreement (this “**Agreement**”) with Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. (each, an “**Agent**” and together, the “**Agents**”), as follows:

1. **Issuance and Sale of Shares.** The Company agrees that, from time to time during the term of this Agreement, on the terms and subject to the conditions set forth herein, it may issue and sell through the Agents ordinary shares (the “**Placement Shares**”) of the Company, nominal value €0.04 per share (the “**Ordinary Shares**”); *provided, however*, that in no event shall the Company issue or sell through the Agents such number or dollar amount of Placement Shares that would (a) exceed the number or dollar amount of shares of Ordinary Shares registered on the effective Registration Statement (defined below) pursuant to which the offering is being made, (b) exceed the number of shares the Company’s board of directors is authorized to issue pursuant to a resolution of the general meeting of shareholders and following approval of the Company’s supervisory board, (c) exceed the number or dollar amount of Ordinary Shares permitted to be sold under Form F-3 (including General Instruction I.B.5 thereof, if applicable) or (d) exceed the number or dollar amount of Ordinary Shares for which the Company has filed a Prospectus Supplement (defined below) (the lesser of (a), (b), (c) and (d), the “**Maximum Amount**”). Notwithstanding anything to the contrary contained herein, the parties hereto agree that compliance with the limitations set forth in this **Section 1** on the amount of Placement Shares issued and sold under this Agreement shall be the sole responsibility of the Company and that the Agents shall have no obligation in connection with such compliance. The issuance and sale of Placement Shares through Agents will be effected pursuant to the Registration Statement (as defined below) filed by the Company and which has been declared effective by the Securities and Exchange Commission (the “**Commission**”), although nothing in this Agreement shall be construed as requiring the Company to use the Registration Statement to issue any Placement Shares.

The Company has filed, in accordance with the provisions of the Securities Act of 1933, as amended (the “**Securities Act**”) and the rules and regulations thereunder (the “**Securities Act Regulations**”), with the Commission a registration statement on Form F-3, including a base prospectus, relating to certain securities, including the Placement Shares to be issued from time to time by the Company, and which incorporates by reference documents that the Company has filed or will file in accordance with the provisions of the Securities Exchange Act of 1934, as amended (the “**Exchange Act**”), and the rules and regulations thereunder. The Company has prepared a prospectus or a prospectus supplement to the base prospectus included as part of the registration statement, which prospectus or prospectus supplement relates to the Placement Shares to be issued from time to time by the Company (the “**Prospectus Supplement**”). The Company will furnish to the Agents, for use by the Agents, copies of the prospectus included as part of such registration statement, as supplemented, by the Prospectus Supplement, relating to the Placement Shares to be issued from time to time by the Company. The Company may file one or more additional registration statements from time to time that will contain a base prospectus and related prospectus or prospectus supplement, if applicable (which shall be a Prospectus Supplement), with respect to the Placement Shares. Except where the context otherwise requires, such registration statement(s), including all documents filed as part thereof or incorporated by reference therein, and including any information contained in a Prospectus (as defined below) subsequently filed with the Commission pursuant to Rule 424(b) under the Securities Act Regulations or deemed to be a part of such registration statement pursuant to Rule 430B of the Securities Act Regulations, is herein called the “**Registration Statement**.” The base prospectus or base prospectuses, including all documents incorporated therein by reference, included in the Registration Statement, as it may be supplemented, if necessary, by the Prospectus Supplement, in the form in which such prospectus or prospectuses and/or Prospectus Supplement have most recently been filed by the Company with the Commission pursuant to Rule 424(b) under the Securities Act Regulations, together with the then issued Issuer Free Writing Prospectus(es), is herein called the “**Prospectus**.”

Any reference herein to the Registration Statement, any Prospectus Supplement, Prospectus or any Issuer Free Writing Prospectus (defined below) shall be deemed to refer to and include the documents, if any, incorporated by reference therein (the “**Incorporated Documents**”), including, unless the context otherwise requires, the documents, if any, filed as exhibits to such Incorporated Documents. Any reference herein to the terms “amend,” “amendment” or “supplement” with respect to the Registration Statement, any Prospectus Supplement, the Prospectus or any Issuer Free Writing Prospectus shall be deemed to refer to and include the filing of any document under the Exchange Act on or after the most-recent effective date of the Registration Statement, or the date of the Prospectus Supplement, Prospectus or such Issuer Free Writing Prospectus, as the case may be, and incorporated therein by reference. For purposes of this Agreement, all references to the Registration Statement, the Prospectus or to any amendment or supplement thereto shall be deemed to include the most recent copy filed with the Commission pursuant to its Electronic Data Gathering Analysis and Retrieval system, or if applicable, the Interactive Data Electronic Application system when used by the Commission (collectively, “**EDGAR**”).

2. **Placements.** Each time that the Company wishes to issue and sell Placement Shares hereunder (each, a “**Placement**”), it will notify one and not more than one Agent (the “**Designated Agent**”) by email notice (or other method mutually agreed to in writing by the parties) of the number or dollar amount of Placement Shares to be issued, the time period during which sales are

requested to be made, any limitation on the number of Placement Shares that may be sold in any one day and any minimum price below which sales may not be made (a “**Placement Notice**”), the form of which is attached hereto as Schedule 1. The Placement Notice shall originate from any of the individuals from the Company set forth on Schedule 3 (with a copy to each of the other individuals from the Company listed on such schedule), and shall be addressed to each of the individuals from the Designated Agent set forth on Schedule 3, as such Schedule 3 may be amended from time to time. The Placement Notice shall be effective unless and until (i) the Designated Agent declines to accept the terms contained therein for any reason, in its sole discretion, in which case the Designated Agent shall, within two Business Days after delivery of the Placement Notice to the Designated Agent, notify the Company, (ii) the entire amount of the Placement Shares thereunder have been sold, (iii) the Company suspends or terminates the Placement Notice or (iv) this Agreement has been terminated under the provisions of Section 12. The amount of any discount, commission or other compensation to be paid by the Company to the Designated Agent in connection with the sale of the Placement Shares shall be calculated in accordance with the terms set forth in Schedule 2. It is expressly acknowledged and agreed that neither the Company nor the Agents will have any obligation whatsoever with respect to a Placement or any Placement Shares unless and until the Company delivers a Placement Notice to the Designated Agent and the Designated Agent does not decline such Placement Notice pursuant to the terms set forth above, and then only upon the terms specified therein and herein. In the event of a conflict between the terms of this Agreement and the terms of a Placement Notice, the terms of the Placement Notice will control.

3. Sale of Placement Shares by the Designated Agent. Subject to the provisions of Section 5(a), the Designated Agent, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Global Market (the “**Exchange**”), to sell the Placement Shares up to the amount specified, and otherwise in accordance with the terms of such Placement Notice. The Designated Agent will provide written confirmation to the Company no later than the opening of the Trading Day (as defined below) immediately following the Trading Day on which it has made sales of Placement Shares hereunder setting forth the number of Placement Shares sold on such day, the compensation payable by the Company to the Designated Agent pursuant to Section 2 with respect to such sales, and the Net Proceeds (as defined below) payable to the Company, with an itemization of the deductions made by the Designated Agent (as set forth in Section 5(b)) from the gross proceeds that it receives from such sales. Subject to the terms of the Placement Notice, the Designated Agent may sell Placement Shares by any method permitted by law deemed to be an “at the market” offering as defined in Rule 415(a)(4) of the Securities Act Regulations, including sales made directly on or through the Exchange or any other existing trading market for the Ordinary Shares, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices and/or any other method permitted by law. “**Trading Day**” means any day on which Ordinary Shares are traded on the Exchange.

4. Suspension of Sales.

(a) The Company or the Designated Agent may, upon notice to the other party in writing (including by email correspondence to each of the individuals of the other party set forth on Schedule 3, if receipt of such correspondence is actually acknowledged by any of the

individuals to whom the notice is sent, other than via auto-reply) or by telephone (confirmed immediately by verifiable facsimile transmission or email correspondence to each of the individuals of the other party set forth on Schedule 3), suspend any sale of Placement Shares (a "Suspension"); provided, however, that such Suspension shall not affect or impair any party's obligations with respect to any Placement Shares sold hereunder prior to the receipt of such notice. While a Suspension is in effect any obligation under Sections 7(l), 7(m), and 7(n) with respect to the delivery of certificates, opinions, or comfort letters to the Agents, shall be waived. Each of the parties agrees that no such notice under this Section 4 shall be effective against any other party unless it is made to one of the individuals named on Schedule 3 hereto, as such Schedule may be amended from time to time.

(b) If either party has reason to believe that the exemptive provisions set forth in Rule 101(c) (1) of Regulation M under the Exchange Act are not satisfied with respect to the Placement Shares, it shall promptly notify the other party and any Agent may, at its sole discretion, suspend sales of the Placement Shares under this Agreement.

(c) Notwithstanding any other provision of this Agreement, during any period in which the Company is in possession of material non-public information, the Company and the Agents agree that (i) no sale of Placement Shares will take place, (ii) the Company shall not request the sale of any Placement Shares, and (iii) the Agents shall not be obligated to sell or offer to sell any Placement Shares.

5. Sale and Delivery to the Designated Agent; Settlement.

(a) Sale of Placement Shares. On the basis of the representations and warranties herein contained and subject to the terms and conditions herein set forth, upon the Designated Agent's acceptance of the terms of a Placement Notice, and unless the sale of the Placement Shares described therein has been declined, suspended, or otherwise terminated in accordance with the terms of this Agreement, the Designated Agent, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable law and regulations to sell such Placement Shares up to the amount specified, and otherwise in accordance with the terms of such Placement Notice. The Company acknowledges and agrees that (i) there can be no assurance that the Designated Agent will be successful in selling Placement Shares, (ii) the Designated Agent will incur no liability or obligation to the Company or any other person or entity if it does not sell Placement Shares for any reason other than a failure by the Designated Agent to use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable law and regulations to sell such Placement Shares as required under this Agreement and (iii) the Designated Agent shall be under no obligation to purchase Placement Shares on a principal basis pursuant to this Agreement, except as otherwise agreed by the Designated Agent and the Company.

(b) Settlement of Placement Shares. Unless otherwise specified in the applicable Placement Notice, settlement for sales of Placement Shares will occur on the second (2nd) Trading Day following the date on which such sales are made (each, a "**Settlement Date**"). The Designated Agent shall notify the Company of each sale of Placement Shares no later than the opening of the Trading Day immediately following the Trading Day on which it has made sales of Placement Shares hereunder. The amount of proceeds to be delivered to the Company on a Settlement Date against receipt of the Placement Shares sold (the "**Net Proceeds**") will be equal

to the aggregate sales price received by the Designated Agent, after deduction for (i) the Designated Agent's commission, discount or other compensation for such sales payable by the Company pursuant to Section 2 hereof, and (ii) any transaction fees imposed by any governmental or self-regulatory organization in respect of such sales.

(c) Delivery of Placement Shares. On or before each Settlement Date, the Company will, or will cause its transfer agent to, electronically transfer the Placement Shares being sold by crediting the Designated Agent's or its designee's account (provided the Designated Agent shall have given the Company written notice of such designee at least one Trading Day prior to the Settlement Date) at The Depository Trust Company through its Deposit and Withdrawal at Custodian System or by such other means of delivery as may be mutually agreed upon by the parties hereto which in all cases shall be freely tradable, transferable, registered shares in good deliverable form. On each Settlement Date, the Designated Agent will deliver the related Net Proceeds in same day funds to an account designated by the Company on, or prior to, the Settlement Date. The Company agrees that if the Company, or its transfer agent (if applicable), defaults in its obligation to deliver Placement Shares on a Settlement Date, the Company agrees that in addition to and in no way limiting the rights and obligations set forth in Section 10(a) hereto, it will (i) hold the Designated Agent harmless against any loss, claim, damage, or expense (including reasonable legal fees and expenses), as incurred, arising out of or in connection with such default by the Company or its transfer agent (if applicable) and (ii) pay to the Designated Agent any commission, discount, or other compensation to which it would otherwise have been entitled absent such default.

(d) Denominations; Registration. Certificates for the Placement Shares, if any, shall be in such denominations and registered in such names as the Agents may request in writing at least one full Business Day (as defined below) before the Settlement Date. The certificates for the Placement Shares, if any, will be made available by the Company for examination and packaging by the Agents in The City of New York not later than noon (New York time) on the Business Day prior to the Settlement Date.

(e) Limitations on Offering Size. Under no circumstances shall the Company cause or request the offer or sale of any Placement Shares if, after giving effect to the sale of such Placement Shares, the number or dollar amount of Placement Shares sold pursuant to this Agreement would exceed the lesser of (A) together with all sales of Placement Shares under this Agreement, the Maximum Amount, (B) the amount available for offer and sale under the currently effective Registration Statement and (C) the number authorized from time to time to be issued and sold under this Agreement by the Company's board of directors or a duly authorized committee thereof and the Company's supervisory board or a duly authorized committee thereof, and notified to the Designated Agent in writing. Under no circumstances shall the Company cause or request the offer or sale of any Placement Shares pursuant to this Agreement at a price lower than the minimum price authorized from time to time by the Company's board of directors or a duly authorized committee thereof and the Company's supervisory board or a duly authorized committee thereof, and notified to the Designated Agent in writing. Further, under no circumstances shall the Company cause or permit the aggregate offering amount of Placement Shares sold pursuant to this Agreement to exceed the Maximum Amount.

(f) Sales Through Agents. With respect to the offering and sale of Placement Shares pursuant to this Agreement, the Company agrees that any offer to sell Placement Shares,

any solicitation of an offer to buy Placement Shares, and any sales of Placement Shares shall only be effected by or through a single Agent on any single given day, and the Company shall in no event request that more than one Agent offer or sell Placement Shares pursuant to this Agreement on the same day.

6. Representations and Warranties of the Company. The Company represents and warrants to, and agrees with each of the Agents that as of the date of this Agreement and, unless otherwise specified, as of each Applicable Time (as defined below):

(a) Registration Statement and Prospectus. The Company and the transactions contemplated by this Agreement meet the requirements for and comply with the applicable conditions set forth in Form F-3 (including General Instruction I.A and I.B) under the Securities Act. As of the date hereof, the Company is a “foreign private issuer” as such term is defined in Rule 3b-4 under the Exchange Act. The Registration Statement has been or will be filed with the Commission and will be declared effective by the Commission under the Securities Act prior to the issuance of any Placement Notices by the Company. The Prospectus Supplement will name the Agents as the agents in the section entitled “Plan of Distribution.” The Company has not received, and has no notice of, any order of the Commission preventing or suspending the use of the Registration Statement, or threatening or instituting proceedings for that purpose. The Registration Statement and the offer and sale of Placement Shares as contemplated hereby meet the requirements of Rule 415 under the Securities Act and comply in all material respects with said Rule. Any statutes, regulations, contracts or other documents that are required to be described in the Registration Statement or the Prospectus or to be filed as exhibits to the Registration Statement have been so described or filed. Copies of the Registration Statement, the Prospectus, and any such amendments or supplements and all documents incorporated by reference therein that were filed with the Commission on or prior to the date of this Agreement have been delivered, or are available through EDGAR, to the Agents and their counsel. The Company has not distributed and, prior to the later to occur of each Settlement Date and completion of the distribution of the Placement Shares, will not distribute any offering material in connection with the offering or sale of the Placement Shares other than the Registration Statement and the Prospectus and any Issuer Free Writing Prospectus (as defined below) to which the Agents have consented. The Ordinary Shares are registered pursuant to Section 12(b) of the Exchange Act and are currently listed on the Exchange under the trading symbol “PRQR.” The Company has taken no action designed to, or likely to have the effect of, terminating the registration of the Ordinary Shares under the Exchange Act, delisting the Ordinary Shares from the Exchange, nor has the Company received any notification that the Commission or the Exchange is contemplating terminating such registration or listing. To the Company’s knowledge, it is in compliance with all applicable listing requirements of the Exchange.

(b) No Misstatement or Omission. The Registration Statement, when it became or becomes effective, and the Prospectus, and any amendment or supplement thereto, on the date of such Prospectus or amendment or supplement, conformed and will conform in all material respects with the requirements of the Securities Act. At each Settlement Date, the Registration Statement and the Prospectus, as of such date, will conform in all material respects with the requirements of the Securities Act. The Registration Statement, when it became or becomes effective, did not, and will not, contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not

misleading. The Prospectus and any amendment and supplement thereto, on the date thereof and at each Applicable Time (defined below), did not or will not include an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in light of the circumstances under which they were made, not misleading. The documents incorporated by reference in the Prospectus or any Prospectus Supplement did not, and any further documents filed and incorporated by reference therein will not, when filed with the Commission, contain an untrue statement of a material fact or omit to state a material fact required to be stated in such document or necessary to make the statements in such document, in light of the circumstances under which they were made, not misleading. The foregoing shall not apply to statements in, or omissions from, any such document made in reliance upon, and in conformity with, information furnished to the Company by either of the Agents specifically for use in the preparation thereof.

(c) Conformity with Securities Act and Exchange Act. The Registration Statement, the Prospectus, any Issuer Free Writing Prospectus or any amendment or supplement thereto, and the documents incorporated by reference in the Registration Statement, the Prospectus or any amendment or supplement thereto, when such documents were or are filed with the Commission under the Securities Act or the Exchange Act or became or become effective under the Securities Act, as the case may be, conformed or will conform in all material respects with the requirements of the Securities Act and the Exchange Act, as applicable.

(d) Company Not Ineligible Issuer. At the time of filing the Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the Company made a *bona fide* offer (within the meaning of Rule 164(h)(2) of the Securities Act Regulations) of the Securities and at the time this Agreement is executed and delivered by the parties hereto, the Company was not and is not an “ineligible issuer,” as defined in Rule 405, without taking account of any determination by the Commission pursuant to Rule 405 that it is not necessary that the Company be considered an ineligible issuer.

(e) Independent Accountants. Deloitte Accountants B.V., the accountants who certified the financial statements and supporting schedules, if any, included in the Registration Statement and the Prospectus, are independent public accountants as required by the Securities Act, the Securities Act Regulations and the Public Company Accounting Oversight Board.

(f) Financial Statements. The financial statements included in the Registration Statement and the Prospectus, together with the related schedules and notes, present fairly, the financial position of the Company at the dates indicated and the statement of operations, shareholders’ equity (*eigen vermogen*) and cash flows of the Company for the periods specified; said financial statements have been prepared in conformity with International Financial Reporting Standards (“IFRS”) as issued by the International Accounting Standards Board (“IASB”) applied on a consistent basis throughout the periods involved, except in the case of unaudited, interim financial statements, subject to normal year-end audit adjustments and the exclusion of certain footnotes. The supporting schedules, if any, present fairly in accordance with IFRS the information required to be stated therein. The summary financial data included in the Registration Statement and the Prospectus present fairly the information shown therein and have been compiled on a basis consistent with that of the audited financial statements included therein. Except as included therein, no historical or pro forma financial statements or supporting schedules are required to be included or incorporated by reference in the Registration Statement or the Prospectus under the Securities Act or the Securities Act Regulations.

(g) No Material Adverse Change in Business. Except as otherwise stated therein, since the respective dates as of which information is given in the Registration Statement or the Prospectus, (A) there has been no material adverse change in the condition, financial or otherwise, or in the earnings, business affairs, properties or prospects of the Company and its subsidiaries, taken as a whole, whether or not arising in the ordinary course of business (a “Material Adverse Effect”), (B) there have been no transactions entered into by the Company, other than those in the ordinary course of business, which are material with respect to the Company, and (C) there has been no dividend or distribution of any kind declared, paid or made by the Company on any class of its share capital.

(h) Good Standing of the Company. The Company has been duly incorporated and is validly existing as a public company with limited liability (*naamloze vennootschap*) under the laws of the Netherlands and has the power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement and the Prospectus and to enter into and perform its obligations under this Agreement; and the Company is duly qualified to transact business and is in good standing (where such concept exists) in each jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where the failure so to qualify or to be in good standing would not reasonably be expected to result in a Material Adverse Effect.

(i) Capitalization. The authorized and issued share capital and outstanding shares in the capital of the Company are as set forth in the Registration Statement and the Prospectus under the caption “Capitalization” (except for subsequent issuances, if any, pursuant to this Agreement, pursuant to reservations, agreements or employee benefit plans referred to in the Registration Statement and the Prospectus or pursuant to the exercise of convertible securities or options referred to in the Registration Statement and the Prospectus). All of the ordinary shares in the capital of the Company existing as of the date of this Agreement have been duly authorized and validly issued and are fully paid. None of the outstanding shares in the capital of the Company were issued in violation of the preemptive or other similar rights of any shareholder of the Company.

(j) Subsidiaries. Each of the Company’s “subsidiaries” (for purposes of this Agreement, as defined in Rule 405 under the Securities Act) has been duly organized and is validly existing in good standing (where such concept exists) under the laws of the jurisdiction of its organization and has the power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement and the Prospectus. Each of the Company’s subsidiaries is duly qualified to transact business and is in good standing (where such concept exists) in each jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where failure to be so qualified or in good standing could not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect. All of the issued and outstanding share capital or other equity or ownership interests of each of the Company’s subsidiaries has been duly authorized and validly issued, is fully paid and nonassessable (where such concept exists) and is owned by the Company, directly or through subsidiaries, free and clear of any security interest, mortgage, pledge, lien, encumbrance or adverse claim, except as disclosed in the Registration Statement and the Prospectus. The Company does not own or control, directly or indirectly, any corporation,

association or other entity other than the subsidiaries listed in or on an exhibit to the Registration Statement.

(k) Authorization of Agreement. This Agreement has been duly authorized, executed and delivered by the Company.

(l) Authorization and Description of Securities. The Securities to be purchased by the Agents from the Company have been duly authorized for issuance and sale to the Agents pursuant to this Agreement and, when issued and delivered by the Company pursuant to this Agreement against payment of the consideration set forth herein, will be validly issued and fully paid; and the issuance of the Securities is not subject to any preemptive or other similar rights. The Ordinary Shares conform, in all material respects, to all statements relating thereto contained in the Registration Statement and the Prospectus and such description conforms, in all material respects, to the rights set forth in the instruments defining the same. No holder of Securities will be subject to personal liability by reason of being such a holder, except for being subject to pay up the Securities acquired by them in full.

(m) Registration Rights. There are no persons with registration rights or other similar rights to have any securities registered for sale pursuant to the Registration Statement or otherwise registered for sale or sold by the Company under the Securities Act pursuant to this Agreement, other than those rights that have been disclosed in the Registration Statement and the Prospectus.

(n) Absence of Violations, Defaults and Conflicts. The Company is not (A) in violation of its articles of association, (B) in default in the performance or observance of any obligation, agreement, covenant or condition contained in any contract, indenture, mortgage, deed of trust, loan or credit agreement, note, lease or other agreement or instrument to which the Company is a party or by which it may be bound or to which any of the properties or assets of the Company is subject (collectively, "Agreements and Instruments"), except, in the case of (B), for such defaults as would not, singly or in the aggregate, reasonably be expected to result in a Material Adverse Effect, or (C) in violation of any law (including in the case of the Company and for the avoidance of doubt, the Exchange Act), statute, rule, regulation (including in the case of the Company and for the avoidance of doubt, the rules and regulations of the Commission under the Exchange Act (the "Exchange Act Regulations")), judgment, order, writ or decree of any arbitrator, court, governmental body, regulatory body, administrative agency or other authority, body or agency having jurisdiction over the Company or any of its respective properties, assets or operations (each, a "Governmental Entity"), except, in the case of (C), for such violations as would not, singly or in the aggregate, reasonably be expected to result in a Material Adverse Effect. The execution, delivery and performance of this Agreement and the consummation of the transactions contemplated herein and in the Registration Statement and the Prospectus (including the issuance and sale of the Securities and the use of the proceeds from the sale of the Securities as described therein under the caption "Use of Proceeds") and compliance by the Company with its obligations hereunder have been duly authorized by all necessary corporate action and do not and will not, whether with or without the giving of notice or passage of time or both, conflict with or constitute a breach of, or default or Repayment Event (as defined below) under, or result in the creation or imposition of any lien, charge or encumbrance upon any properties or assets of the Company pursuant to, the Agreements and Instruments (except for such conflicts, breaches, defaults or Repayment Events or liens, charges or encumbrances as would not, singly or in the aggregate,

reasonably be expected to result in a Material Adverse Effect), nor will such action result in any violation of the provisions of the articles of association of the Company or any law, statute, rule, regulation, judgment, order, writ or decree of any Governmental Entity, except for such violations as would not, singly or in the aggregate, result in a Material Adverse Effect. As used herein, a “Repayment Event” means any event or condition which gives the holder of any note, debenture or other evidence of indebtedness (or any person acting on such holder’s behalf) the right to require the repurchase, redemption or repayment of all or a portion of such indebtedness by the Company.

(o) Absence of Labor Dispute. No material labor dispute with the employees of the Company exists or, to the knowledge of the Company, is imminent, and the Company is not aware of any material existing or imminent labor disturbance by the employees of any of its principal suppliers, manufacturers, customers or contractors.

(p) Absence of Proceedings. There is no action, suit, proceeding, inquiry or investigation before or brought by any Governmental Entity now pending or, to the knowledge of the Company, threatened, against or affecting the Company, which would reasonably be expected to result in a Material Adverse Effect, or which would reasonably be expected to materially and adversely affect its respective properties or assets or the consummation of the transactions contemplated in this Agreement or the performance by the Company of its obligations hereunder; and the aggregate of all pending legal or governmental proceedings to which the Company is a party or of which its properties or assets are the subject, including ordinary routine litigation incidental to the business, if determined adversely to the Company, would not reasonably be expected to result in a Material Adverse Effect.

(q) Accuracy of Exhibits. There are no contracts or documents which are required to be described in the Registration Statement or the Prospectus or to be filed as exhibits to the Registration Statement which have not been so described and filed as required.

(r) Absence of Further Requirements. No filing with, or authorization, approval, consent, license, order, registration, qualification or decree of, any Governmental Entity is necessary or required for the performance by the Company of its obligations hereunder, in connection with the offering, issuance or sale of the Placement Shares hereunder or the consummation of the transactions contemplated by this Agreement, except such as have been already obtained or as may be required under the Securities Act, the Securities Act Regulations, the rules of the Nasdaq Stock Market LLC (“Nasdaq”), U.S. state securities laws or the rules of FINRA.

(s) Possession of Licenses and Permits. The Company possesses such permits, licenses, approvals, consents and other authorizations (collectively, “Governmental Licenses”) issued by the appropriate Governmental Entities necessary to conduct the business now operated by it, including without limitation, all such permits, licenses, approvals, consents and other authorizations required by the United States Food and Drug Administration (the “FDA”), the European Medicines Agency (the “EMA”), or any other federal, state, local or foreign agencies or bodies engaged in the regulation of clinical trials, pharmaceuticals, biologics or biohazardous substances or materials, except where the failure so to possess such Governmental Licenses would not, singly or in the aggregate, reasonably be expected to result in a Material Adverse Effect. The Company is in compliance with the terms and conditions of all Governmental Licenses, except where the failure so to comply would not, singly or in the aggregate, reasonably be expected to

result in a Material Adverse Effect. All of the Governmental Licenses are valid and in full force and effect, except where the invalidity of such Governmental Licenses or the failure of such Governmental Licenses to be in full force and effect would not, singly or in the aggregate, reasonably be expected to result in a Material Adverse Effect. The Company has not received any written notice of proceedings relating to the actual revocation or modification of any Governmental Licenses, which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would reasonably be expected to result in a Material Adverse Effect. To the extent required by applicable laws and regulations of the FDA, the Company has submitted to the FDA an Investigational New Drug Application or amendment or supplement thereto for each clinical trial it has conducted or sponsored or is conducting or sponsoring in the United States; all such submissions, if any, were in material compliance with applicable laws and regulations when submitted and no material deficiencies have been asserted by the FDA with respect to any such submissions. To the extent required by applicable laws and regulations of countries within the European Union, the Company has submitted to the national medicinal agencies of such countries a Clinical Trial Authorization application or amendment or supplement thereto for each clinical trial it has conducted or sponsored or is conducting or sponsoring in such countries; all such submissions, if any, were in material compliance with applicable laws and regulations when submitted and no material deficiencies have been asserted by the national medicinal agencies with respect to any such submissions.

(t) Title to Property. The Company does not own real property. The Company has good and marketable title to all personal and other properties owned by it (excluding for the purpose of this Section 6(t), Intellectual Property (as defined below)), in each case, free and clear of all mortgages, pledges, liens, security interests, claims, restrictions or encumbrances of any kind except such as (A) are described in the Registration Statement and the Prospectus or (B) do not, singly or in the aggregate, materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company; and all of the leases and subleases material to the business of the Company and under which the Company holds properties described in the Registration Statement or the Prospectus, are in full force and effect, and the Company has no notice of any material claim of any sort that has been asserted by anyone adverse to the rights of the Company under any of the leases or subleases mentioned above, or affecting or questioning the rights of the Company to the continued possession of the leased or subleased premises under any such lease or sublease.

(u) Intellectual Property. The Company owns, or has obtained valid, binding and enforceable licenses for the right to use, patents, patent applications, inventions, copyrights, know how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures), trademarks, service marks, trade names or other intellectual property (collectively, "Intellectual Property") necessary to carry on the business of the Company as now conducted and as proposed to be conducted, insofar as such Intellectual Property is described in the Registration Statement and the Prospectus (collectively, the "Company Intellectual Property"), except where failure to own, license or have such rights would not, individually or in the aggregate, have a Material Adverse Effect; and to the knowledge of the Company, the patents, trademarks, and copyrights, if any, included within the Company Intellectual Property are valid, enforceable, and subsisting. Other than as disclosed in the Registration Statement and the Prospectus, (A) the Company is not obligated to pay a material royalty, grant a license, or provide other material consideration to any third party in connection

with the Company Intellectual Property, (B) the Company has not received any notice of any claim of infringement, misappropriation or conflict with any Intellectual Property rights of others with respect to any of the Company's product candidates or processes or the Company Intellectual Property, (C) to the knowledge of the Company, neither the manufacture nor the sale or use of any of the product candidates or processes of the Company referred to in the Registration Statement or the Prospectus do or will infringe, misappropriate or violate any existing, non-patent Intellectual Property right or any existing valid, granted patent claim of any third party, (D) to the knowledge of the Company, no third party has any ownership rights in or to any Intellectual Property that is owned by the Company and, to the knowledge of the Company, no third party has any ownership right in or to any Intellectual Property that is exclusively licensed to the Company in any field of use other than any licensor to the Company of such Intellectual Property, (E) there is no pending or, to the knowledge of the Company, threatened action, suit, proceeding or claim by others challenging the Company's rights in or to any Company Intellectual Property, (F) to the Company's knowledge, no employee of the Company is or has been in violation of any term of any employment contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement, nondisclosure agreement or any restrictive covenant to or with a former employer where the basis of such violation relates to such employee's employment with the Company, and (G) to the knowledge of the Company, the Company has complied with the terms of each agreement pursuant to which Intellectual Property has been licensed to the Company, except where failure to comply would not, individually or in the aggregate, have a Material Adverse Effect, and, to the knowledge of the Company, all such agreements are in full force and effect. The statements relating to the Company's intellectual property rights contained in the Registration Statement and the Prospectus are complete and accurate in all material respects. The Registration Statement and the Prospectus did not and do not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the intellectual property statements, in light of the circumstance under which they were made, not misleading.

(v) Patents and Patent Applications. All patents and patent applications owned by or licensed to the Company or under which the Company has rights have, to the knowledge of the Company, been duly and properly filed and maintained; except for routine *ex parte* patent prosecution activities before patent offices, there is no pending or, to the knowledge of the Company, threatened legal proceeding, including, but not limited to, any government or patent office proceeding, such as inter partes review, reexamination, opposition, or other patent office proceeding, in any jurisdiction challenging the validity, enforceability, or scope of any patents and/or pending patent applications owned by or licensed to the Company; to the knowledge of the Company, each individual associated with the filing and prosecution of such patents and applications has complied with their duty of candor and disclosure to the U.S. Patent and Trademark Office (the "USPTO") in connection with such patents and applications; and the Company is not aware of any information required to be disclosed to the USPTO that was not disclosed to the USPTO in connection with the prosecution of the aforementioned patents and applications.

(w) Environmental Laws. Except as would not, singly or in the aggregate, reasonably be expected to result in a Material Adverse Effect, (A) the Company is not in violation of any applicable federal, state, local or foreign statute, law, rule, regulation, ordinance, code, policy or rule of common law or any judicial or administrative interpretation thereof, including any

judicial or administrative order, consent, decree or judgment, relating to pollution or protection of human health, the environment (including, without limitation, ambient air, surface water, groundwater, land surface or subsurface strata) or wildlife, including, without limitation, laws and regulations relating to the release or threatened release of chemicals, pollutants, contaminants, wastes, toxic substances, hazardous substances, petroleum or petroleum products, asbestos-containing materials or mold (collectively, “Hazardous Materials”) or to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of Hazardous Materials (collectively, “Environmental Laws”), (B) the Company has all permits, authorizations and approvals required for its operations under any applicable Environmental Laws and is in compliance with its requirements, (C) there are no pending or, to the knowledge of the Company, threatened, administrative, regulatory or judicial actions, suits, demands, demand letters, claims, liens, notices of noncompliance or violation, investigation or proceedings relating to any Environmental Law against the Company and (D) to the knowledge of the Company, there are no events or circumstances that would reasonably be expected to form the basis of an order for clean-up or remediation, or an action, suit or proceeding by any private party or Governmental Entity, against or affecting the Company relating to Hazardous Materials or any Environmental Laws.

(x) Accounting Controls. The Company maintains an effective system of “internal control over financial reporting” (as defined under Rule 13-a15(f) and 15d-15(f) under the Exchange Act Regulations) that complies with the requirements of the Exchange Act and a system of internal accounting controls sufficient to provide reasonable assurances that (A) transactions are executed in accordance with management’s general or specific authorization; (B) transactions are recorded as necessary to permit preparation of financial statements in conformity with IFRS as issued by the IASB and to maintain accountability for assets; (C) access to assets is permitted only in accordance with management’s general or specific authorization; (D) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences; and (E) the interactive data in XBRL included or incorporated by reference in the Registration Statement or the Prospectus is in compliance with the SEC’s published rules, regulations and guidelines applicable thereto . Since the end of the Company’s most recent audited fiscal year, there has been no material weakness in the Company’s internal control over financial reporting (whether or not remediated) and except as described in the Registration Statement and the Prospectus, there has been no change in the Company’s internal control over financial reporting that has materially adversely affected, or is reasonably likely to materially adversely affect, the Company’s internal control over financial reporting.

(y) Disclosure Controls. The Company has established “disclosure controls and procedures” (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act Regulations) that complies with the requirements of the Exchange Act; the Company’s “disclosure controls and procedures” are reasonably designed to ensure that all information (both financial and non-financial) required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and regulations under the Exchange Act, and that all such information will be accumulated and communicated to the Company’s management as appropriate to allow timely decisions regarding required disclosure and to make the certifications of the Chief Executive Officer and Chief Financial Officer of the Company required under the Exchange Act with respect to such reports.

(z) Preclinical and Clinical Data and Regulatory Compliance. The preclinical tests and clinical trials that are described in, or the results of which are referred to in, the Registration Statement or the Prospectus (collectively, “Studies”) were and, if still pending, are being conducted in all material respects in accordance with the protocols, procedures and controls designed and approved for such Studies and with standard medical and scientific research procedures; each description of the results of such Studies is accurate and complete in all material respects and fairly presents the data derived from such Studies; and the Company has no knowledge of any other Studies the results of which are inconsistent with, or otherwise call into question, the results described or referred to in the Registration Statement or the Prospectus. Except as described in the Registration Statement and the Prospectus, the Company has not received any written notice of, or correspondence from, any Governmental Entity requiring the termination, suspension or material modification of any Studies. The Company has operated and currently is in compliance with the United States Federal Food, Drug, and Cosmetic Act (21 U.S.C. §301 et seq.), all applicable regulations of the FDA (collectively, the “FDCA”), the EMA and other federal, state, local and foreign governmental bodies exercising comparable authority, except where the failure to so operate or be in compliance would not have a Material Adverse Effect.

(aa) Compliance with Health Care Laws. The Company is, and at all times has been, in material compliance with all applicable Health Care Laws. For purposes of this Agreement, “Health Care Laws” means: (i) the FDCA and the Public Health Service Act (42 U.S.C. § 201 et seq.); (ii) all applicable federal, state, local and all applicable foreign health care related fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute (42 U.S.C. § 1320a-7b(b)), the federal criminal false claims law (42 U.S.C. § 1320a-7b(a)), the federal civil monetary penalties law (42 U.S.C. § 1320a-7a), the federal Civil False Claims Act (31 U.S.C. § 3729 et seq.), the exclusions law (42 U.S.C. § 1320a-7), the Physician Payments Sunshine Act (42 U.S.C. § 1320a-7h), federal criminal laws relating to health care fraud and abuse, including but not limited to, 18 U.S.C. §§ 286, 287, 1347 and 1349, the health care fraud criminal provisions under the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) (42 U.S.C. § 1320d et seq.), and the regulations promulgated pursuant to such statutes; (iii) HIPAA as amended by the Health Information Technology for Economic and Clinical Health Act (“HITECH Act”) (42 U.S.C. § 17921 et seq.), each as amended, and their implementing regulations; (iv) Medicare (Title XVIII of the Social Security Act) and Medicaid (Title XIX of the Social Security Act), and the regulations promulgated pursuant to such statutes; (v) the Patient Protection and Affordable Care Act of 2010 (Public Law 111-148), as amended by the Health Care and Education Reconciliation Act of 2010 (Public Law 111-152), and the regulations promulgated thereunder; and (vi) all other local, state, federal, national, supranational and foreign health care laws relating to the regulation of the Company. The Company: (a) has not received written notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any Governmental Entity or other party alleging that any operation or activity is in violation of any Health Care Laws (collectively, “Action”); (b) has no knowledge that any Action is threatened; and (c) has no knowledge of any event or condition that would reasonably be expected to result in an Action. The Company has filed, maintained and submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Health Care Laws, and all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and accurate on the date filed in all material respects (or were corrected or supplemented by a subsequent submission). Neither the

Company nor any of their employees, officers, directors or agents is a party to any corporate integrity agreements, plans of correction, monitoring agreements, consent decrees, settlement orders, or similar agreements with or imposed by any Governmental Entity regarding any Health Care Laws. Additionally, neither the Company nor any of their employees, officers, directors or agents has been excluded, suspended or debarred from participation in any U.S. federal health care program or human clinical research or, to the knowledge of the Company, is subject to a governmental inquiry, investigation, proceeding, or other similar action that could reasonably be expected to result in debarment, suspension, or exclusion.

(bb) Payment of Taxes. The Company has filed all necessary Dutch and United States national, federal, state and foreign income and franchise tax returns that are required to have been filed by it pursuant to applicable national, federal, state, local, foreign or other law except insofar as the failure to file such returns would not reasonably be expected to result in a Material Adverse Effect, and has paid all taxes required to be paid by any of them pursuant to such returns or pursuant to any assessment received by the Company, except for such taxes, if any, as are being contested in good faith and as to which adequate reserves have been established by the Company or except insofar as the failure to pay such taxes would not reasonably be expected to result in a Material Adverse Effect. The charges, accruals and reserves on the books of the Company in respect of any income and corporation tax liability for any years not finally determined are adequate to meet any assessments or re-assessments for additional income and corporation tax for any years not finally determined, except to the extent of any inadequacy that would not reasonably be expected to result in a Material Adverse Effect. The Company is not involved in any current material dispute with any tax authority and the Company is currently not subject to any material investigation or audit from any tax authority. To the Company's knowledge, except for any net (corporate) income taxes imposed on the Agents by the Netherlands or any political subdivision or taxing authority thereof or therein as a result of any present or former connection between any Agent and the Netherlands, no transaction, value added ("VAT"), stamp, capital or other issuance, registration, transaction, transfer or withholding tax or duty is payable in the Netherlands by or on behalf of the Agents to any taxing authority in connection with (i) the issuance, sale and delivery of the Securities by the Company in the manner contemplated herein; (ii) the purchase from the Company, and the initial sale and delivery by the Agents of the Securities to purchasers thereof as contemplated herein; or (iii) the execution and delivery of this Agreement or any other document to be furnished hereunder.

(cc) Insurance. The Company carries or is entitled to the benefits of insurance, with financially sound and reputable insurers, in such amounts and covering such risks as is customary and adequate for the conduct of its business, and all such insurance is in full force and effect. The Company has not received any notice that it will not be able (A) to renew its existing insurance coverage as and when such policies expire or (B) to obtain comparable coverage from similar institutions as may be necessary or appropriate to conduct its business as now conducted and at a cost that would not reasonably be expected to result in a Material Adverse Effect. The Company has not been denied any insurance coverage which it has sought or for which it has applied.

(dd) Investment Company Act. The Company is not required, and upon the issuance and sale of the Securities as herein contemplated and the application of the net proceeds therefrom as described in the Registration Statement and the Prospectus will not be required, to

register as an “investment company” under the Investment Company Act of 1940, as amended (the “1940 Act”).

(ee) Absence of Manipulation. Neither the Company nor, to the Company’s knowledge, any affiliate of the Company has taken, nor will the Company or any affiliate take, directly or indirectly any action which is designed, or would reasonably be expected, to cause or result in, or which constitutes, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Securities or to result in a violation of Regulation M under the Exchange Act.

(ff) FCPA. Neither the Company nor any of its subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee, affiliate or other person acting on behalf of the Company or any of its subsidiaries is aware of or has taken any action, directly or indirectly, that would result in a violation or a sanction for violation by such persons of the Foreign Corrupt Practices Act of 1977 or the U.K. Bribery Act 2010, each as may be amended, or similar law of any other relevant jurisdiction, or the rules or regulations thereunder; and the Company and its subsidiaries have instituted and maintain policies and procedures to ensure compliance therewith. No part of the proceeds of the offering of the Placement Shares will be used, directly or indirectly, in violation of the Foreign Corrupt Practices Act of 1977 or the U.K. Bribery Act 2010, each as may be amended, or similar law of any other relevant jurisdiction, or the rules or regulations thereunder.

(gg) AML. The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements and the money laundering statutes and the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental agency (collectively, the “Money Laundering Laws”) and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its subsidiaries with respect to the Money Laundering Laws is pending or, to the best knowledge of the Company, threatened.

(hh) Sanctions. Neither the Company nor any of its subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company or any of its subsidiaries (i) is, or is controlled or 50% or more owned in the aggregate by or is acting on behalf of, one or more individuals or entities that are currently the subject of any sanctions administered or enforced by the United States (including any administered or enforced by the Office of Foreign Assets Control of the U.S. Department of the Treasury, the U.S. Department of State or the Bureau of Industry and Security of the U.S. Department of Commerce), the United Nations Security Council, the European Union, a member state of the European Union (including sanctions administered or enforced by Her Majesty’s Treasury of the United Kingdom) or other relevant sanctions authority (collectively, “Sanctions” and such persons, “Sanctioned Persons” and each such person, a “Sanctioned Person”), (ii) is located, organized or resident in a country or territory that is, or whose government is, the subject of Sanctions that broadly prohibit dealings with that country or territory (collectively, “Sanctioned Countries” and each, a “Sanctioned Country”) or (iii) will, directly or indirectly, use the proceeds of this offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other individual or entity in any manner that would result in a violation of any Sanctions by, or could result in the imposition of Sanctions against, any individual or entity (including any individual or entity

participating in the offering, whether as underwriter, advisor, investor or otherwise). Neither the Company nor any of its subsidiaries has engaged in any dealings or transactions with or for the benefit of a Sanctioned Person, or with or in a Sanctioned Country, in the preceding 5 years, nor does the Company or any of its subsidiaries have any plans to engage in dealings or transactions with or for the benefit of a Sanctioned Person, or with or in a Sanctioned Country.

(ii) Lending Relationships. Except as disclosed in the Registration Statement and the Prospectus, the Company (i) does not have any material lending or other relationship with any banking or lending affiliate of any Agent and (ii) does not intend to use any of the proceeds from the sale of the Securities to repay any outstanding debt owed to any affiliate of any Agent.

(jj) Statistical and Market-Related Data. Any statistical and market-related data included in the Registration Statement or the Prospectus are based on or derived from sources that the Company believes, after reasonable inquiry, to be reliable and accurate and, to the extent required, the Company has obtained the written consent to the use of such data from such sources.

(kk) Listing Approval. The Ordinary Shares are registered pursuant to Section 12(b) of the Exchange Act. The Company has filed a Notice of Listing of Additional Shares with The Nasdaq Global Market, and the Company has taken no action designed to, or likely to have the effect of, terminating the registration of the Ordinary Shares under the Exchange Act or delisting the Securities from the Nasdaq Global Market, nor has the Company received any written notification that the Commission or the Nasdaq Global Market is contemplating terminating such registration or listing. The Company is in compliance with all applicable listing requirements of the Nasdaq Global Market, except to the extent as would not reasonably be expected to result in a Material Adverse Effect.

(ll) FINRA Matters. There are no affiliations or associations between any member of FINRA and any of the Company's officers, directors or 5% or greater shareholders. There are no relationships, direct or indirect, or related-party transactions involving the Company or any other person required to be described in the Registration Statement and the Prospectus which have not been described in such documents as required.

(mm) Finder's Fees. Neither the Company nor any of the Subsidiaries has incurred any liability for any finder's fees, brokerage commissions or similar payments in connection with the transactions herein contemplated, except as may otherwise exist with respect to the Agents pursuant to this Agreement.

(nn) Submission to Jurisdiction. The Company has the power to submit, and pursuant to Section 18 of this Agreement, has legally, validly, effectively and irrevocably submitted, to the personal jurisdiction of each United States federal court and New York state court located in the City and County of New York, Borough of Manhattan, State of New York, U.S.A., and the Company has the power to designate and pursuant to Section 18 of this Agreement, has legally, validly, effectively and irrevocably designated the notice address provided in Section 11 of this Agreement for the effective service of process in any action arising out of or relating to this Agreement or the Securities in any of the above courts, and service of process effected on such address will be effective to confer valid personal jurisdiction over the Company as provided in Section 18 hereof.

(oo) No Rights of Immunity. Except as provided by laws or statutes generally applicable to transactions of the type described in this Agreement, neither the Company nor any of its respective properties, assets or revenues has any right of immunity under the laws of the Netherlands, New York State law or United States federal law, from any legal action, suit or proceeding, from the giving of any relief in any such legal action, suit or proceeding, from set-off or counterclaim, from the jurisdiction of any Dutch, New York or United States federal court, from service of process, attachment upon or prior to judgment, or attachment in aid of execution of judgment, or from execution of a judgment, or other legal process or proceeding for the giving of any relief or for the enforcement of a judgment, in any such court, with respect to its obligations, liabilities or any other matter under or arising out of or in connection with this Agreement. To the extent that the Company or any of its respective properties, assets or revenues may have or may hereafter become entitled to any such right of immunity in any such court in which proceedings may at any time be commenced, the Company waives or will waive such right to the extent permitted by law and has consented to such relief and enforcement as provided in Section 17 and Section 18 of this Agreement.

(pp) Agent Purchases. The Company acknowledges and agrees that Agents have informed the Company that the Agents may, to the extent permitted under the Securities Act and the Exchange Act, purchase and sell Ordinary Shares for their own accounts while this Agreement is in effect, *provided*, that the Company shall not be deemed to have authorized or consented to any such purchases or sales by the Agents.

(qq) Forward-Looking Statements. Each financial or operational projection or other “forward-looking statement” (as defined by Section 27A of the Securities Act or Section 21E of the Exchange Act, as applicable) contained in the Registration Statement or the Prospectus (i) was so included by the Company in good faith and with reasonable basis after due consideration by the Company of the underlying assumptions, estimates and other applicable facts and circumstances and (ii) is accompanied by meaningful cautionary statements identifying those factors that could cause actual results to differ materially from those in such forward-looking statement. No such statement was made with the knowledge of a director or senior manager of the Company that is was false or misleading.

(rr) XBRL. The interactive data in the eXtensible Business Reporting Language (“XBRL”) included as an exhibit or incorporated by reference to the Registration Statement fairly presents the information called for in all material respects and has been prepared in accordance with the SEC’s rules and guidelines applicable thereto.

(ss) Data Privacy and Security Laws. The Company and its subsidiaries are, and at all prior times were, in material compliance with all applicable data privacy and security laws and regulations, including without limitation HIPAA, HITECH Act, and the European Union General Data Protection Regulation (“GDPR”) (EU 2016/679) (and all other applicable laws and regulations with respect to Personal Data (defined below) that have been announced as of the date hereof as becoming effective within 12 months after the date hereof, and for which any non-compliance with same would be reasonably likely to create a material liability) (collectively, the “Privacy Laws”). To ensure compliance with the Privacy Laws, the Company and its subsidiaries have in place, comply with, and take appropriate steps reasonably designed to ensure compliance in all material respects with their policies and procedures relating to data privacy and security and the collection, storage, use, disclosure, handling, and analysis of Personal Data (the

“Policies”). The Company provides accurate notice of its Policies then in effect to its customers, employees, third party vendors and representatives in material compliance with Privacy Laws. Each of the Company Policies provides accurate and sufficient notice of the Company’s privacy practices relating to its subject matter and such Company Policies do not contain any material omissions of the Company’s privacy practices. “Personal Data” means (i) a natural person’s name, street address, telephone number, e-mail address, photograph, social security number or tax identification number, driver’s license number, passport number, credit card number, bank information, or customer or account number; (ii) any information which would qualify as “personally identifying information” under the Federal Trade Commission Act, as amended; (iii) Protected Health Information as defined by HIPAA; (iv) “personal data” as defined by GDPR, and (v) any other piece of information that allows the identification of such natural person, or his or her family, or permits the collection or analysis of any data related to an identified person’s health or sexual orientation. The execution, delivery and performance of this Agreement or any other agreement referred to in this Agreement will not result in a breach of violation of any Privacy Laws or Policies. The Company further certifies that neither it nor any subsidiary: (i) has received notice of any actual or potential material liability under or relating to, or actual or potential violation of, any of the Privacy Laws; (ii) is currently conducting or paying for, in whole or in part, any investigation, remediation, or other corrective action pursuant to any Privacy Law; or (iii) is a party to any order, decree, or agreement that imposes any obligation or liability under any Privacy Law.

(tt) Cybersecurity; Data Protection. The Company and its subsidiaries’ information technology and computer systems and assets, networks, hardware, software, websites, applications, databases (including all Personal Data, and sensitive, confidential or regulated data, and the data of their respective customers, employees, suppliers, vendors and any third party data maintained by or on behalf of them), equipment or technology (collectively, “IT Systems and Data”) are adequate for, and operate and perform in all material respects as required in connection with the operation of the business of the Company and its subsidiaries as currently conducted, free and clear of all material bugs, errors, defects, Trojan horses, time bombs, malware and other corruptants. The Company and its subsidiaries have implemented and maintained commercially reasonable controls, policies, procedures, and safeguards to maintain and protect their material confidential information and the integrity, continuous operation, redundancy and security of all IT Systems and Data used in connection with their businesses. (i) Except as may be included or incorporated by reference in the Registration Statement and the Prospectus, (x) to the Company’s knowledge, the Company has not had any material security breach, violations, outages or unauthorized uses of or accesses to same, or other material compromise of or relating to any of the Company’s or its subsidiaries’ IT Systems and Data, and (y) the Company and its subsidiaries have not been notified of, and have no knowledge of any event or condition that would reasonably be expected to result in, any material security breach or other material compromise to their IT Systems and Data; (ii) the Company and its subsidiaries are presently in compliance with all applicable laws or statutes and all judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, internal policies and contractual obligations relating to the privacy and security of IT Systems and Data and to the protection of such IT Systems and Data from unauthorized use, access, misappropriation or modification, except as would not, in the case of this clause (ii), individually or in the aggregate, have a Material Adverse Effect; and (iii) the Company and its subsidiaries have implemented backup and disaster recovery technology consistent with industry standards and practices.

(uu) Compliance with ERISA. The Company does not maintain any “employee benefit plan” subject to Title IV of the Employee Retirement Income Security Act of 1974, as amended (“ERISA”), or the regulations and published interpretations thereunder.

(vv) Stock Transfer Taxes. On each Settlement Date, all stock transfer or other taxes (other than income taxes) which are required to be paid in connection with the sale and transfer of the Placement Shares to be sold hereunder will be, or will have been, fully paid or provided for by the Company and all laws imposing such taxes will be or will have been fully complied with.

(ww) Underwriter Agreements. The Company is not a party to any agreement with an agent or underwriter for any other “at the market” or continuous equity transaction.

(xx) Margin Rules. Neither the issuance, sale and delivery of the Placement Shares nor the application of the proceeds thereof by the Company as described in the Registration Statement and the Prospectus will violate Regulation T, U or X of the Board of Governors of the Federal Reserve System or any other regulation of such Board of Governors.

Any certificate signed by an officer of the Company and delivered to the Agents or to counsel for the Agents pursuant to or in connection with this Agreement shall be deemed to be a representation and warranty by the Company, as applicable, to the Agents as to the matters set forth therein.

7. Covenants of the Company. The Company covenants and agrees with each of the Agents that:

(a) Registration Statement Amendments. After the date of this Agreement and during any period in which a Prospectus relating to any Placement Shares is required to be delivered by the Agents under the Securities Act (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), (i) the Company will notify the Agents promptly of the time when any subsequent amendment to the Registration Statement, other than documents incorporated by reference, has been filed with the Commission and/or has become effective or any subsequent supplement to the Prospectus has been filed and of any request by the Commission for any amendment or supplement to the Registration Statement or Prospectus or for additional information, (ii) the Company will prepare and file with the Commission, promptly upon the Agents’ request, any amendments or supplements to the Registration Statement or Prospectus that, in the Agents’ reasonable opinion, may be necessary or advisable in connection with the distribution of the Placement Shares by the Agents (*provided, however, that the failure of the Agents to make such request shall not relieve the Company of any obligation or liability hereunder, or affect the Agents’ right to rely on the representations and warranties made by the Company in this Agreement and provided, further, that the only remedy the Agents shall have with respect to the failure to make such filing shall be to cease making sales under this Agreement until such amendment or supplement is filed*); (iii) the Company will not file any amendment or supplement to the Registration Statement or Prospectus relating to the Placement Shares or a security convertible into the Placement Shares unless a copy thereof has been submitted to Agents within a reasonable period of time before the filing and the Agents have not objected thereto (*provided, however, that the failure of the Agent to make such objection shall not relieve the Company of any obligation or liability hereunder, or affect the Agents’ right to rely*

on the representations and warranties made by the Company in this Agreement and *provided, further*, that the only remedy the Agents shall have with respect to the failure by the Company to obtain such consent shall be to cease making sales under this Agreement) and the Company will furnish to the Agents at the time of filing thereof a copy of any document that upon filing is deemed to be incorporated by reference into the Registration Statement or Prospectus, except for those documents available via EDGAR; and (iv) the Company will cause each amendment or supplement to the Prospectus to be filed with the Commission as required pursuant to the applicable paragraph of Rule 424(b) of the Securities Act or, in the case of any document to be incorporated therein by reference, to be filed with the Commission as required pursuant to the Exchange Act, within the time period prescribed (the determination to file or not file any amendment or supplement with the Commission under this Section 7(a), based on the Company's reasonable opinion or reasonable objections, shall be made exclusively by the Company). Notwithstanding anything to the contrary herein, the Company has no obligation to provide the Agents any advanced copy of any supplement to the Prospect if such supplement does not relate to the Placement Shares or to the transactions contemplated by this Agreement.

(b) Notice of Commission Stop Orders. The Company will advise the Agents, promptly after it receives notice or obtains knowledge thereof, of the issuance or threatened issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement, of the suspension of the qualification of the Placement Shares for offering or sale in any jurisdiction, or of the initiation or threatening of any proceeding for any such purpose; and it will promptly use its commercially reasonable efforts to prevent the issuance of any stop order or to obtain its withdrawal if such a stop order should be issued. The Company will advise the Agents promptly after it receives any request by the Commission for any amendments to the Registration Statement or any amendment or supplements to the Prospectus or any Issuer Free Writing Prospectus or for additional information related to the offering of the Placement Shares or for additional information related to the Registration Statement, the Prospectus or any Issuer Free Writing Prospectus.

(c) Delivery of Prospectus; Subsequent Changes. During any period in which a Prospectus relating to the Placement Shares is required to be delivered by the Agents under the Securities Act with respect to the offer and sale of the Placement Shares, (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), the Company will comply with all requirements imposed upon it by the Securities Act, as from time to time in force, and to file on or before their respective due dates all reports and any definitive proxy or information statements required to be filed by the Company with the Commission pursuant to Sections 13(a), 13(c), 14, 15(d) or any other provision of or under the Exchange Act. If the Company has omitted any information from the Registration Statement pursuant to Rule 430B under the Securities Act, it will use its best efforts to comply with the provisions of and make all requisite filings with the Commission pursuant to said Rule 430B and to notify the Agents promptly of all such filings. If during such period any event occurs as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances then existing, not misleading, or if during such period it is necessary to amend or supplement the Registration Statement or Prospectus to comply with the Securities Act, the Company will promptly notify the Agents to suspend the offering of Placement Shares during such period and the Company will promptly amend or supplement the Registration Statement or

Prospectus (at the expense of the Company) so as to correct such statement or omission or effect such compliance.

(d) Listing of Placement Shares. During any period in which the Prospectus relating to the Placement Shares is required to be delivered by the Agents under the Securities Act with respect to the offer and sale of the Placement Shares, the Company will use its reasonable best efforts to cause the Placement Shares to be listed on the Exchange.

(e) Delivery of Registration Statement and Prospectus. The Company will furnish to the Agents and their counsel (at the expense of the Company) copies of the Registration Statement, the Prospectus (including all documents incorporated by reference therein) and all amendments and supplements to the Registration Statement or Prospectus that are filed with the Commission during any period in which a Prospectus relating to the Placement Shares is required to be delivered under the Securities Act (including all documents filed with the Commission during such period that are deemed to be incorporated by reference therein), in each case as soon as reasonably practicable and in such quantities as the Agents may from time to time reasonably request and, at the Agents' request, will also furnish copies of the Prospectus to each exchange or market on which sales of the Placement Shares may be made; *provided, however*, that the Company shall not be required to furnish any document (other than the Prospectus) to the Agents to the extent such document is available on EDGAR.

(f) Earning Statement. The Company will make generally available to its security holders as soon as practicable, but in any event not later than 15 months after the end of the Company's current fiscal quarter, an earning statement covering a 12-month period that satisfies the provisions of Section 11(a) and Rule 158 of the Securities Act.

(g) Use of Proceeds. The Company will use the Net Proceeds as described in the Prospectus in the section entitled "Use of Proceeds."

(h) Notice of Other Sales. Without the prior written consent of the Agents, the Company will not, directly or indirectly, offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Ordinary Shares (other than the Placement Shares offered pursuant to this Agreement) or securities convertible into or exchangeable for Ordinary Shares, warrants or any rights to purchase or acquire, Ordinary Shares during the period beginning on the fifth (5th) Trading Day immediately prior to the date on which any Placement Notice is delivered to the Agents hereunder and ending on the fifth (5th) Trading Day immediately following the final Settlement Date with respect to Placement Shares sold pursuant to such Placement Notice (or, if the Placement Notice has been terminated or suspended prior to the sale of all Placement Shares covered by a Placement Notice, the date of such suspension or termination); and will not directly or indirectly in any other "at the market" or continuous equity transaction offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Ordinary Shares (other than the Placement Shares offered pursuant to this Agreement) or securities convertible into or exchangeable for Ordinary Shares, warrants or any rights to purchase or acquire, Ordinary Shares prior to the later of the termination of this Agreement and the sixtieth (60th) day immediately following the final Settlement Date with respect to Placement Shares sold pursuant to such Placement Notice; *provided, however*, that such restrictions will not be required in connection with the Company's issuance or sale of (i) Ordinary Shares, options to purchase Ordinary Shares or Ordinary Shares issuable upon the exercise of options or other compensatory share awards,

pursuant to any employee, director or similar stock option or benefits plan, stock ownership plan or dividend reinvestment plan (but not Ordinary Shares subject to a waiver to exceed plan limits in its dividend reinvestment plan) of the Company whether now in effect or hereafter implemented, (ii) Ordinary Shares issuable upon conversion of securities or the exercise of warrants, options or other rights in effect or outstanding, and disclosed in filings by the Company available on EDGAR or otherwise in writing to the Agents and (iii) Ordinary Shares or securities convertible into or exchangeable for shares of Ordinary Shares as consideration for mergers, acquisitions, other business combinations, strategic alliances, collaborations, partnerships, joint ventures or similar transactions occurring after the date of this Agreement which are not issued primarily for capital raising purposes.

(i) Change of Circumstances. The Company will, at any time during the pendency of a Placement Notice advise the Agents promptly after it shall have received notice or obtained knowledge thereof, of any information or fact that would alter or affect in any material respect any opinion, certificate, letter or other document required to be provided to the Agents pursuant to this Agreement.

(j) Due Diligence Cooperation. The Company will cooperate with any reasonable due diligence review conducted by the Agents or its representatives in connection with the transactions contemplated hereby, including, without limitation, providing information and making available documents and senior corporate officers, during regular business hours and at the Company's principal offices, as the Agents may reasonably request.

(k) Required Filings Relating to Placement of Placement Shares. The Company shall disclose, in its reports on Form 6-K containing its quarterly or semi-annual financial statements and in its annual report on Form 20-F to be filed by the Company with the Commission from time to time, the number of the Placement Shares sold through the Agents under this Agreement, and the net proceeds to the Company from the sale of the Placement Shares pursuant to this Agreement during the relevant quarter or, in the case of an annual report on Form 20-F, during the fiscal year covered by such annual report and the fourth quarter of such fiscal year. The Company agrees that on such dates as the Securities Act shall require, the Company will (i) file a prospectus supplement with the Commission under the applicable paragraph of Rule 424(b) under the Securities Act (each and every filing date under Rule 424(b), a "**Filing Date**"), which prospectus supplement will set forth, within the relevant period, the amount of Placement Shares sold through the Agents, the Net Proceeds to the Company and the compensation payable by the Company to the Agents with respect to such Placement Shares, and (ii) deliver such number of copies of each such prospectus supplement to each exchange or market on which such sales were effected as may be required by the rules or regulations of such exchange or market.

(l) Representation Dates; Certificate. (1) Prior to the date of the first Placement Notice and (2) each time the Company:

(i) files the Prospectus relating to the Placement Shares or amends or supplements (other than a prospectus supplement relating solely to an offering of securities other than the Placement Shares) the Registration Statement or the Prospectus relating to the Placement Shares by means of a post-effective amendment, sticker, or supplement but not by means of incorporation of documents by reference into the Registration Statement or the Prospectus relating to the Placement Shares;

(ii) files an annual report on Form 20-F under the Exchange Act (including any Form 20-F/A containing amended financial information or a material amendment to the previously filed Form 20-F);

(iii) files a report on Form 6-K under the Exchange Act containing its quarterly or semi-annual financial statements; or

(iv) files a report on Form 6-K containing amended financial information under the Exchange Act (each date of filing of one or more of the documents referred to in clauses (i) through (iv) shall be a "**Representation Date**");

the Company shall furnish the Agents (but in the case of clause (iv) above only if the Agents reasonably determine that the information contained in such Form 6-K is material) with a certificate dated the Representation Date, in the form and substance satisfactory to the Agents and its counsel, substantially similar to the form previously provided to the Agents and their counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as amended or supplemented. The requirement to provide a certificate under this Section 7(l) shall be waived for any Representation Date occurring at a time a Suspension is in effect, which waiver shall continue until the earlier to occur of the date the Company delivers instructions for the sale of Placement Shares hereunder (which for such calendar quarter shall be considered a Representation Date) and the next occurring Representation Date. Notwithstanding the foregoing, if the Company subsequently decides to sell Placement Shares following a Representation Date when a Suspension was in effect and did not provide the Agents with a certificate under this Section 7(l), then before the Company delivers the instructions for the sale of Placement Shares or either of the Agents sells any Placement Shares pursuant to such instructions, the Company shall provide the Agents with a certificate in conformity with this Section 7(l) dated as of the date that the instructions for the sale of Placement Shares are issued.

(m) Legal Opinions. (1) Prior to the date of the first Placement Notice and (2) within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(l) for which no waiver is applicable and excluding the date of this Agreement, the Company shall cause to be furnished to the Agents a written opinion of Goodwin Procter LLP, U.S. counsel to the Company, and Allen & Overy LLP, Dutch counsel for the Company (together, "**Company Counsel**"), or other counsel satisfactory to the Agents, in form and substance satisfactory to the Agents and their counsel, substantially similar to a form previously provided to the Agents and their counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented; *provided, however*, the Company shall be required to furnish to Agent no more than one opinion hereunder per calendar quarter; *provided, further*, that in lieu of such opinions for subsequent periodic filings under the Exchange Act, counsel may furnish the Agent with a letter (a "**Reliance Letter**") to the effect that the Agent may rely on a prior opinion delivered under this Section 7(m) to the same extent as if it were dated the date of such letter (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of the date of the Reliance Letter).

(n) Comfort Letter. (1) Prior to the date of the first Placement Notice and (2) within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(l) for which no waiver is applicable and

excluding the date of this Agreement, the Company shall cause its independent registered public accounting firm to furnish the Agents letters (the “**Comfort Letters**”), dated the date the Comfort Letter is delivered, which shall meet the requirements set forth in this Section 7(n); *provided*, that if requested by the Agents, the Company shall cause a Comfort Letter to be furnished to the Agent within ten (10) Trading Days of the date of occurrence of any material transaction or event, including the restatement of the Company’s financial statements. The Comfort Letter from the Company’s independent registered public accounting firm shall be in a form and substance satisfactory to the Agent, (i) confirming that they are an independent registered public accounting firm within the meaning of the Securities Act and the PCAOB, (ii) stating, as of such date, the conclusions and findings of such firm with respect to the financial information and other matters ordinarily covered by accountants’ “comfort letters” to underwriters in connection with registered public offerings (the first such letter, the “**Initial Comfort Letter**”) and (iii) updating the Initial Comfort Letter with any information that would have been included in the Initial Comfort Letter had it been given on such date and modified as necessary to relate to the Registration Statement and the Prospectus, as amended and supplemented to the date of such letter.

(o) Market Activities. The Company will not, directly or indirectly, (i) take any action designed to cause or result in, or that constitutes or might reasonably be expected to constitute, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of Ordinary Shares or (ii) sell, bid for, or purchase Ordinary Shares in violation of Regulation M, or pay anyone any compensation for soliciting purchases of the Placement Shares other than the Agents.

(p) Investment Company Act. The Company will conduct its affairs in such a manner so as to reasonably ensure that neither it nor any of its Subsidiaries will be or become, at any time prior to the termination of this Agreement, required to register as an “investment company,” as such term is defined in the Investment Company Act.

(q) No Offer to Sell. Other than an Issuer Free Writing Prospectus approved in advance by the Company and the Agents in their capacity as agents hereunder, neither the Agents nor the Company (including its agents and representatives, other than the Agent in its capacity as such) will make, use, prepare, authorize, approve or refer to any written communication (as defined in Rule 405 under the Securities Act), required to be filed with the Commission, that constitutes an offer to sell or solicitation of an offer to buy Placement Shares hereunder.

(r) Blue Sky and Other Qualifications. The Company will use its commercially reasonable efforts, in cooperation with the Agents, to qualify the Placement Shares for offering and sale, or to obtain an exemption for the Placement Shares to be offered and sold, under the applicable securities laws of such states and other jurisdictions (domestic or foreign) as the Agents may designate and to maintain such qualifications and exemptions in effect for so long as required for the distribution of the Placement Shares (but in no event for less than one year from the date of this Agreement); *provided, however*, that the Company shall not be obligated to file any general consent to service of process or to qualify as a foreign corporation or as a dealer in securities in any jurisdiction in which it is not so qualified or to subject itself to taxation in respect of doing business in any jurisdiction in which it is not otherwise so subject. In each jurisdiction in which the Placement Shares have been so qualified or exempt, the Company will file such statements and reports as may be required by the laws of such jurisdiction to continue such qualification or

exemption, as the case may be, in effect for so long as required for the distribution of the Placement Shares (but in no event for less than one year from the date of this Agreement).

(s) Sarbanes-Oxley Act. The Company and the Subsidiaries will maintain and keep accurate books and records reflecting their assets and maintain internal accounting controls in a manner designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and including those policies and procedures that (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company, (ii) provide reasonable assurance that transactions are recorded as necessary to permit the preparation of the Company's consolidated financial statements in accordance with generally accepted accounting principles, (iii) that receipts and expenditures of the Company are being made only in accordance with management's and the Company's directors' authorization, and (iv) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on its financial statements. The Company and the Subsidiaries will maintain such controls and other procedures, including, without limitation, those required by Sections 302 and 906 of the Sarbanes-Oxley Act, and the applicable regulations thereunder that are designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Commission's rules and forms, including, without limitation, controls and procedures designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure and to ensure that material information relating to the Company or the Subsidiaries is made known to them by others within those entities, particularly during the period in which such periodic reports are being prepared.

(t) Certificate; Further Documentation. Prior to the date of the first Placement Notice, the Company shall deliver to the Agents a certificate of a member of the Company's board of directors, dated as of such date, certifying as to (i) the articles of association of the Company, (ii) the resolutions of the board of directors and the supervisory board of the Company authorizing the execution, delivery and performance of this Agreement and the issuance of the Placement Shares and (iii) the incumbency of the representatives of the Company duly authorized to execute this Agreement and the other documents contemplated by this Agreement. Within five (5) Trading Days of each Representation Date, the Company shall have furnished to the Agents such further information, certificates and documents as the Agents may reasonably request.

(u) *Intentionally omitted.*

8. Payment of Expenses. The Company will pay all expenses incident to the performance of its obligations under this Agreement, including (i) the preparation and filing of the Registration Statement, including any fees required by the Commission, and the printing or electronic delivery of the Prospectus as originally filed and of each amendment and supplement thereto, in such number as the Agents shall deem necessary, (ii) the printing and delivery to the Agents of this Agreement and such other documents as may be required in connection with the offering, purchase, sale, issuance or delivery of the Placement Shares, (iii) the preparation,

issuance and delivery of the certificates, if any, for the Placement Shares to the Agents, including any stock or other transfer taxes and any capital duties, stamp duties or other similar duties or taxes payable upon the sale, issuance or delivery of the Placement Shares to the Agents, (iv) the fees and disbursements of the counsel, accountants and other advisors to the Company, (v) the fees and expenses of Agent including but not limited to the fees and expenses of the counsel to the Agent, payable upon the execution of this Agreement, in an amount not to exceed \$25,000, (vi) the qualification or exemption of the Placement Shares under state securities laws in accordance with the provisions of Section 7(r) hereof, including filing fees, but excluding fees of the Agent's counsel, (vii) the printing and delivery to the Agents of copies of any Permitted Issuer Free Writing Prospectus and the Prospectus and any amendments or supplements thereto in such number as the Agents shall deem necessary, (viii) the preparation, printing and delivery to the Agents of copies of the blue sky survey, (ix) the fees and expenses of the transfer agent and registrar for the Ordinary Shares, (x) the filing and other fees incident to any review by FINRA of the terms of the sale of the Placement Shares including the fees of the Agents' counsel (subject to the cap, set forth in clause (v) above), and (xi) the fees and expenses incurred in connection with the listing of the Placement Shares on the Exchange.

9. Conditions to Agent's Obligations. The obligations of the Agents hereunder with respect to a Placement will be subject to the continuing accuracy and completeness of the representations and warranties made by the Company herein, to the due performance by the Company of its obligations hereunder, to the completion by the Agents of a due diligence review satisfactory to it in its reasonable judgment, and to the continuing satisfaction (or waiver by each of the Agents in its sole discretion) of the following additional conditions:

(a) Registration Statement Effective. The Registration Statement shall have become effective and shall be available for the (i) resale of all Placement Shares issued to an Agent and not yet sold by such Agent and (ii) sale of all Placement Shares contemplated to be issued by any Placement Notice.

(b) No Material Notices. None of the following events shall have occurred and be continuing: (i) receipt by the Company of any request for additional information from the Commission or any other federal or state Governmental Entity during the period of effectiveness of the Registration Statement, the response to which would require any post-effective amendments or supplements to the Registration Statement or the Prospectus; (ii) the issuance by the Commission or any other federal or state Governmental Entity of any stop order suspending the effectiveness of the Registration Statement or the initiation of any proceedings for that purpose; (iii) receipt by the Company of any notification with respect to the suspension of the qualification or exemption from qualification of any of the Placement Shares for sale in any jurisdiction or the initiation or threatening of any proceeding for such purpose; or (iv) the occurrence of any event that makes any statement of a material fact made in the Registration Statement or the Prospectus or any document incorporated or deemed to be incorporated therein by reference untrue or that requires the making of any changes in the Registration Statement, the Prospectus or documents so that, in the case of the Registration Statement, it will not contain an untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading and, that in the case of the Prospectus, it will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or

necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(c) No Misstatement or Material Omission. The Agents shall not have advised the Company that the Registration Statement or Prospectus, or any amendment or supplement thereto, contains an untrue statement of fact that in the Agents' reasonable opinion is material, or omits to state a fact that in the Agents' reasonable opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

(d) Material Changes. Except as contemplated in the Prospectus, or disclosed in the Company's reports filed with the Commission, there shall not have been any material adverse change in the authorized capital stock of the Company or any Material Adverse Effect or any development that could cause a Material Adverse Effect, or a downgrading in or withdrawal of the rating assigned to any of the Company's securities (other than asset backed securities) by any rating organization or a public announcement by any rating organization that it has under surveillance or review its rating of any of the Company's securities (other than asset backed securities), the effect of which, in the case of any such action by a rating organization described above, in the reasonable judgment of the Agents (without relieving the Company of any obligation or liability it may otherwise have), is so material as to make it impracticable or inadvisable to proceed with the offering of the Placement Shares on the terms and in the manner contemplated in the Prospectus.

(e) Legal Opinions. The Agents shall have received the opinions of Company Counsel required to be delivered pursuant to Section 7(m) on or before the date on which such delivery of such opinion is required pursuant to Section 7(m).

(f) Comfort Letter. The Agents shall have received the Comfort Letter required to be delivered pursuant to Section 7(n) on or before the date on which such delivery of such Comfort Letter is required pursuant to Section 7(n).

(g) Representation Certificate. The Agents shall have received the certificate required to be delivered pursuant to Section 7(l) on or before the date on which delivery of such certificate is required pursuant to Section 7(l).

(h) No Suspension. Trading in the Ordinary Shares shall not have been suspended on the Exchange and the Ordinary Shares shall not have been delisted from the Exchange.

(i) Other Materials. On each date on which the Company is required to deliver a certificate pursuant to Section 7(l), the Company shall have furnished to the Agents such appropriate further information, opinions, certificates, letters and other documents as the Agents may reasonably request. All such opinions, certificates, letters and other documents will be in compliance with the provisions hereof.

(j) Securities Act Filings Made. All filings with the Commission required by Rule 424 under the Securities Act to have been filed prior to the issuance of any Placement Notice hereunder shall have been made within the applicable time period prescribed for such filing by Rule 424.

(k) Approval for Listing. The Placement Shares shall either have been (i) approved for listing on the Exchange, subject only to notice of issuance, or (ii) the Company shall have filed an application for listing of the Placement Shares on the Exchange at, or prior to, the issuance of any Placement Notice and the Exchange shall have reviewed such application and not provided any objections thereto.

(l) FINRA. If applicable, FINRA shall have raised no objection to the terms of this offering and the amount of compensation allowable or payable to the Agents as described in the Prospectus.

(m) No Termination Event. There shall not have occurred any event that would permit the Agents to terminate this Agreement pursuant to Section 12(a).

10. Indemnification and Contribution.

(a) Company Indemnification. The Company agrees to indemnify and hold harmless the Agents, their partners, members, directors, officers, employees and agents and each person, if any, who controls the applicable Agent within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act as follows:

(i) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, joint or several, arising out of or based upon any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement (or any amendment thereto), or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading, or arising out of any untrue statement or alleged untrue statement of a material fact included in any related Issuer Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading;

(ii) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, joint or several, to the extent of the aggregate amount paid in settlement of any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or of any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission; *provided* that (subject to Section 10(d) below) any such settlement is effected with the written consent of the Company, which consent shall not unreasonably be delayed or withheld; and

(iii) against any and all expense whatsoever, as incurred (including the fees and disbursements of counsel), reasonably incurred in investigating, preparing or defending against any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission, to the extent that any such expense is not paid under (i) or (ii) above,

provided, however, that this indemnity agreement shall not apply to any loss, liability, claim, damage or expense to the extent arising out of any untrue statement or omission or alleged untrue statement or omission made solely in reliance upon and in conformity with written information

furnished to the Company by the Agents expressly for use in the Registration Statement (or any amendment thereto), or in any related Issuer Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto).

(b) Agent Indemnification. Each Agent, severally but not jointly, agrees to indemnify and hold harmless the Company and its directors and each officer of the Company who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act against any and all loss, liability, claim, damage and expense described in the indemnity contained in Section 10(a), as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in the Registration Statement (or any amendments thereto) or the Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with information relating to such Agent and furnished to the Company in writing by such Agent expressly for use therein. The Company hereby acknowledges that the only information that the Agents have furnished to the Company expressly for use in the Registration Statement, the Prospectus or any Issuer Free Writing Prospectus (or any amendment or supplement thereto) are the statements set forth in the last sentence of the first paragraph under the caption “Plan of Distribution” in the Prospectus.

(c) Procedure. Any party that proposes to assert the right to be indemnified under this Section 10 will, promptly after receipt of notice of commencement of any action against such party in respect of which a claim is to be made against an indemnifying party or parties under this Section 10, notify each such indemnifying party of the commencement of such action, enclosing a copy of all papers served, but the omission so to notify such indemnifying party will not relieve the indemnifying party from (i) any liability that it might have to any indemnified party otherwise than under this Section 10 and (ii) any liability that it may have to any indemnified party under the foregoing provision of this Section 10 unless, and only to the extent that, such omission results in the forfeiture of substantive rights or defenses by the indemnifying party. If any such action is brought against any indemnified party and it notifies the indemnifying party of its commencement, the indemnifying party will be entitled to participate in and, to the extent that it elects by delivering written notice to the indemnified party promptly after receiving notice of the commencement of the action from the indemnified party, jointly with any other indemnifying party similarly notified, to assume the defense of the action, with counsel reasonably satisfactory to the indemnified party, and after notice from the indemnifying party to the indemnified party of its election to assume the defense, the indemnifying party will not be liable to the indemnified party for any other legal expenses except as provided below and except for the reasonable costs of investigation subsequently incurred by the indemnified party in connection with the defense. The indemnified party will have the right to employ its own counsel in any such action, but the fees, expenses and other charges of such counsel will be at the expense of such indemnified party unless (1) the employment of counsel by the indemnified party has been authorized in writing by the indemnifying party, (2) the indemnified party has reasonably concluded (based on advice of counsel) that there may be legal defenses available to it or other indemnified parties that are different from or in addition to those available to the indemnifying party, (3) a conflict or potential conflict exists (based on advice of counsel to the indemnified party) between the indemnified party and the indemnifying party (in which case the indemnifying party will not have the right to direct the defense of such action on behalf of the indemnified party) or (4) the indemnifying party has not in fact employed counsel to assume the defense of such action within a reasonable time after

receiving notice of the commencement of the action, in each of which cases the reasonable fees, disbursements and other charges of counsel will be at the expense of the indemnifying party or parties. It is understood that the indemnifying party or parties shall not, in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the reasonable fees, disbursements and other charges of more than one separate firm admitted to practice in such jurisdiction at any one time for all such indemnified party or parties. All such fees, disbursements and other charges will be reimbursed by the indemnifying party promptly as they are incurred. An indemnifying party will not, in any event, be liable for any settlement of any action or claim effected without its written consent. No indemnifying party shall, without the prior written consent of each indemnified party, settle or compromise or consent to the entry of any judgment in any pending or threatened claim, action or proceeding relating to the matters contemplated by this Section 10 (whether or not any indemnified party is a party thereto), unless such settlement, compromise or consent (1) includes an unconditional release of each indemnified party from all liability arising out of such litigation, investigation, proceeding or claim and (2) does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party.

(d) Settlement Without Consent if Failure to Reimburse. If an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for reasonable fees and expenses of counsel, such indemnifying party agrees that it shall be liable for any settlement of the nature contemplated by Section 10(a)(ii) effected without its written consent if (1) such settlement is entered into more than 45 days after receipt by such indemnifying party of the aforesaid request, (2) such indemnifying party shall have received notice of the terms of such settlement at least 30 days prior to such settlement being entered into and (3) such indemnifying party shall not have reimbursed such indemnified party in accordance with such request prior to the date of such settlement.

(e) Contribution. In order to provide for just and equitable contribution in circumstances in which the indemnification provided for in the foregoing paragraphs of this Section 10 is applicable in accordance with its terms but for any reason is held to be unavailable or insufficient from the Company or an Agent, the Company and such Agent will contribute to the total losses, claims, liabilities, expenses and damages (including any investigative, legal and other expenses reasonably incurred in connection with, and any amount paid in settlement of, any action, suit or proceeding or any claim asserted) to which the Company and such Agent may be subject in such proportion as shall be appropriate to reflect the relative benefits received by the Company on the one hand and the Agents on the other hand. The relative benefits received by the Company on the one hand and such Agent on the other hand shall be deemed to be in the same proportion as the total net proceeds from the sale of the Placement Shares (before deducting expenses) received by the Company bear to the total compensation received by the Agents from the sale of Placement Shares on behalf of the Company. If, but only if, the allocation provided by the foregoing sentence is not permitted by applicable law, the allocation of contribution shall be made in such proportion as is appropriate to reflect not only the relative benefits referred to in the foregoing sentence but also the relative fault of the Company, on the one hand, and such Agent, on the other hand, with respect to the statements or omission that resulted in such loss, claim, liability, expense or damage, or action in respect thereof, as well as any other relevant equitable considerations with respect to such offering. Such relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or omission or alleged omission to state a

material fact relates to information supplied by the Company or such Agent, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and each Agent agree that it would not be just and equitable if contributions pursuant to this Section 10(e) were to be determined by pro rata allocation or by any other method of allocation that does not take into account the equitable considerations referred to herein. The amount paid or payable by an indemnified party as a result of the loss, claim, liability, expense, or damage, or action in respect thereof, referred to above in this Section 10(e) shall be deemed to include, for the purpose of this Section 10(e), any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim to the extent consistent with Section 10(c) hereof. Notwithstanding the foregoing provisions of this Section 10(e), no Agent shall be required to contribute any amount in excess of the commissions received by such Agent under this Agreement and no person found guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 10(e), any person who controls a party to this Agreement within the meaning of the Securities Act, and any officers, directors, partners, employees or agents of an Agent, will have the same rights to contribution as that party, and each director of the Company and each officer of the Company who signed the Registration Statement will have the same rights to contribution as the Company, subject in each case to the provisions hereof. Any party entitled to contribution, promptly after receipt of notice of commencement of any action against such party in respect of which a claim for contribution may be made under this Section 10(e), will notify any such party or parties from whom contribution may be sought, but the omission to so notify will not relieve that party or parties from whom contribution may be sought from any other obligation it or they may have under this Section 10(e) except to the extent that the failure to so notify such other party materially prejudiced the substantive rights or defenses of the party from whom contribution is sought. Except for a settlement entered into pursuant to the last sentence of Section 10(c) hereof, no party will be liable for contribution with respect to any action or claim settled without its written consent if such consent is required pursuant to Section 10(c) hereof. The Agents' respective obligations to contribute pursuant to this Section 10(e) are several in proportion to the respective number of Placement Shares they have sold hereunder, and not joint.

11. Representations and Agreements to Survive Delivery. The indemnity and contribution agreements contained in Section 10 of this Agreement and all representations and warranties of the Company herein or in certificates delivered pursuant hereto shall survive, as of their respective dates, regardless of (i) any investigation made by or on behalf of any Agent, any controlling persons, or the Company (or any of their respective officers, directors, employees or controlling persons), (ii) delivery and acceptance of the Placement Shares and payment therefor or (iii) any termination of this Agreement.

12. Termination.

(a) An Agent may terminate this Agreement with respect to itself, by notice to the Company, as hereinafter specified at any time (1) if there has been, since the time of execution of this Agreement or since the date as of which information is given in the Prospectus, any change, or any development or event involving a prospective change, in the condition, financial or otherwise, or in the business, properties, earnings, results of operations or prospects of the

Company and its Subsidiaries considered as one enterprise, whether or not arising in the ordinary course of business, which individually or in the aggregate, in the sole judgment of such Agent is material and adverse and makes it impractical or inadvisable to market the Placement Shares or to enforce contracts for the sale of the Placement Shares, (2) if there has occurred any material adverse change in the financial markets in the United States or the international financial markets, any outbreak of hostilities or escalation thereof or other calamity or crisis or any change or development involving a prospective change in national or international political, financial or economic conditions, in each case the effect of which is such as to make it, in the judgment of such Agent, impracticable or inadvisable to market the Placement Shares or to enforce contracts for the sale of the Placement Shares, (3) if trading in the Ordinary Shares has been suspended or limited by the Commission or the Exchange, or if trading generally on the Exchange has been suspended or limited, or minimum prices for trading have been fixed on the Exchange, (4) if any suspension of trading of any securities of the Company on any exchange or in the over-the-counter market shall have occurred and be continuing, (5) if a major disruption of securities settlements or clearance services in the United States shall have occurred and be continuing, or (6) if a banking moratorium has been declared by either U.S. Federal or New York authorities. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8 (Payment of Expenses), Section 10 (Indemnification and Contribution), Section 11 (Representations and Agreements to Survive Delivery), Section 17 (Governing Law and Time; Waiver of Jury Trial), Section 18 (Consent to Jurisdiction), Section 19 (Recognition of the U.S. Special Resolution Regimes), Section 20 (Appointment of Agent for Service) and Section 21 (Judgment Currency) hereof shall remain in full force and effect notwithstanding such termination. If an Agent elects to terminate this Agreement as provided in this Section 12(a), such Agent shall provide the required notice as specified in Section 13 (Notices). For the avoidance of doubt, the termination by one Agent of its rights and obligations under this Agreement pursuant to this Section 12(a) shall not affect the rights and obligations of the other Agent under this Agreement.

(b) The Company shall have the right, by giving ten (10) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8, Section 10, Section 11, Section 17, Section 18, Section 19, Section 20 and Section 21 hereof shall remain in full force and effect notwithstanding such termination.

(c) Each of the Agents shall have the right, by giving ten (10) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement, with respect to such Agent's rights and obligations under this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8, Section 10, Section 11, Section 17, Section 18, Section 19, Section 20 and Section 21 hereof shall remain in full force and effect notwithstanding such termination. For the avoidance of doubt, the termination by one Agent of its rights and obligations under this Agreement pursuant to this Section 12(c) shall not affect the rights and obligations of the other Agent under this Agreement.

(d) This Agreement shall remain in full force and effect unless terminated pursuant to Sections 12(a), (b), or (c) above or otherwise by mutual agreement of the parties; *provided, however*, that any such termination by mutual agreement shall in all cases be deemed to

provide that Section 8, Section 10, Section 11, Section 17, Section 18, Section 19, Section 20 and Section 21 shall remain in full force and effect.

(e) Any termination of this Agreement shall be effective on the date specified in such notice of termination; *provided, however*, that such termination shall not be effective until the close of business on the date of receipt of such notice by an Agent or the Company, as the case may be. If such termination shall occur prior to the Settlement Date for any sale of Placement Shares, such Placement Shares shall settle in accordance with the provisions of this Agreement.

13. Notices. All notices or other communications required or permitted to be given by any party to any other party pursuant to the terms of this Agreement shall be in writing, unless otherwise specified, and if sent to the Agents, shall be delivered to:

Citigroup Global Markets Inc.
388 Greenwich Street
New York, New York, 10013
Attention: General Counsel
Facsimile: (646) 291 1469

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022
Attention: Capital Markets
Facsimile: (212) 307-3730

with copies to:

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022
Attention: General Counsel
Facsimile: (212) 829-4708

and with a copy to (such copy not to constitute notice):

Cooley LLP
55 Hudson Yards
New York, NY 10001-2157
Attention: Daniel I. Goldberg, Esq.
Email: dgoldberg@cooley.com

and if to the Company, shall be delivered to:

ProQR Therapeutics N.V.
Zernikedreef 9
2333 CK Leiden

The Netherlands
Attention: Daniel de Boer
Email: DdeBoer@proqr.com

with a copy to (such copy not to constitute notice):

Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210
Attention: Mitchell S. Bloom, Esq. and Danielle M. Lauzon, Esq.
Email: mbloom@goodwinlaw.com; dlauzon@goodwinlaw.com

Each party to this Agreement may change such address for notices by sending to the parties to this Agreement written notice of a new address for such purpose. Each such notice or other communication shall be deemed given (i) when delivered personally or by verifiable facsimile transmission (with an original to follow) on or before 4:30 p.m., New York City time, on a Business Day or, if such day is not a Business Day, on the next succeeding Business Day, (ii) on the next Business Day after timely delivery to a nationally-recognized overnight courier and (iii) on the Business Day actually received if deposited in the U.S. mail (certified or registered mail, return receipt requested, postage prepaid). For purposes of this Agreement, “**Business Day**” shall mean any day on which the Exchange and commercial banks in the City of New York are open for business.

An electronic communication (“**Electronic Notice**”) shall be deemed written notice for purposes of this Section 13 if sent to the electronic mail address specified by the receiving party under separate cover or as specified above by Company. Electronic Notice shall be deemed received at the time the party sending Electronic Notice receives verification of receipt by the receiving party. Any party receiving Electronic Notice may request and shall be entitled to receive the notice on paper, in a nonelectronic form (“**Nonelectronic Notice**”) which shall be sent to the requesting party within ten (10) days of receipt of the written request for Nonelectronic Notice.

14. Successors and Assigns. This Agreement shall inure to the benefit of and be binding upon the Company and the Agents and their respective successors and the parties referred to in Section 10 hereof. References to any of the parties contained in this Agreement shall be deemed to include the successors and permitted assigns of such party. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assigns any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement. Neither party may assign its rights or obligations under this Agreement without the prior written consent of the other party; *provided, however*, that each Agent may assign its rights and obligations hereunder to an affiliate thereof who is a registered broker dealer without obtaining the Company’s consent.

15. Adjustments for Stock Splits. The parties acknowledge and agree that all share-related numbers contained in this Agreement shall be adjusted to take into account any stock split, stock dividend or similar event effected with respect to the Placement Shares.

16. Entire Agreement; Amendment; Severability. This Agreement (including all schedules and exhibits attached hereto and Placement Notices issued pursuant hereto) constitutes

the entire agreement and supersedes all other prior and contemporaneous agreements and undertakings, both written and oral, among the parties hereto with regard to the subject matter hereof. Neither this Agreement nor any term hereof may be amended except pursuant to a written instrument executed by the Company and each of the Agents. In the event that any one or more of the provisions contained herein, or the application thereof in any circumstance, is held invalid, illegal or unenforceable as written by a court of competent jurisdiction, then such provision shall be given full force and effect to the fullest possible extent that it is valid, legal and enforceable, and the remainder of the terms and provisions herein shall be construed as if such invalid, illegal or unenforceable term or provision was not contained herein, but only to the extent that giving effect to such provision and the remainder of the terms and provisions hereof shall be in accordance with the intent of the parties as reflected in this Agreement. No implied waiver by a party shall arise in the absence of a waiver in writing signed by such party. No failure or delay in exercising any right, power, or privilege hereunder shall operate as a waiver thereof, nor shall any single or partial exercise thereof preclude any other or further exercise thereof or the exercise of any right, power, or privilege hereunder.

17. **GOVERNING LAW AND TIME; WAIVER OF JURY TRIAL.** THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO THE PRINCIPLES OF CONFLICTS OF LAWS. SPECIFIED TIMES OF DAY REFER TO NEW YORK CITY TIME. EACH PARTY HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY.

18. **CONSENT TO JURISDICTION.** EACH PARTY HEREBY IRREVOCABLY SUBMITS TO THE NON-EXCLUSIVE JURISDICTION OF THE STATE AND FEDERAL COURTS SITTING IN THE CITY OF NEW YORK, BOROUGH OF MANHATTAN, FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION WITH ANY TRANSACTION CONTEMPLATED HEREBY, AND HEREBY IRREVOCABLY WAIVES, AND AGREES NOT TO ASSERT IN ANY SUIT, ACTION OR PROCEEDING, ANY CLAIM THAT IT IS NOT PERSONALLY SUBJECT TO THE JURISDICTION OF ANY SUCH COURT, THAT SUCH SUIT, ACTION OR PROCEEDING IS BROUGHT IN AN INCONVENIENT FORUM OR THAT THE VENUE OF SUCH SUIT, ACTION OR PROCEEDING IS IMPROPER. EACH PARTY HEREBY IRREVOCABLY WAIVES PERSONAL SERVICE OF PROCESS AND CONSENTS TO PROCESS BEING SERVED IN ANY SUCH SUIT, ACTION OR PROCEEDING BY MAILING A COPY THEREOF (CERTIFIED OR REGISTERED MAIL, RETURN RECEIPT REQUESTED) TO SUCH PARTY AT THE ADDRESS IN EFFECT FOR NOTICES TO IT UNDER THIS AGREEMENT AND AGREES THAT SUCH SERVICE SHALL CONSTITUTE GOOD AND SUFFICIENT SERVICE OF PROCESS AND NOTICE THEREOF. NOTHING CONTAINED HEREIN SHALL BE DEEMED TO LIMIT IN ANY WAY ANY RIGHT TO SERVE PROCESS IN ANY MANNER PERMITTED BY LAW. NOTHING CONTAINED HEREIN SHALL BE DEEMED TO LIMIT IN ANY WAY ANY RIGHT TO SERVE PROCESS IN ANY MANNER PERMITTED BY LAW. TO THE EXTENT THAT THE COMPANY HAS OR HEREAFTER MAY ACQUIRE ANY IMMUNITY (ON THE GROUNDS OF

SOVEREIGNTY OR OTHERWISE) FROM THE JURISDICTION OF ANY COURT OR FROM ANY LEGAL PROCESS WITH RESPECT TO ITSELF OR ITS PROPERTY, THE COMPANY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY LAW, SUCH IMMUNITY IN RESPECT OF ANY SUCH SUIT, ACTION OR PROCEEDING.

19. Recognition of the U.S. Special Resolution Regimes.

(a) In the event that any Agent that is a Covered Entity becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer from such Agent of this Agreement, and any interest and obligation in or under this Agreement, will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if this Agreement, and any such interest and obligation, were governed by the laws of the United States or a state of the United States.

(b) In the event that any Agent that is a Covered Entity or a BHC Act Affiliate of such Underwriter becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under this Agreement that may be exercised against such Underwriter are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if this Agreement were governed by the laws of the United States or a state of the United States.

As used in this Section 19, “**BHC Act Affiliate**” has the meaning assigned to the term “affiliate” in, and shall be interpreted in accordance with, 12 U.S.C. § 1841(k); “**Covered Entity**” means any of the following: (i) a “covered entity” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b), (ii) a “covered bank” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b) or (iii) a “covered FSI” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b); “Default Right” has the meaning assigned to that term in, and shall be interpreted in accordance with, 12 C.F.R. §§ 252.81, 47.2 or 382.1, as applicable; and “U.S. Special Resolution Regime” means each of (i) the Federal Deposit Insurance Act and the regulations promulgated thereunder and (ii) Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act and the regulations promulgated thereunder.

20. Appointment of Agent for Service. The Company hereby irrevocably appoints CT Corporation System, with offices at 111 Eighth Avenue, New York, New York 10011 as its agent for service of process in any suit, action or proceeding described in Section 18 and agrees that service of process in any such suit, action or proceeding may be made upon it at the office of such agent. The Company waives, to the fullest extent permitted by law, any other requirements of or objections to personal jurisdiction with respect thereto. The Company represents and warrants that such agent has agreed to act as the Company’s agent for service of process, and the Company agrees to take any and all action, including the filing of any and all documents and instruments, that may be necessary to continue such appointment in full force and effect.

21. Judgment Currency. If for the purposes of obtaining judgment in any court it is necessary to convert a sum due hereunder into any currency other than United States dollars, the parties hereto agree, to the fullest extent permitted by law, that the rate of exchange used shall be the rate at which in accordance with normal banking procedures an Agent could purchase United States dollars with such other currency in The City of New York on the Business Day preceding

that on which final judgment is given. The obligation of the Company with respect to any sum due from it to an Agent or any person controlling such Agent shall, notwithstanding any judgment in a currency other than United States dollars, not be discharged until the first Business Day following receipt by such Agent or any person controlling such Agent of any sum in such other currency, and only to the extent that such Agent or controlling person may in accordance with normal banking procedures purchase United States dollars with such other currency. If the United States dollars so purchased are less than the sum originally due to an Agent or controlling person hereunder, the Company agrees as a separate obligation and notwithstanding any such judgment, to indemnify such Agent or controlling person against such loss. If the United States dollars so purchased are greater than the sum originally due to an Agent or controlling person hereunder, such Agent or controlling person agrees to pay to the Company an amount equal to the excess of the dollars so purchased over the sum originally due to such Agent or controlling person hereunder.

22. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Delivery of an executed Agreement by one party to the other may be made by facsimile or electronic transmission.

23. Construction. The section and exhibit headings herein are for convenience only and shall not affect the construction hereof. References herein to any law, statute, ordinance, code, regulation, rule or other requirement of any Governmental Entity shall be deemed to refer to such law, statute, ordinance, code, regulation, rule or other requirement of any Governmental Entity as amended, reenacted, supplemented or superseded in whole or in part and in effect from time to time and also to all rules and regulations promulgated thereunder.

24. Permitted Free Writing Prospectuses. The Company represents, warrants and agrees that, unless it obtains the prior consent of each of the Agents, and each of the Agents represents, warrants and agrees that, unless it obtains the prior consent of the Company, it has not made and will not make any offer relating to the Placement Shares that would constitute an Issuer Free Writing Prospectus, or that would otherwise constitute a “free writing prospectus,” as defined in Rule 405, required to be filed with the Commission. Any such free writing prospectus consented to by the Agents or by the Company, as the case may be, is hereinafter referred to as a “Permitted Free Writing Prospectus.” The Company represents and warrants that it has treated and agrees that it will treat each Permitted Free Writing Prospectus as an “issuer free writing prospectus,” as defined in Rule 433, and has complied and will comply with the requirements of Rule 433 applicable to any Permitted Free Writing Prospectus, including timely filing with the Commission where required, legending and record keeping. For the purposes of clarity, the parties hereto agree that all free writing prospectuses, if any, listed in Exhibit 24 hereto are Permitted Free Writing Prospectuses.

25. Absence of Fiduciary Relationship. The Company acknowledges and agrees that:

(a) each Agent is acting solely as agent in connection with the public offering of the Placement Shares and in connection with each transaction contemplated by this Agreement and the process leading to such transactions, and no fiduciary or advisory relationship between the Company or any of its respective affiliates, stockholders (or other equity holders), creditors or employees or any other party, on the one hand, and the Agents, on the other hand, has been or will be created in respect of any of the transactions contemplated by this Agreement, irrespective of

whether or not such Agent has advised or is advising the Company on other matters, and no Agent has any obligation to the Company with respect to the transactions contemplated by this Agreement except the obligations expressly set forth in this Agreement;

(b) it is capable of evaluating and understanding, and understands and accepts, the terms, risks and conditions of the transactions contemplated by this Agreement;

(c) neither the Agents nor their affiliates have provided any legal, accounting, regulatory or tax advice with respect to the transactions contemplated by this Agreement and it has consulted its own legal, accounting, regulatory and tax advisors to the extent it has deemed appropriate;

(d) it is aware that each Agent and their respective affiliates are engaged in a broad range of transactions which may involve interests that differ from those of the Company and the Agents and their affiliates have no obligation to disclose such interests and transactions to the Company by virtue of any fiduciary, advisory or agency relationship or otherwise; and

(e) it waives, to the fullest extent permitted by law, any claims it may have against an Agent or its affiliates for breach of fiduciary duty or alleged breach of fiduciary duty in connection with the sale of Placement Shares under this Agreement and agrees that such Agent and its affiliates shall not have any liability (whether direct or indirect, in contract, tort or otherwise) to it in respect of such a fiduciary duty claim or to any person asserting a fiduciary duty claim on its behalf or in right of it or the Company, employees or creditors of Company.

26. **Definitions.** As used in this Agreement, the following terms have the respective meanings set forth below:

“Applicable Time” means (i) each Representation Date, (ii) the time of each sale of any Placement Shares pursuant to this Agreement and (iii) each Settlement Date.

“Issuer Free Writing Prospectus” means any “issuer free writing prospectus,” as defined in Rule 433, relating to the Placement Shares that (1) is required to be filed with the Commission by the Company, (2) is a “road show” that is a “written communication” within the meaning of Rule 433(d)(8)(i) whether or not required to be filed with the Commission, or (3) is exempt from filing pursuant to Rule 433(d)(5)(i) because it contains a description of the Placement Shares or of the offering that does not reflect the final terms, in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company’s records pursuant to Rule 433(g) under the Securities Act Regulations.

“Rule 164,” “Rule 172,” “Rule 405,” “Rule 415,” “Rule 424,” “Rule 424(b),” “Rule 430B,” and **“Rule 433”** refer to such rules under the Securities Act Regulations.

All references in this Agreement to financial statements and schedules and other information that is “contained,” “included” or “stated” in the Registration Statement or the Prospectus (and all other references of like import) shall be deemed to mean and include all such financial statements and schedules and other information that is incorporated by reference in the Registration Statement or the Prospectus, as the case may be.

All references in this Agreement to the Registration Statement, the Prospectus or any amendment or supplement to any of the foregoing shall be deemed to include the copy filed with the Commission pursuant to EDGAR; all references in this Agreement to any Issuer Free Writing Prospectus (other than any Issuer Free Writing Prospectuses that, pursuant to Rule 433, are not required to be filed with the Commission) shall be deemed to include the copy thereof filed with the Commission pursuant to EDGAR; and all references in this Agreement to “supplements” to the Prospectus shall include, without limitation, any supplements, “wrappers” or similar materials prepared in connection with any offering, sale or private placement of any Placement Shares by the Agents outside of the United States.

[Signature Page Follows]

If the foregoing correctly sets forth the understanding among the Company and the Agents, please so indicate in the space provided below for that purpose, whereupon this letter shall constitute a binding agreement between the Company and the Agents.

Very truly yours,

PROQR THERAPEUTICS N.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: CEO

ACCEPTED as of the date first-above written:

Citigroup Global Markets Inc.

By: /s/ Bradley Wolff

Name: Bradley Wolff

Title: Managing Director

Cantor Fitzgerald & Co.

By: /s/ Bala Murty

Name: Bala Murty

Title: Chief Operating Officer, Investment Banking

SCHEDULE 1

Form of Placement Notice

From: ProQR Therapeutics N.V.

To: [Designated Agent] the (“**Designated Agent**”)
Attention: []

Subject: Placement Notice

Date: [], 202[0]

Ladies and Gentlemen:

Pursuant to the terms and subject to the conditions contained in the Sales Agreement among ProQR Therapeutics N.V., a Dutch public company with limited liability (the “**Company**”), Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. (each individually an “**Agent**” and collectively the “**Agents**”), dated March [], 2020, the Company hereby requests that the Designated Agent sell up to [] of the Company’s ordinary shares, nominal value €0.04 per share, at a minimum market price of \$[] per share, during the time period beginning [month, day, time] and ending [month, day, time].

SCHEDULE 2

Compensation

The Company shall pay to the Designated Agent in cash, upon each sale of Placement Shares pursuant to this Agreement, an amount equal to 3.0% of the aggregate gross proceeds from each sale of Placement Shares.

SCHEDULE 3

Notice Parties

The Company.

Smital Shah (sshah@proqr.com)

Daniel de Boer (DdeBoer@proqr.com)

Citigroup Global Markets Inc.

Matthew Morris (matthew.t.morris@citi.com)

Robert Leonard (robert.g.leonard@citi.com)

Cantor Fitzgerald & Co.

Sameer Vasudev (svasudev@cantor.com)

With copies to:

CFControlledEquityOffering@cantor.com

SCHEDULE 4

Subsidiaries

ProQR Therapeutics Holding B.V. (the Netherlands)
ProQR Therapeutics I B.V. (the Netherlands)
ProQR Therapeutics II B.V. (the Netherlands)
ProQR Therapeutics III B.V. (the Netherlands)
ProQR Therapeutics IV B.V. (the Netherlands)
ProQR Therapeutics VI B.V. (the Netherlands)
ProQR Therapeutics VII B.V. (the Netherlands)
ProQR Therapeutics VIII B.V. (the Netherlands)
ProQR Therapeutics IX B.V. (the Netherlands)
Amylon Therapeutics B.V. (the Netherlands)
Amylon Therapeutics Inc. (Delaware, United States)
ProQR Therapeutics I Inc. (Delaware, United States)

Form of Representation Date Certificate Pursuant to Section 7(l)

The undersigned, the duly qualified and elected [], of ProQR Therapeutics N.V., a Dutch public company with limited liability (the “Company”), does hereby certify in such capacity and on behalf of the Company, pursuant to Section 7(l) of the Sales Agreement, dated March [], 2020 (the “Sales Agreement”), among the Company, Citigroup Global Markets Inc. and Cantor Fitzgerald & Co., that to the best of the knowledge of the undersigned:

(i) The representations and warranties of the Company in Section 6 of the Sales Agreement (A) to the extent such representations and warranties are subject to qualifications and exceptions contained therein relating to materiality or Material Adverse Effect, are true and correct on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof, except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date, and (B) to the extent such representations and warranties are not subject to any qualifications or exceptions, are true and correct in all material respects as of the date hereof as if made on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof, except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date; *provided, however*, that in the case of clauses (A) and (B), such representations and warranties also shall be qualified by the disclosure included or incorporated by reference in the Registration Statement and Prospectus; and

(ii) The Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied pursuant to the Sales Agreement at or prior to the date hereof.

PROQR THERAPEUTICS N.V.

By: _____

Name: _____

Title: _____

Date: []

Exhibit 24

Permitted Free Writing Prospectus

[None.]

**DESCRIPTION OF THE REGISTRANT'S SECURITIES PURSUANT TO
SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED**

The ordinary shares, nominal value €0.04 per share ("Ordinary Shares"), of ProQR Therapeutics N.V. (the "Company," "we," "us," and "our"), is registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The following description sets forth certain general terms and provisions of our Ordinary Shares. These descriptions are in all respects subject to and qualified in their entirety by, and should be read in conjunction with, the applicable provisions of, our amended articles of association (the "Articles of Association") previously filed with the Securities and Exchange Commission (the "SEC") and incorporated by reference as exhibits to the Annual Report on Form 20-F of which this Exhibit 4.18 is a part, and the applicable provisions of Dutch law.

Authorized Share Capital

Our authorized capital is €7,200,000, divided into 90,000,000 Ordinary Shares and 90,000,000 preferred shares, nominal value of €0.04 per share ("Preferred Shares"). Under Dutch law, our authorized share capital is the maximum capital that we may issue without amending our Articles of Association.

Ordinary 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 of shareholders 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.

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 of shareholders 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", is an irrevocable and repeatedly exercisable right to subscribe for preferred shares.

On May 16, 2018, our general meeting of shareholders adopted a resolution pursuant to which our management board, subject to approval of the supervisory board, is authorized to, in accordance with applicable laws and Nasdaq listing rules and for a period of 5 years from the date of the resolution of the general meeting of shareholders: (a) issue ordinary shares up to 100% of the Company's authorized share capital for general purposes and issuances under Company's stock option plans with the proviso that the issuances under stock option plans is limited to 15% of the Company's issued share capital (minus any treasury shares) at the date of the general meeting of shareholders; (b) grant rights to subscribe for ordinary shares as described under (a); and (c) limit or exclude the pre-emptive rights of holders of ordinary shares, which delegation shall include the authority to determine the price and further terms and conditions of any such share issuance or grant.

Voting Rights

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.

Dividend Rights

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. 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 Rights

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.

Registration Rights

Certain holders of our Ordinary Shares, or their permitted transferees, are entitled to rights with respect to the registration of these shares under the Securities Act. These rights are provided under the terms of a Registration Rights Agreement dated as of September 17, 2014 (the "Registration Rights Agreement") between us and the holders of these shares, which was entered into following our initial public offering, and includes demand registration rights, short-form registration rights and piggyback registration rights. These registration rights are assignable, subject to certain conditions, including that the assignee be bound by the terms and conditions of the Registration Rights Agreement. In addition, we have agreed, under certain circumstances, to register the Ordinary Shares that we may issue to Ionis Pharmaceuticals, Inc. from time to time in connection with our license agreement with Ionis Pharmaceuticals, Inc.

Demand Registration Rights

Under the terms of the Registration Rights Agreement, we are required, upon the written request of the holders of at least one-third of the shares that are then outstanding and entitled to rights under the Registration Rights Agreement, that we file a Form F-1 registration statement with respect to such securities having an anticipated aggregate offering price, net of selling expense, of at least \$10,000,000, then we must give notice of such initiating holders' request to all holders of shares entitled to rights under the Registration Rights Agreement, and as soon as practicable within 60 days of such request file a Form F-1 registration statement covering all shares entitled to rights under the Registration Rights Agreement requested to be included by either the initiating holders or by any other holders of shares entitled to rights under the Registration Rights Agreement as specified by notice given by each such holder within 20 days of receiving notice of the initiating holders' request. We are not required to effect a registration pursuant to this provision of the Registration Rights Agreement: (i) during the period that is 30 days before our good faith estimate of the date of filing of, and ending on a date that is 90 days after the effective date of, a registration initiated by us; provided that we are actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; (ii) after we have effected two registration statements pursuant

to this provision of the Registration Rights Agreement; or (iii) if the initiating holders propose to dispose of securities that may be registered on a Form F-3 registration statement. We may defer the filing of a registration statement twice during any twelve-month period for a period of not more than 90 days, if we provide a certificate signed by our chief executive officer stating that in the good faith judgment of our board of directors it would be materially detrimental to us and our shareholders for such registration statement to be effected at this time.

Short Form Registration Rights

If we are eligible to file a registration statement on Form F-3 and have not effected more than two such registrations within the preceding twelve-month period, these holders have the right, upon written notice to us from the holders of at least 30% of the shares that are then outstanding and entitled to rights under the Registration Rights Agreement, that we file a Form F-3 registration statement with respect to securities of such holders having an anticipated aggregate offering price, net of selling expenses, of at least \$5,000,000, then we must give notice to all other holders of such initiating holders' request to all holders of shares entitled to rights under the Registration Rights Agreement, and as soon as practicable within 45 days of such request file a Form F-3 registration statement covering all shares entitled to registration rights requested to be included by either the initiating holders or by any other holders of shares entitled to registration rights within 20 days of receiving notice of the initiating holders' request. We are not required to effect a registration pursuant to this provision of the Registration Rights Agreement during the period that is 30 days before our good faith estimate of the date of filing of, and ending on a date that is 90 days after the effective date of, a registration initiated by us; provided that we are actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective. We may defer the filing of a registration statement twice during any twelve-month period for a period of not more than 90 days, if we provide a certificate signed by our chief executive officer stating that in the good faith judgment of our board of directors it would be materially detrimental to us and our shareholders for such registration statement to be effected at this time.

Piggyback Registration Rights

If we propose to register any of our Ordinary Shares, the holders of these shares are entitled to include their shares in the registration. If such registration is to be an underwritten offering, then the holders' registration rights are conditioned on such holders' participation in such underwriting.

Articles of Association and Dutch Law

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

Anti-Takeover Measure

To enable us to pursue our business strategy and the successful development of our product pipeline and to protect our interests and those of our stakeholders (including shareholders, employees and patient populations), our business strategy, our continuity and our independence against actual and potential threats, we have adopted an anti-takeover measure by granting a perpetual and repeatedly exercisable call option to a 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 equals, at the time of exercise of the call option, the lesser of: (i) the total number of shares equal to our issued share capital at that time, minus the number of Preferred Shares already held by the protection foundation at that time (if any) or (ii) the maximum number of Preferred Shares that may be issued under

our authorized share capital under our Articles of Association from time to time. The protection foundation's Articles of Association provide that it will act to promote and protect the best interests of us, our business and our stakeholders, including patient populations that may benefit from our products and pipeline, by opposing any influences that conflict with these interests and threaten to undermine our strategy, continuity, independence and/or identity. The board of the protection foundation is 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/or 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.

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. The ordinary shares listed on Nasdaq Global Market are held through DTC, therefore DTC is recorded in the shareholders register as the holder of those ordinary shares.

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 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 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.

On May 16, 2018, our general meeting of shareholders adopted a resolution pursuant to which our management board will be authorized to acquire (i) up to 10% of the issued share capital of the Company plus, in case of a material reorganization of the capital structure of the Company, (ii) an additional 10% of the issued share capital of the Company, by any means, including through derivative products, purchases on any stock exchange, through any private purchase or block trade, or otherwise, for a price that is between 0.01 US Dollar and an amount which is not higher than 110% of the average market price of such 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), for a period of eighteen (18) months with effect from the general meeting of shareholders. In this respect, the words “issued share capital” means the Company’s issued share capital from time to time. For the avoidance of doubt, the issued share capital includes treasury shares.

Capital Reductions; Cancellation

At a general meeting of shareholders, 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 of shareholders 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 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 disproportionate 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, bringing to market 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 make our products available to the patient populations that may benefit from such products and to maintain a suitable pipeline of products that may be beneficial for relevant patient populations;
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- 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, in the municipality of Haarlemmermeer (Schiphol Airport), Oegstgeest, Leidschendam, Katwijk, Noordwijk or Wassenaar, 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 eight 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 of shareholders 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 of shareholders. 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 of shareholders. 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 management board member present at the meeting and, if none of them is present, the general meeting of shareholders 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 of shareholders may decide at his discretion to admit other persons to the meeting. The chairman of the general meeting of shareholders 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 of shareholders 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 of shareholders 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

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 of shareholders 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.

Each year within five months after the end of our financial year, save where this period is extended for a maximum of five 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."

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.

In Dutch public takeover practice, depending on the circumstances, an asset sale transaction is sometimes used as a way to squeeze out minority shareholders, for example, after a successful public offer, or tender offer, through which the offeror acquires a supermajority, but less than all, of the shares. In such a scenario, the business of the target company would be sold to an offeror, a buyer or a special purpose vehicle, followed by the liquidation of the target company. The purchase price would be distributed to all

shareholders in proportion to their respective shareholding as liquidation proceeds, thus separating the business from the company in which minority shareholders participated.

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 Stock Market 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 Global Market.

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

- Best practice provision 4.1.3 (vii) 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 this provision.
 - Best practice provision 2.1.7 (i) stipulates that any one of the criteria referred to in best practice provision 2.1.8, sections i. to v. inclusive should be applicable to at most one supervisory board member. 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 3.3.2 prohibits the granting of shares or rights to shares to members of the supervisory board as remuneration. 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,
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and we have granted and expect to grant options to acquire ordinary shares to our supervisory board members.

- Pursuant to the best practice provision 3.1.2 (vi) and (vii) of the DCGC, options granted to our management board members should not be exercisable during the first three years after the date of grant; shares granted to our management board members should be retained by them for a period of at least five years; We do not intend to comply with all of the above requirements.
- Best practice provision 4.3.3 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, this best practice provision 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 4.2.3 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 intend to post analyst presentations on our website after meetings with analysts.
- Pursuant to best practice provision 3.2.3 the remuneration of the management board in the event of dismissal may not exceed one year's salary. The management services agreements with our management board members provide for a lump-sum equal to 24 months of the individual's monthly gross fixed salary. Based on the risk profile of the company and to be able to attract highly skilled management, we assumed this period to be appropriate.

Market Abuse

The Market Abuse section described in our other filings with the Securities and Exchange Commission, including our annual report on Form 20-F for the year ended December 31, 2015, and the base prospectus included in our registration statement on Form F-3 (File No. 333-207245), is no longer applicable following the EU Market Abuse Regulation, which became effective as of July 3, 2016. The EU Market Abuse Regulation has direct effect in the Netherlands and other EU member states. The EU Market Abuse Regulation replaces the provisions on market abuse, insider trading and notifications set out in the Dutch Financial Supervision Act. The EU Market Abuse Regulation does not apply to companies whose shares are not admitted to trading or are not listed on a regulated market in the EU/EEA, but only on NASDAQ. Accordingly, the provisions of the EU Market Abuse Regulation do not currently apply to us.

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 are listed on the Nasdaq Global Market, 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.

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

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).

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

corporation who take any action designed to defeat a threatened change in control of the corporation.

In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

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.

its business requires shareholders' approval. The management 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.

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 a supervisory board member is appointed for a period of four years and may then be reappointed once for another four-year period. The supervisory board member may then subsequently be reappointed again for a period of two years, which appointment may be extended by at most two years. In the event of a reappointment after an eight-year period, reasons should be given in the report of the supervisory board.

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 management board 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.

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

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.

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.

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 abuses 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.

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.

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 the meeting is held. The determination of the shareholders of record entitled to notice or to vote at a meeting of shareholders shall apply to any adjournment of the meeting, but the board of directors may fix a new record date for the adjourned meeting.

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.

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 of shareholders. 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 of shareholders 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.

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. An 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.

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.

On May 16, 2018, our general meeting of shareholders adopted a resolution pursuant to which our management board will be authorized to acquire (i) up to 10% of the issued share capital of the Company plus, in case of a material reorganization of the capital structure of the Company, (ii) an additional 10% of the issued share capital of the Company, by any means, including through derivative products, purchases on any stock exchange, through any private purchase or block trade, or otherwise, for a price that is between 0.01 US Dollar and an amount which is not higher than 110% of the average market price of such 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), for a period of eighteen (18) months with effect from the general meeting of shareholders. In this respect, the words "issued share capital" means the Company's issued share capital from time to time. For the avoidance of doubt, the issued share capital includes treasury shares.

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;

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.

As indicated above, we have adopted an anti-takeover measure 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, the number of Preferred Shares described above. 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.

In addition, our boards need to act in the interest of ProQR, our business and take into account the interests of all our stakeholders, including by promoting the sustainable success of our business and the creation of long term value for us and our business. The boards are responsible to determine our strategy and choosing our strategic direction. In doing so and depending on the circumstances they may decide to not entertain a proposed takeover or other strategic proposal, even if the proposal is supported by the majority of our shareholders and/or would create more shareholder value. The boards may also use their general authority under Dutch corporate law and the DCGC to not co-operate with a proposal, e.g. by not providing due diligence and or by not cooperating with shareholder proposals to adopt resolutions in a general shareholder meeting that may change our strategy for instance

by invoking the maximum 180 days response time set out in the DCGC.

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 usufructuaries and pledgees whose particulars must be registered therein.

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 reasonably requests unless doing so would be contrary to an overriding interest of ours. Our management board or our supervisory board will in principle give a 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.

On May 16, 2018, our general meeting of shareholders adopted a resolution pursuant to which our management board, subject to approval of the supervisory board, is authorized to, in accordance with applicable laws and Nasdaq listing rules and for a period of 5 years from the date of the resolution of the general meeting of shareholders: (a) issue Ordinary Shares up to 100% of the Company's authorized share capital for general purposes and issuances under Company's stock option plans with the proviso that the issuances under stock option

plans is limited to 15% of the Company's issued share capital (minus any treasury shares) at the date of the general meeting of shareholders; (b) grant rights to subscribe for Ordinary Shares as described under (a); and (c) limit or exclude the pre-emptive rights of holders of Ordinary Shares, which delegation shall include the authority to determine the price and further terms and conditions of any such share issuance or grant.

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.

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.

The Delaware General Corporation Law provides for stockholder appraisal rights, or the right to demand payment

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

in cash of the judicially determined fair value of the stockholder's shares, in connection with certain mergers and consolidations.

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.

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 compensation of supervisory board members. The supervisory directors will be reimbursed for their expenses.

Stock Exchange Listing

Our Ordinary Shares are listed on the Nasdaq Global Market under the symbol "PRQR." We have listed our ordinary shares in registered form and our shares are not certificated. Our ordinary shares are traded on the Nasdaq Global Market in book-entry form.

Transfer Agent and Registrar

We have appointed American Stock Transfer & Trust Company, LLC as our agent to maintain our shareholders register and to act as transfer agent, registrar and paying agent for the ordinary shares

SUBSIDIARIES OF PROQR THERAPEUTICS N.V.

The following is a list of subsidiaries of the Company (and jurisdiction of incorporation) as of December 31, 2019.

<u>Name of Subsidiary</u>	<u>Jurisdiction of Incorporation or Organization</u>
ProQR Therapeutics Holding B.V.	Netherlands
ProQR Therapeutics I B.V.	Netherlands
ProQR Therapeutics II B.V.	Netherlands
ProQR Therapeutics III B.V.	Netherlands
ProQR Therapeutics IV B.V.	Netherlands
ProQR Therapeutics VI B.V.	Netherlands
ProQR Therapeutics VII B.V.	Netherlands
ProQR Therapeutics VIII B.V.	Netherlands
ProQR Therapeutics IX B.V.	Netherlands
ProQR Therapeutics I Inc.	United States
Amylon Therapeutics B.V.	Netherlands
Amylon Therapeutics, Inc.	United States

**Certification by the Principal Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Daniel de Boer, certify that:

1. I have reviewed this annual report on Form 20-F of ProQR Therapeutics N.V. (the “Company”);
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;
4. The Company’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the Company’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the Company’s internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company’s internal control over financial reporting; and
5. The Company’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company’s auditors and the audit committee of the Company’s board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company’s ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company’s internal control over financial reporting.

Date: March 31, 2020

By: /S/ Daniel de Boer

Name: Daniel de Boer

Title: *Chief Executive Officer*
(Principal Executive Officer)

**Certification by the Principal Financial Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Smital Shah, certify that:

1. I have reviewed this annual report on Form 20-F of ProQR Therapeutics N.V. (the “Company”);
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;
4. The Company’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the Company’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the Company’s internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company’s internal control over financial reporting; and
5. The Company’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company’s auditors and the audit committee of the Company’s board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company’s ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company’s internal control over financial reporting.

Date: March 31, 2020

By: /S/ Smital Shah
Name: Smital Shah
Title: *Chief Business and Financial Officer*
(Principal Financial Officer)

**Certification Pursuant to 18 U.S.C. Section 1350,
as Adopted Pursuant to Section 906 Of The Sarbanes-Oxley Act of 2002**

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Daniel de Boer, the Chief Executive Officer, and Smital Shah, the Chief Business and Financial Officer, of ProQR Therapeutics N.V. (the "Company"), hereby certify, that, to their knowledge:

- (1) The Annual Report on Form 20-F for the year ended December 31, 2019 (the "Report") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 31, 2020

By: _____ /s/ Daniel de Boer
Name: Daniel de Boer
Title: Chief Executive Officer
(Principal Executive Officer)

By: _____ /s/ Smital Shah
Name: Smital Shah
Title: Chief Business and Financial
Officer
(Principal Financial Officer)

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To: the Supervisory Board and Shareholders of ProQR Therapeutics N.V.

We consent to the incorporation by reference in Registration Statement No. 333-199451 on Form S-8 and Registration Statement No. 333-228251 on Form F-3 of our reports dated March 31, 2020 relating to the financial statements of ProQR Therapeutics N.V. and the effectiveness of ProQR Therapeutics N.V.'s internal control over financial reporting appearing in this Annual Report on Form 20-F of ProQR Therapeutics N.V. for the year ended December 31, 2019.

/s/ Deloitte Accountants B.V.

Amsterdam, the Netherlands
March 31, 2020

To

ProQR Therapeutics N.V.
Zemikedreef 9
2333 CK Leiden
The Netherlands

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1070 AK Amsterdam The Netherlands

Tel +31 20 674 1000
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Amsterdam, 31 March 2020
Subject **Dutch law legal opinion**

Dear Sirs, Madam,

1. We have acted as legal counsel to you, ProQR Therapeutics N.V., a public limited liability company (*naamloze vennootschap*) incorporated under the laws of the Netherlands, with its corporate seat in Leiden (the Netherlands) (the **Company**) on matters of Dutch law in connection with the sale for a consideration of up to USD 75,000,000 of ordinary shares, with a nominal value of EUR 0,04 each (the **Future Shares**), in the Company's share capital, to be issued after the date hereof to Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. pursuant to a Prospectus (as defined below) incorporated into the Registration Statement (as defined below) under a sales agreement between the Company and Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. (the **Sales Agreement**).

On 7 November 2018, the Company filed a registration statement on Form F-3 (File No. 333-228251) with the U.S. Securities and Exchange Commission (the **SEC**) relating to the registration by the Company of up to \$300,000,000 of any combination of securities of the types specified therein, which was declared effective on 19 November 2018 (the **Registration Statement**), and the form of prospectus included in it (the **Base Prospectus**), as supplemented by the prospectus supplement dated 31 March 2020, and filed with the SEC on 31 March 2020, pursuant to Rule 424 under the Securities Act. The term **Prospectus** shall mean the final prospectus supplement (the **Final Prospectus Supplement**) to the Base Prospectus, together with the Base Prospectus. References herein to the Prospectus shall refer to both the prospectus supplement and the Base Prospectus components of such prospectus.

This legal opinion is rendered to you in order to be filed as an exhibit to the Registration Statement.

2. We have examined and relied upon the following documents in rendering this legal opinion:
 - (a) a pdf copy of the Registration Statement;
 - (b) a pdf copy of the Base Prospectus;

Allen & Overy LLP is a limited liability partnership registered in England and Wales with registered number OC306763. It is authorised and regulated by the Solicitors Regulation Authority of England and Wales. The term partner is used to refer to a member of Allen & Overy LLP or an employee or consultant with equivalent standing and qualifications. A list of the members of Allen & Overy LLP and of the non-members who are designated as partners is open to inspection at its registered office, One Bishops Square, London E1 6AD.

Allen & Overy LLP or an affiliated undertaking has an office in each of: Abu Dhabi, Amsterdam, Antwerp, Athens, Bangkok, Beijing, Belfast, Bratislava, Brussels, Bucharest (associated office), Budapest, Casablanca, Doha, Dubai, Düsseldorf, Frankfurt, Hamburg, Hanoi, Ho Chi Minh City, Hong Kong, Istanbul, Jakarta (associated office), London, Luxembourg, Madrid, Mannheim, Milan, Moscow, Munich, New York, Paris, Perth, Prague, Riyadh (associated office), Rome, São Paulo, Shanghai, Singapore, Sydney, Tokyo, Warsaw and Washington, D.C. and Yangon.

- (c) a pdf copy of the Final Prospectus Supplement;
- (d) a pdf copy of the Form 20-F;
- (e) a pdf copy of the executed Sales Agreement;
- (f) an electronic copy of the registration of the Company in the trade register of the Chamber of Commerce (**Trade Register**, *Handelsregister*) dated 31 March 2020 (the **Excerpt**);
- (g) a copy of the minutes of the annual general meeting of the Company held on 16 May 2018 (the **AGM Resolution**);
- (h) a pdf copy of the written resolution of the Company's supervisory board (the **Supervisory Board**) dated 30 March 2020 (the **Supervisory Board Resolution**);
- (i) a pdf copy of the written resolution of the Management Board dated 30 March 2020 (the **Management Board Resolution**);
- (j) a pdf copy of the internal rules for the Management Board adopted by the Management Board on 23 September 2014 (the **Management Board Rules**);
- (k) a pdf copy of the internal rules for the Supervisory Board adopted by the Supervisory Board on 23 September 2014 (the **Supervisory Board Rules**);
- (l) a pdf copy of the recent articles of association (*statuten*) of the Company dated 27 February 2018 (the **Articles of Association**);
- (m) a pdf copy of the deed of incorporation (*akte van oprichting*) of the Company (the **Deed of Incorporation**), as executed by a civil-law notary on 21 February 2012;
- (n) a pdf copy of the deed of conversion and amendment to the articles of association of the Company, pursuant to which deed the Company converted from a B.V. to a N.V. (the **Deed of Conversion**); and
- (o) a copy of the Company's shareholders' register within the meaning of Article 2:85 of the Dutch Civil Code (the **Shareholders' Register**).

The documents (g) up to and including (i) are collectively referred to as the **Resolutions**.

Unless explicitly stated in this legal opinion, we have not examined any other agreement, deed or document entered into by or affecting the Company or any other corporate records of the Company and have not made any other inquiry concerning it.

3. We assume:

- (a) the genuineness of all signatures on the documents referred to in paragraph 1 above;
- (b) the authenticity and completeness of all documents submitted to us as originals and the completeness and conformity to originals of all documents submitted to us as copies or by electronic means;
- (c) that the Registration Statement has been or shall be filed with the SEC, and shall become effective, in the form referred to in this legal opinion;
- (d) (i) that the Management Board Rules and the Supervisory Board Rules are the regulations as in force on the date hereof; and (ii) the Articles of Association of the Company are its articles

of association (*statuten*) currently in force. Although not constituting conclusive evidence thereof, the Extract supports item (ii) of this assumption;

- (e) that at the time of issue of the Future Shares, the Company has not been dissolved (*ontbonden*), granted a moratorium (*surseance verleend*) or declared bankrupt (*failliet verklaard*) (although not constituting conclusive evidence thereof, this assumption is supported by (a) the contents of the Excerpt, and (b) an online search in the central insolvency register on 31 March 2019;
 - (f) that the Deed of Incorporation is a valid notarial deed (*authentieke akte*), the contents thereof complied with the statutory requirements at the date of incorporation and there were no defects in the incorporation of the Company (not appearing on the face of the Deed of Incorporation) on the basis of which a court might dissolve the Company or deem it never to have existed;
 - (g) that the Deed of Conversion is a valid notarial deed (*authentieke akte*), the contents thereof complied with the statutory requirements at the date of conversion and there were no defects in the conversion of the Company from a B.V. into a N.V. (not appearing on the face of the Deed of Conversion) on the basis of which a court might nullify the conversion of the Company;
 - (h) the Resolutions, including any power of attorney therein have not been and will not be annulled, modified, revoked or rescinded and are in full force and effect as at the date hereof and that the Resolutions have been made with due observance of the statutory requirements and the provisions of the Articles of Association relating to the convening of meetings and the making of resolutions (although not constituting conclusive evidence thereof, failure to observe such provisions is not apparent on the face thereof) and that each factual confirmation and statement in the Resolutions (including any confirmation or statement on conflict of interest (*tegenstrijdig belang*)) is correct;
 - (i) that at the time of issue of the Future Shares, the Company will have taken all necessary corporate action required by (i) the Company's articles of association; and (ii) applicable laws of the Netherlands, to (a) issue of the Future Shares and (b) exclude any pre-emption rights with respect to such issuance;
 - (j) that at the time of issue of the Future Shares, the authorised share capital of the Company will allow such issue of Future Shares (or the granting of any rights to subscribe for such Future Shares);
 - (k) that at the time of issue of the Future Shares, the Future Shares will be issued in the form and manner required by applicable law, the Company's articles of association and its other internal rules and regulations at the time of issue, and otherwise offered to, issued to and accepted by their subscribers in accordance with all applicable laws (including, for the avoidance of doubt, Dutch law);
 - (l) that at the time of issue of the Future Shares, the Future Shares will be paid for with due observance of the relevant formalities under all applicable laws (including, for the avoidance of doubt, Dutch law);
 - (m) none of the opinions stated in this opinion letter will be affected by any foreign law; and
 - (n) that the documents referred to in paragraph 1 above were at their date (where applicable), and have through the date hereof remained, valid, accurate and in full force and effect.
4. This legal opinion is limited to the laws of the Netherlands currently in force (unpublished case law not included), excluding tax law (except as specifically referred to herein), the laws of the EU (insofar

as not implemented in Dutch law or directly applicable in the Netherlands), market abuse laws and competition or procurement laws.

No undertaking is assumed on our part to revise, update or amend this opinion letter in connection with or to notify or inform you of, any developments and/or changes of Dutch law subsequent to the date hereof.

We express no opinion as to matters of fact in this legal opinion. We assume that there are no facts not disclosed to us, which could affect the conclusions in this legal opinion.

Our willingness to render this opinion letter is based on the condition that you accept and agree that (i) the competent courts at Amsterdam, the Netherlands have exclusive jurisdiction to settle any issues of interpretation or liability arising out of or in connection with this opinion letter, (ii) all matters related to the legal relationship between yourself and Allen & Overy LLP and all individuals associated with Allen & Overy LLP, including the above submission to jurisdiction, are governed by Dutch law and the general terms and conditions of Allen & Overy LLP, (iii) any liability arising out of or in connection with this opinion letter shall be limited to the amount which is paid out under the insurance policy of Allen & Overy LLP in the matter concerned and (iv) no person other than Allen & Overy LLP may be held liable in connection with this legal opinion.

This legal opinion is strictly limited to the matters stated in it and does not relate to any other agreement or matter and may not be read as extending by implication to any matters not specifically referred to. Nothing in this opinion should be taken as expressing an opinion in respect of any representation, warranty or other statement or other information as to factual matters contained in any document referred to herein or examined in connection with this opinion except as expressly confirmed herein.

5. Based on the foregoing and subject to the qualifications set out below, we are of the opinion that:
 - (a) **Future Shares:** When issued, the Future Shares will have been validly issued, will have been fully paid and will be non-assessable.
6. This legal opinion is subject to the following qualifications:
 - (a) The opinions expressed in this legal opinion may be affected or limited by (i) the general defences available to obligors under Netherlands law in respect of the validity and enforceability of agreements; and (ii) the provisions of any applicable bankruptcy (*faillissement*), insolvency, moratorium (*surseance van betaling*), fraudulent conveyance (*Actio Pauliana*), reorganisation and other or similar laws of general application now or hereafter in effect, relating to or affecting the enforcement or protection of creditors' rights.
 - (b) As used in the opinions in paragraph 5 of this opinion letter, the term "non-assessable" – which term has no equivalent in Dutch – means that a holder of a share will not by reason of merely being such a holder, be subject to assessment or calls by the Company or its creditors for further payment on such share.
 - (c) Under Dutch law, each power of attorney (*volmacht*) or mandate (*lastgeving*), whether or not irrevocable, granted by the Company will terminate by force of law and without notice, upon bankruptcy of the Company. To the extent that the appointment by the Company of a process agent would be deemed to constitute a power of attorney or a mandate, this qualification would apply.
 - (d) This opinion letter does not purport to express any opinion or view on the operational rules and procedures of any clearing or settlement system or agency.

7. In this opinion, Dutch legal concepts are expressed in English terms and not in their original Dutch terms. The concepts concerned may not always be identical to the concepts described by the English terms as such terms may be understood under the laws of other jurisdictions. This legal opinion is given on the express basis, accepted by each person who is entitled to rely on it, that this legal opinion and all rights, obligations or liability in relation to it are governed by Dutch law.
8. This legal opinion is given exclusively in connection with our representation of the Company and for no other purpose.
9. Notwithstanding the previous sentence, this opinion may be disclosed, quoted, or referred to without our written express consent (i) if such disclosure, quotation or reference without our written consent is required by law, court order or any competent regulatory authority, *provided* that you shall notify us immediately or as soon as otherwise possible after such disclosure, quotation or reference or (ii) to the extent that such disclosure, quotation or reference is required (a) to any of your insurers in respect of any claim or potential claim against you or (b) for evidence in court or similar proceedings in which you are a defendant, *provided*, in each of the events referred to in (a) and (b), that you shall notify us prior to any such disclosure, reference or quotation being made.
10. We consent to the filing of this opinion letter as an exhibit to the Registration Statement and also consent to the reference to Allen & Overy LLP in the Registration Statement under the caption "Legal Matters".

Yours faithfully,

Allen & Overy LLP