PROQR THERAPEUTICS N.V.

FORM 20-F

(Annual and Transition Report (foreign private issuer))

Filed 03/13/25 for the Period Ending 12/31/24

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SIC Code	2834 - Pharmaceutical Preparations
Industry	Biotechnology & Medical Research
Sector	Healthcare
Fiscal Year	12/31

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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, 2024

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)

Jurriaan Dekkers, Chief Financial Officer
Tel: +31 88 166 7000
jdekkers@proqr.com, Zernikedreef 9, 2333 CK Leiden, The Netherlands
(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	The Nasdaq Stock Market LLC

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: 105,212,527

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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 whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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 as issued by the International Accounting Standards Board	☐ Other

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

Summary of the Material and Other Risks Associated with Our Business

Our business is subject to numerous material risks and uncertainties that you should be aware of in evaluating our business, including those described in Part I, Item 3.D: "Risk Factors" in this Annual Report on Form 20-F, or this Annual Report. These risks include, but are not limited to, the following:

- We are a 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 will require additional capital to fund our operations and if we fail to obtain the necessary financing, we will not be able to complete the development and commercialization of our product candidates.
- While we were founded in 2012, we announced our plans to refocus our business on our RNA editing platform in 2022, and it may make it difficult to assess the future viability of our business and our strategy.
- Our business depends in part on the success of our different product candidates, which are currently in different phases of preclinical and clinical development. We cannot be certain that we will be able to successfully complete the clinical development of, obtain regulatory approval for, or successfully commercialize our product candidates.
- We may not be able to file investigational new drug applications ("INDs") or IND amendments or similar applications to commence clinical trials of our product candidates on the timelines we expect, and even if we are able to, the U.S. Food and Drug Administration (the "FDA") or similar foreign regulatory authority may not permit us to proceed.
- The regulatory approval processes of the FDA, the European Medicines Agency (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.
- Failures or delays in the commencement or completion of our preclinical studies 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.
- Our RNA technologies are unproven in the disease indications for which they are being developed and tested and may not lead to the development of, or result in, marketable products.
- Failure to obtain regulatory approval in jurisdictions outside the United States ("U.S.") and the European Union ("EU") would prevent our product candidates from being marketed in those jurisdictions.
- 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.
- 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.
- We rely on third-party manufacturers and suppliers and we intend to rely on third parties to produce preclinical, clinical, and, if approved, commercial supplies of our product candidates.
- If third parties on which we depend to conduct our preclinical- and clinical studies 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.

- Our collaboration partnerships with pharmaceutical companies are important to our business. If these companies do not successfully develop drugs pursuant to these agreements, our business could be adversely affected.
- We license patent rights from third-party owners or licensees and if we fail to comply with our obligations in our intellectual property licenses, we could lose rights that are fundamental to our business.
- 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.
- We or our licensors or any current or 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.
- 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.
- 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.
- 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.
- Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.
- Members of our Board of Directors (the "Board" or "board") and our principal shareholders and their affiliates have significant control over our company, which will limit other stakeholders' ability to influence corporate matters and could delay or prevent a change in corporate control.
- We are a foreign private issuer and, as a result, we are not subject to U.S. proxy rules and are subject to the Securities and Exchange Act of 1934, as amended (the "Exchange Act") reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.
- Certain U.S. holders of our ordinary shares may suffer adverse tax consequences if we are characterized as a passive foreign investment company ("PFIC") for U.S. federal income tax purposes.
- 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.

The material and other risks summarized above should be read together with the text of the full risk factors discussed in the section entitled "Risk Factors" and the other information set forth in this Annual Report, including our consolidated financial statements and the related notes, as well as in other documents that we file with the Securities and Exchange Commission (the "SEC"). If any such material and other risks and uncertainties occur, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks summarized above or described in full elsewhere in this Annual Report are not the only risks that we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, prospects, financial condition and results of operations.

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From time to time, we may use our website or our LinkedIn profile at www.linkedin.com/company/proqr-therapeutics/ to distribute material information. Our financial and other material information is routinely posted to and accessible on the Investors & Media section of our website, available at www.ProQR.com. Investors are encouraged to review the Investors & Media section of our website because we may post material information on that site that is not otherwise disseminated by us. Information that is contained in and can be accessed through our website or our LinkedIn page is not incorporated into, and does not form a part of, this Annual Report on Form 20-F.

Introduction

This document contains information required for the Annual Report on Form 20-F for the year ended December 31, 2024, of ProQR Therapeutics N.V. (the "Annual Report"). Unless the context specifically indicates otherwise, references in this Annual Report to "ProQR Therapeutics N.V.", "ProQR Therapeutics", "ProQR", "we", "our", "ours", "us", the "Company" and similar designations refer to ProQR Therapeutics N.V., a company organized under the laws of the Netherlands, and where appropriate, its consolidated subsidiaries.

IFRS Based Information

The audited financial statements as at December 31, 2024 and 2023, and for the years ended December 31, 2024, December 31, 2023 and December 31, 2022, included in the Annual Report 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-Generally Accepted Accounting Principles ("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

We use various trademarks and tradenames, including without limitation "ProQR", "Axiomer", "Trident" and our corporate logo, that we use in connection with the operation of our business. Other trademarks, trade names or service marks of third parties referred to or incorporated by reference in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks, trade names and service marks in this Annual Report may be referred to without the ®, ™ or SM symbols, but the omission of 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. We do not intend to use or display other companies' trademarks, trade names and service marks to imply a relationship with, or endorsement or sponsorship of us, any other companies.

Market, Industry and Other Data

Market data and certain other statistical information used throughout this Annual Report are based on independent industry publications, governmental publications, reports by market research firms or other independent sources that we believe to be reliable sources. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. In some cases, we do not expressly refer to the sources from which this data is derived. We are responsible for all of the disclosure contained in this Annual Report, and we believe that these sources are reliable. While we are not aware of any misstatements regarding any third-party information presented in this Annual Report, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed under the section titled “Risk Factors” and elsewhere in this Annual Report and in the documents incorporated by reference herein. Some data are also based on our good faith estimates. These and other factors could cause results to differ materially from those expressed in the estimates made by the third parties or by us.

Cautionary Language Regarding Forward-looking Statements

This Annual Report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 4.B "Business Overview," Part I, Item 3.D. "Risk Factors," and Part I, Item 5. "Operating and Financial Review and Prospects," but are also contained elsewhere in this Annual Report. 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," or the negative of these terms, or other comparable terminology intended to identify statements about the future, although not all forward-looking statements contain these identifying words. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The forward-looking statements contained in this Annual Report are based upon information available to us as of the date of this Annual Report and, while we believe we have a reasonable basis for each forward-looking statement contained this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that forward-looking statements are not guarantees of future performance and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. Known and unknown risks, uncertainties and other factors may cause our actual results, performance or achievements, including in relation to the research and (pre-)clinical development of our RNA editing platform or any of our pipeline programs, to be materially different from our expectations. These forward-looking statements include, without limitation, statements about the following:

- our development programs, including the cost, timing, plans, results of preclinical studies and clinical trials and other development activities by us and our collaborative partners and therapeutic potential with respect to our product candidates;
- the likelihood of our clinical programs being executed on timelines provided and reliance on our contract research organizations ("CROs") 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, and the ability to successfully submit the necessary applications or to obtain the necessary clearances;
- our business operations and our ability to secure, maintain and realize the intended benefits of collaborations with partners, including the timing of commencing clinical trials and enrollment of patients and/or healthy volunteers therein;
- 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;
- our ability to attract and retain key scientific and/or management personnel;
- our other programs and business operations (including Axiomer™);
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates, if approved;
- our collaboration with Eli Lilly and Company ("Lilly") and the intended benefits thereof, including milestone and royalty payments from commercial product sales, if any, from the products covered by the collaboration, as well as the potential of our technologies and product candidates;

- the accuracy of our estimates of our future revenue, expenses, capital requirements and needs for additional financing;
- our estimates regarding the market opportunities for our current and future programs and any future product candidates;
- the impact of global economic and political developments on our business, including rising inflation and capital market disruptions, tariffs (including tariffs that have been or may in the future be imposed by the United States or other countries), trade protection measures or other trade barriers (including further legislation or actions taken by the United States or other countries that restrict trade), economic sanctions and economic slowdowns or recessions that may result from such developments which could harm our research and development efforts as well as the value of our ordinary shares and our ability to access capital markets;
- the impact on our operations and activities that may be slowed or halted by shortage and/or pressure on supply and logistics on the global market and/or the impact of health epidemics, pandemics and other widespread outbreaks of contagious diseases;
- general business, financial and accounting risks and risks related to litigation and disputes with third parties; and
- the other risks and uncertainties, including those listed under the caption “Risk Factors.”

In addition, even if our results, performance, financial condition and liquidity, and the development of the industry in which we operate are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. Among the factors that may result in differences are our expectations regarding risks and uncertainties related to the impact of geopolitical developments on our business, operations, strategy, goals and anticipated milestones, including our ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products, and our ability to obtain and maintain requisite regulatory approvals and to enroll patients and/or healthy volunteers in our planned clinical trials, additional interactions with regulatory authorities and expectations regarding future regulatory filings, our reliance on collaborations with third parties, estimating the commercial potential of our development programs and other risks indicated in the risk factors included in this report and other filings with the SEC.

Actual results could differ materially from our forward-looking statements due to a number of factors, including the risks set forth under the section “Risk Factors” and elsewhere in this Annual Report.

Any forward-looking statements that we make in this Annual Report are valid only as of the date of such statements, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this Annual Report 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. [Reserved]

Not applicable.

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report, including the financial statements and the related notes included elsewhere in this Annual Report. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that adversely affect our business. If any of the following risks actually occurs, our business, financial condition, results of operations, and future prospects could be materially and adversely affected.

Risks Related to Our Capital Needs and Financial Position

We are a 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 biopharmaceutical company with a limited operating history, engaged in the discovery and development of RNA-based therapeutics with our proprietary Axiomer RNA editing platform technology which could be used to develop new product candidates across multiple therapeutic areas. Since our inception in February 2012, we have devoted a significant portion of our resources to the development of our product candidates in inherited retinal disorders, including sepofarsen for Leber Congenital Amaurosis ("LCA"), ultevursen for Usher syndrome, and QR-1123 for autosomal dominant retinitis pigmentosa. Past resources have also been expended for the development of QR-504a for Fuchs endothelial corneal dystrophy, and eluforsen for cystic fibrosis, for which we have ceased making investments, and QR-313 for epidermolysis bullosa, which we have spun off. In August 2022 we announced our strategy to exclusively focus our resources on the development of our RNA editing platform. As a result, we have ended the clinical development of sepofarsen and ultevursen, which we have sold to Laboratoires Théa S.A.S. ("Théa") in December 2023. We have had significant operating losses since our inception. Our net losses for the years ended December 31, 2024, December 31, 2023 and December 31, 2022 were, € 27,763,000, € 27,735,000 and € 64,204,000, respectively. At December 31, 2024, we had an accumulated deficit of € 427,158,000. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our RNA editing platform is still in early stages of development and we are subject to

the risks of failure inherent in the development of novel technologies and product candidates based on novel technologies.

To date, the only material income we have generated has been from the receipt of government research grants and collaboration agreements. Our ability to generate revenue from product sales depends upon our ability to successfully develop candidates with our RNA editing platform, subsequently obtain regulatory approval for these candidates and successfully commercialize them and any other product candidates that we might develop, in-license or acquire in the future, enter into new collaboration agreements and generate milestone and royalty payments under existing or future collaboration agreements.

Even if we are able to successfully achieve regulatory approval for our 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 of both RNA editing platform and product candidates, 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, our ability to develop product candidates with our RNA editing platform, us or any current or 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 current or 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 planned clinical studies for our product candidates;
- complete and submit New Drug Applications (“NDAs”) to the FDA, Marketing Authorization Applications (“MAAs”) to the EMA, and comparable applications to other regulatory authorities and obtain regulatory approval for indications for which there is a commercial market;
- set a commercially viable price for any products for which we may receive approval;
- obtain commercial quantities of our products at acceptable cost levels;
- develop a commercial organization capable of sales, marketing and distribution for any product that we might 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, as has been the case for product candidates for which we have suspended or ceased development activities, or be shown to be not 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 for product candidates that do advance through development.

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.

In February, 2018, we entered into an agreement with Foundation Fighting Blindness ("FFB"), under which FFB has provided funding of $ 6.8 million to advance ultevursen into the clinic. Pursuant to the terms of the agreement, we were obligated to make certain repayments to FFB subject to development milestones. In December 2023, upon the occurrence of the sale of ultevursen to Théa, these payables were settled by means of a lump-sum payment in the amount of € 1.13 million and a percentage of earn-out payments for milestones and sales to be received by us from Théa, ranging from 5-10%.

Even if we are able to generate revenues from the sale of any of our product candidates or receive royalties from any of our collaboration partners, 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, which could result in a decline in the market value of our ordinary shares.

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 of cash to conduct further research and development, including with respect to our Axiomer platform, 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 U.S., the EU and certain other markets. As at December 31, 2024, we had € 149,408,000 in cash and cash equivalents. Based on our current operating plans, we believe that such existing cash and cash equivalents will be sufficient to fund our anticipated level of operations into mid-2027. 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 RNA editing platform and 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 relating to product candidates. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the preclinical and clinical development plans we establish for our product candidates;
- the number and characteristics of product candidates that we develop or may in-license;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies;
- the number and characteristics of programs that we may pursue in our innovation unit, including the development of RNA editing platform;
- the achievement of milestones that trigger payments under our existing or future collaboration agreements;

- our ability to establish collaboration arrangements for the development of our product candidates on favorable terms, if at all;
- 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 any 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. For instance, the trading prices for our ordinary shares and for other biopharmaceutical companies have been highly volatile. As a result, we may face difficulties raising capital through sales of our equity or debt securities or such sales may be on unfavorable terms. Similarly, adverse market or macroeconomic conditions or market volatility resulting from global economic developments, geopolitical developments, high inflation, rising interest rates, international tariffs, trade protection measures, economic sanctions, potential for significant changes in U.S. policies or regulatory environment, future public health epidemics or other factors, could materially and adversely affect our ability to consummate an equity or debt financing on favorable 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 such as our RNA editing platform. In order to raise additional capital, we may seek 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. 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 acceptable or relinquish or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

While we were founded in 2012, we announced our plans to refocus our business on our RNA editing platform in 2022, and it may be difficult to assess the future viability of our business and our strategy.

We were founded in February 2012 and began operations in May 2012, since which time we have primarily focused our efforts on development activities for our product candidates, including acquiring and developing product and technology rights and entering into collaborations. We have revised our strategy from time to time, including most recently in August 2022 when we announced our plan to focus exclusively on our RNA editing platform, therewith withdrawing from the ophthalmology space. 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 research and development initiatives and clinical development or approved products on the market.

We or third parties upon whom we depend may be adversely affected by natural disasters, geopolitical developments and/or global health pandemics, and our business, financial condition and results of operations could be adversely affected.

The occurrence of unforeseen or catastrophic events, including extreme weather events and other natural disasters, man-made disasters, or the emergence of epidemics or pandemics, acts of war, or geopolitical events, such as the ongoing conflict between Russia and Ukraine, depending on their scale, may cause different degrees of damage to the national and local economies, such as recessions, rising interest rates, inflation, fuel prices fluctuations, foreign currency fluctuations, international tariffs, boycotts, curtailment of trade and other business restrictions, and could cause a disruption in our operations and have a material adverse effect on our financial condition and results of operations. Man-made disasters, pandemics, and other events connected with the regions in which we operate could have similar effects. If a natural disaster, health pandemic, or other event beyond our control occurred that prevented us from using all or a significant portion of our office and/or lab spaces, damaged critical infrastructure, such as our manufacturing facilities or our manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations or supplies, it may be difficult for us to continue our business for a substantial period of time.

Increased attention to, and evolving expectations for, environmental, social, and governance ("ESG") initiatives could increase our costs, harm our reputation, or otherwise adversely impact our business.

Companies across industries are facing increasing scrutiny from a variety of stakeholders related to their ESG and sustainability practices. Investor advocacy groups, certain institutional investors, investment funds, and other influential investors have increasingly focused on ESG practices and have placed increasing importance on the non-financial impacts of their investments. Expectations regarding voluntary ESG initiatives and disclosures may result in increased costs (including but not limited to increased costs related to compliance, stakeholder engagement, contracting and insurance), enhanced compliance or disclosure obligations, or other adverse impacts to our business, financial condition, or results of operations.

While we may at times engage in voluntary initiatives (such as voluntary disclosures, certifications, or goals, among others) to improve the ESG profile of the Company, such initiatives may be costly and may not have the desired effect. Moreover, we may not be able to successfully complete such voluntary initiatives due to factors that are within or outside of our control. Even if this is not the case, our actions may subsequently be determined to be insufficient by various stakeholders, and we may be subject to investor or regulator engagement on our ESG efforts, even if such initiatives are currently voluntary.

Certain market participants, including major institutional investors and capital providers, use third-party benchmarks and scores to assess companies' ESG profiles in making investment or voting decisions. Unfavorable ESG ratings could lead to increased negative investor sentiment towards us, which could negatively impact our share price as well as our access to and cost of capital. In addition, in recent years "anti-ESG" sentiment has gained momentum across the United States, with several states and Congress having proposed or enacted "anti-ESG" policies, legislation, or initiatives or issued related legal opinions, and the President having recently issued an executive order opposing diversity equity and inclusion (DEI) initiatives in the private sector. Such anti-ESG and anti-DEI-related policies, legislation, initiatives, litigation, legal opinions, and scrutiny could result in us facing additional compliance obligations, becoming the subject of investigations and enforcement actions, or sustaining reputational harm. Therefore, to the extent we take actions that are seen as positive to some investors, other investors may take issue with such actions or face regulatory pressure to refrain from investing in, or divest from, our business. To the extent ESG matters negatively impact our reputation, it may also impede our ability to compete as effectively to attract and retain employees, which may adversely impact our operations.

In addition, we expect there will likely be increasing levels of regulation, disclosure-related and otherwise, with respect to ESG matters. For example, the SEC has published propose rules that would require companies to provide significantly expanded climate-related disclosures in their periodic reporting. The new climate disclosure rules were the subject of multiple legal challenges, and the SEC voluntarily stayed the climate disclosure rules pending the completion of judicial review. Therefore, it is unknown whether the new rules will go into effect and if they do, whether there will be significant changes. If the new rules go into effect and are not substantially different than the rules adopted by the SEC, we may be required to incur significant additional costs to comply, including the implementation of significant additional internal controls processes and procedures regarding matters that have not been subject to such controls in the past, and impose increased oversight obligations on our management and board of directors. Even if the SEC rules are not adopted, states or ex-U.S. jurisdictions in which we currently or may in the future operate may also have or adopt ESG or climate-related disclosure rules requiring similar or broader disclosure obligations. These and other changes in stakeholder expectations will likely lead to increased costs as well as scrutiny that could heighten all of the risks identified in this risk factor. Additionally, our business partners may be subject to similar expectations, which may augment or create additional risks, including risks that may not be known to us.

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

Our business depends in part on the success of our programs and product candidates, which are currently in different stages of preclinical and clinical development. We cannot be certain that we will be able to successfully complete the clinical development of, obtain regulatory approval for, or successfully commercialize our product candidates.

Our business depends in part on our ability to develop, secure regulatory approval for and commercialize one or more product candidates, including any product candidates resulting from our initial pipeline programs using our Axiomer technology, including our lead program AX-0810 for Cholestatic Diseases targeting Na-taurocholate cotransporting polypeptide ("NTCP"). However, the development of drug candidates is lengthy, uncertain and expensive, and there can be no assurance that we will achieve such goals. For example, in the past, we have focused our efforts on the development of product candidates in our ophthalmology portfolio and, previously, for cystic fibrosis, none of which we are planning to continue developing at this time. In February 2022, we announced that top-line results from our Phase 2/3 pivotal trial of sepofarsen did not meet its primary endpoint.

In August 2022, we announced our strategy to shift our focus and resources exclusively to the development of our RNA editing platform, ending the clinical development of sepofarsen and ultevursen and ultimately ending all activity related to the broader ophthalmology portfolio. In December 2023, we have sold the assets sepofarsen and ultevursen to Théa, which Théa will further develop.

The clinical trials and manufacturing and marketing of our future product candidates will be subject to extensive and rigorous review and regulation by numerous government authorities in the U.S., the EU 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 U.S. and the EU, 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.

In addition, if Théa or a third party collaborator resumes or were to resume the advancement of sepofarsen or ultevursen or QR-1011, or commence new clinical programs of our product candidates in the future, the successful clinical development, regulatory approval and commercialization of any of these product candidates would require additional or new preclinical and clinical testing and substantial additional or new clinical development and regulatory approval efforts before we are permitted to commence their commercialization, if ever. It would be several years before a pivotal trial could be completed for any of such other product candidates, if ever.

We may not be able to file INDs or IND amendments or similar applications to commence clinical trials of our product candidates on the timelines we expect, and even if we are able to, the FDA or similar foreign regulatory authority may not permit us to proceed.

We may not be able to file INDs or similar applications for our product candidates on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND or similar application will result in the FDA or similar foreign regulatory authority allowing clinical trials to begin, or that, once begun, issues will not arise that result in the suspension or termination of clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND or similar application, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations apply to new clinical trials we may submit as amendments to existing INDs or to a new IND or similar application. Any failure to file INDs or similar applications on the timelines we expect or to obtain authorization to begin our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

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 U.S. or the EU 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 any product candidate, we will need to complete preclinical and toxicology studies, as well as proof-of-concept studies and Phase 1, Phase 2 and Phase 3 clinical trials for such candidate. 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 an 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, including pivotal 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 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 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.

We may never realize a return on our investment of resources and cash from our drug discovery collaborations.

In addition to developing our own pipeline of product candidates, we also conduct drug discovery activities for or with collaborators who are also engaged in drug discovery and development, which could include pre-commercial biotechnology companies and large pharmaceutical companies. Under these collaborations, we might provide the benefit of our drug discovery platform and platform experts who identify molecules that have activity against one or more specified targets, among other resources. In consideration, we have received, and might receive in the future, (i) equity investments; (ii) upfront fees; and/or (iii) the right to receive option fees, cash milestone payments upon the achievement of specified development, regulatory, or commercial sales milestones for the drug discovery targets, and potential royalties. Our ability to receive fees and payments and realize returns from our drug discovery collaborations in a timely manner, or at all, is subject to a number of risks, including but not limited to the following:

- our collaborators may incur unanticipated costs or experience delays in completing, or may be unable to complete, the development and commercialization of any drug candidates;

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to our collaborations and may not perform their obligations as expected;

- collaborators may decide not to pursue development or commercialization of drug candidates for various reasons, including results of clinical trials or other studies, changes in the collaborator's strategic focus or available funding, their desire to develop products that compete directly or indirectly with our drug candidates, or external factors (such as an acquisition or industry slowdown) that divert resources or create competing priorities;

- existing collaborators and potential future collaborators may begin to perceive us to be a competitor more generally, particularly as we advance our internal drug discovery programs, and therefore may be unwilling to continue existing collaborations, or enter into new collaborations, with us;

- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution, or marketing of a drug candidate or product;

- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation, or the preferred course of development, might cause delays or terminations of the research, development, or commercialization of drug candidates, or might result in litigation or arbitration;

- collaborators may not properly obtain, maintain, enforce, defend, or protect our or their intellectual property or proprietary rights, or they may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our or their intellectual property or proprietary rights;

- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;

- collaborators may infringe, misappropriate, or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and

- drug discovery collaborations may be terminated prior to our receipt of any significant value.

Failures or delays in the commencement or completion of our preclinical studies or planned or future clinical trials of our future 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 preclinical studies and clinical trials is a prerequisite to submitting an NDA to the FDA or an 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 future clinical trials will begin or be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including, among others:

- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- inadequate quantity or quality of a product candidate or other materials necessary to conduct clinical trials;

- difficulties obtaining Institutional Review Board (“IRB”) or ethics committee approval to conduct a clinical trial at a prospective site or sites, or where applicable, institutional biosafety committee (“IBC”) approval;

- 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;

- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to lack of efficacy, side effects, personal reasons or loss of interest; or

- force majeure events.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the EMA, the IRBs at the sites where the IRBs are overseeing a clinical trial, upon recommendation of a data safety monitoring board ("DSMB") overseeing the clinical trial at issue, or by 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, administrative actions, or policy;
- problems with clinical supply materials; and
- lack of adequate funding to continue the clinical trial.

Positive results from early-stage clinical trials and preclinical testing of our product candidates are not necessarily predictive of the results of later clinical trials for these product candidates. If we cannot achieve positive results in our later stage clinical trials for our product candidates, we may be unable to successfully develop, obtain regulatory approval for and commercialize them.

We may from time to time publish results from preclinical studies and clinical trials of our product candidates. Positive results from early-stage clinical trials and preclinical testing of our product candidates *in vitro* and *in vivo* may not necessarily be predictive of the results from later-stage clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials after achieving positive results in preclinical and early-stage clinical trials, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings that emerged while clinical trials were already underway or safety or efficacy observations made in clinical trials, including adverse events. 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 European Commission approval. If we fail to produce positive results in our clinical trials for any 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.

Additionally, some of our clinical trials have utilized and may in the future utilize an "open-label" trial design. An open-label clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a patient bias where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an investigator bias where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates when studied in a controlled environment with a placebo or active control.

Changes in regulatory requirements or guidance from the FDA, EMA or other applicable regulatory authorities, or unanticipated events during our preclinical or clinical development activities may occur, which may result in changes to requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, or guidance from the FDA, EMA, or other applicable regulatory authorities, imposition of additional preclinical or clinical study requirements by applicable regulatory authorities or unanticipated events during our preclinical or clinical development may force us to amend study protocols or conduct additional studies or trials or involve delays to our preclinical and clinical studies and overall development strategy, all of which could result in increased costs for the development of our product candidates. We may experience delays if we are required by the FDA, EMA, or other applicable regulatory authorities, or if we voluntarily decide to, redesign or restructure a clinical trial once initiated. Amendments to our clinical trial protocols may require resubmission to the applicable regulatory authorities and IRBs or ethics committees for review and approval, which may adversely impact the cost, timing and/or successful completion of a clinical trial. We may be delayed in our clinical development if we are unable to obtain alignment with the FDA, EMA, or other applicable regulatory authorities on an acceptable clinical trial design or statistical analysis plan for any of our clinical trials. Additionally, the FDA, EMA, or other applicable regulatory authorities may require us to conduct additional clinical trials, including pivotal trials, to support a marketing application. If we experience delays completing, or if we terminate, any of our clinical trials, or if we are required to conduct additional clinical trials, the commercial prospects for our product candidates may be harmed and our ability to generate product revenue will be delayed.

Our RNA technologies are unproven in the disease indications for which they are being developed and tested and may not lead to the development of, or result in, marketable products.

We are developing an RNA editing platform and a pipeline of product candidates using our proprietary Axiomer RNA editing technology for genetic disorders with unmet need. We believe that editing at the RNA level to, for example, 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 preliminary, ongoing, and yet to be clinically validated. The mechanism of action of our compounds could be different from what we today hypothesize. Also, we may discover that the molecules that 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 RNA editing platform and will focus our resources exclusively on this RNA editing platform, 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, and in turn we may not become profitable and the value of our ordinary shares would decline.

While there are a number of approved therapies based on the oligonucleotide modality, there are no approved therapies based on the editing technology underlying our novel editing mechanism which uses Adenosine Deaminase Acting on RNA ("ADAR"). This may increase the complexity, uncertainty and length of the development and 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 U.S. and the EU, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The regulatory approval process outside the U.S. and the EU generally includes all of the risks associated with obtaining FDA and European Commission approval, but can involve additional testing. We may need to partner with third parties in order to obtain approvals outside the U.S. and the EU. 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 U.S. and the EU on a timely basis, if at all. Even if we were to receive approval in the U.S. or the EU, approval by the FDA or the European Commission does not ensure approval by regulatory authorities in other countries or jurisdictions. Similarly, approval by one regulatory authority outside the U.S. and the EU would not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA or the European Commission. 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.

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 may seek a breakthrough therapy designation for our product candidates in the future. 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 available 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 may also be 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. 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 also 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 such qualification or decide that the time period for FDA review or approval will not be shortened.

We may seek designation for our Axiomer RNA editing platform as a designated platform technology, but we might not receive such a designation, and even if we do, such a designation may not lead to a faster development, regulatory review or approval process.

We may seek designation for our Axiomer RNA editing platform as a designated platform technology. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), a platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA or biologics license application ("BLA"); (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated

platform technology concurrently with, or at any time after, submission of an IND for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA or BLA for a drug that uses or incorporates the platform technology. Even if we believe our Axiomer platform meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not ensure that a drug will be developed more quickly, be reviewed by the FDA faster, or receive FDA approval. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

Our therapeutic candidates are based on a novel mechanism of action, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all.

Although we have discovered and are developing our novel RNA editing platform and will focus our resources exclusively on this RNA editing platform, as announced as part of our strategy update in August 2022, 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 or our partners may never succeed in developing a marketable product based on our platform, and in turn 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.

Risks Related to Our Dependence on Third Parties

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 party to, and we may from time to time in the future pursue, collaborative arrangements for the development and commercialization of product candidates, if approved. We have executed and continue to consider strategic alternatives that include spinouts, out-licensing or collaborative partnerships to develop and commercialize our RNA technologies, including our Axiomer program, or programs. For example, in 2021, we entered into a licensing and research collaboration agreement with Lilly, as amended in 2022, which expanded our collaboration, focused on the discovery, development, and commercialization of potential new medicines primarily in the peripheral nervous system ("PNS") and central nervous system ("CNS") and metabolic diseases, and in 2024, we announced a new research partnership with the Rett Syndrome Research Trust ("RSRT") focused on utilizing Axiomer to develop editing oligonucleotides ("EONs") targeting an underlying genetic variant that causes Rett syndrome, a rare neurodevelopment disorder, which is included on our pipeline as AX-2402. If any of our collaborative partners in future collaborative arrangements for the commercialization of 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.

Moreover, 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. The failure of any current or future collaboration partners to develop or effectively commercialize our product candidates, if approved, for any of these reasons would have a material adverse effect on our operating results and financial condition.

For sepofarsen and ultevursen, we will depend on Théa to develop and conduct clinical trials with, obtain regulatory approvals for, and if approved, market and sell these product candidates. We may also pursue similar relationships with other development and commercialization collaborators for additional product candidates in the future or expand the reach with current collaborators. If such collaborators fail to perform as expected, the potential for us to generate future revenue from such product candidates would be significantly reduced and our business would be harmed.

For certain product candidates, we depend, or will depend, on our development and commercial collaborators to develop, conduct clinical trials of, and, if approved, commercialize product candidates.

Our current collaborations and any future collaborations that we enter into are subject to numerous risks, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to the collaborations;

- collaborators may not perform their obligations as expected or fail to fulfill their responsibilities in a timely manner, or at all;

- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;

- collaborators may delay preclinical studies or clinical trials, provide insufficient funding for clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our shareholders about the status of such product candidates;

- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- the collaborations may not result in product candidates to develop and/or preclinical studies or clinical trials conducted as part of the collaborations may not be successful;

- product candidates developed with collaborators may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to stop commercialization of our product candidates;

- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate; and

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation.

In addition, certain collaboration and commercialization agreements provide our collaborators with rights to terminate such agreements, which rights may or may not be subject to conditions, and which rights, if exercised, would adversely affect our product development efforts and could make it difficult for us to attract new collaborators. In that event, we would likely be required to limit the size and scope of efforts for the development and commercialization of such product candidates or products; we would likely be required to seek additional financing to fund further development or identify alternative strategic collaborations; our potential to generate future revenue from royalties and milestone payments from such product candidates or products would be significantly reduced, delayed or eliminated; and it could have an adverse effect on our business and future growth prospects. Our rights to recover tangible and intangible assets and intellectual property rights needed to advance a product candidate or product after termination of a collaboration may be limited by contract, and we may not be able to advance a program post-termination.

We rely on third-party manufacturers and suppliers and we intend to rely on third parties to produce preclinical, clinical and, if approved, 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 current Good Manufacturing Practice ("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. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturer or manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA, the EMA or another regulatory authority. The delays associated with the verification of a new manufacturer or manufacturing process 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 but not limited to:

- 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;
- subjection of 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 third parties on which we depend to conduct our preclinical and clinical studies 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 and consultants to design, conduct, supervise and monitor preclinical studies for our product candidates and expect to rely on CROs, clinical data management organizations, institutions, and clinical investigators for the conduct of our future clinical trials. We and our CROs are required to comply with various regulations, including Good Laboratory Practices ("GLP") and 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 that study data integrity is assured. Regulatory authorities ensure compliance with these requirements through periodic inspections of study sponsors, principal investigators and study sites. If we or any of our investigators or CROs fail to comply with applicable requirements, the data generated in our studies may be deemed unreliable and the FDA, the EMA or other comparable foreign regulatory authorities may require us to perform additional studies. We cannot be certain that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our studies comply with such requirements.

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 studies. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the study data they obtain is compromised due to their failure to adhere to our protocols, regulatory requirements or for other reasons, our preclinical or clinical studies may be extended, delayed or terminated.

Because we have relied and continue to rely on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves a 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 relatively 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. Even though we carefully manage our relationships with our CROs, there can be no assurance that we will not be impacted by this type of 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. Regional or single-source dependencies may in some cases accentuate these risks. For example, the pharmaceutical industry generally, and in some instances our collaborators or other third parties depend on China-based suppliers or service providers for certain raw materials, products and services, or other activities. The ability of our collaborators or such other third parties to continue to engage these China-based suppliers or service providers for certain preclinical research programs and clinical development programs could be restricted due to geopolitical developments between the United States and China, including as a result of the escalation of tariffs or other trade restrictions or if the previously proposed federal legislation known as the BIOSECURE Act or a similar law were to be enacted. In any such circumstances, we may not be able to engage a backup or alternative supplier or service provider in a timely manner or at all. This, in turn, could materially and adversely affect our or our collaborators' ability to manufacture or supply marketed products and product candidates or advance our or our collaborators' preclinical research or clinical development programs, which could materially and adversely affect our business and future 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 or clinical studies or meet expected deadlines, our studies could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our studies is conducted in accordance with the general investigational plan and protocols for the trial.

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 and entities 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. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback statute is violated. Violations are subject to significant civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, a claim submitted for payment to any federal healthcare program that includes items or services that were made as a result of a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act ("FCA"). The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers, among others, on the other;

- federal civil and criminal false claims laws, including the FCA 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. A claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the FCA. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring qui tam actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery or settlement. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- 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. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA fraud provisions without actual knowledge of the statute or specific intent to violate it;

- 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 on certain covered healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their respective "business associates", being those independent contractors or agents of covered entities that create, receive, maintain, transmit or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal 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 U.S. Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies to report annually to the Department of Health and Human Services ("HHS") information related to direct or indirect payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other licensed healthcare professionals (such as physician assistants, nurse practitioners, and others), and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- analogous state, local 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 any 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.

The distribution of biopharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of biopharmaceutical products.

Comparable laws and regulations exist in the countries within the EEA and other countries where we may market our products in the future, including without limitation the United Kingdom ("UK"), Canada and Brazil. Although in the EEA such laws are partially based upon EU 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, disgorgement, imprisonment, reputational harm, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, as well as additional

reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. 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 similar penalties. In addition, the approval and commercialization of any product candidate we develop outside the U.S. will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. All of these could harm our ability to operate our business and our financial results.

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 and any imposition of significant fines or other sanctions could have a significant impact on our business and results of operations.

Our collaboration partnerships with pharmaceutical companies are important to our business. If these companies do not successfully develop drugs pursuant to these agreements, our business could be adversely affected.

Under the amended and restated research and collaboration agreement which we entered into with Lilly in December 2022, Lilly has been granted certain exclusive and non-exclusive rights to our Axiomer platform IP to exploit compounds and develop and commercialize products based on this platform. Should Lilly decide not to pursue or be unable to pursue further development and subsequent commercialization, we would not be able to receive milestone payments or royalty revenues associated with this partnership, which could have a substantial impact on our revenue.

Risks Related to Our Intellectual Property

We may become involved in legal proceedings with third parties that infringe our intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

We may from time to time become involved in legal proceedings challenging our intellectual property rights, including with respect to Axiomer. For example, one or more third parties may seek to invalidate these intellectual property rights. Our success will depend in part on our ability to obtain, maintain and enforce patent protection for our inventions. We may not be able to successfully prosecute the patent applications. If patents are issued or granted, we may fail to maintain these patents due to oppositions and/or other post grant procedures initiated by third parties, we may determine not to pursue litigation against other companies that are infringing these patents, or we may pursue litigation in a variety of ways. For example, we currently are facing oppositions in Australia and Europe with respect to patents relating to our Axiomer platform. If we are unsuccessful in defending our patents against these oppositions, we could lose patent protection for Axiomer and product candidates developed thereunder in these jurisdictions. Further, intellectual property

rights may not provide us with complete exclusivity in the respective fields, which would allow for third parties to develop competing products and technologies, which could adversely affect our business and harm our 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, EPO 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.

Further, 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's 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 business depends upon our ability to develop, manufacture and, if approved, 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 be 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.

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 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, regardless of the exclusive or non-exclusive nature of these rights. Our licensors may not successfully prosecute the patent applications licensed to us. Even if patents are issued or granted, our 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.

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 have executed a confidentiality 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 in the future 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 2022) 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

If any of our product candidates are 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 are 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 are approved, we will need to enter into collaborations with third parties to provide sales, marketing and distribution capabilities to commercialize such products or develop these capabilities internally, which would be expensive and time-consuming. If we decide to 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 such 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 have adequate sales and distribution capabilities for our products or be successful in gaining market acceptance of any approved product. If we decide to market our products directly, we would 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 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.

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. whether on our own or with a collaborator, 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 may 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 may 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 may 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.

Even if we are able to commercialize any of our product candidates, whether on our own or with a collaborator, 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, by us or a collaborator 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 or our collaborators 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. Moreover, 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. Factors payors consider in determining reimbursement are based on whether the product is: (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational.

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 U.S., particularly in Member States of the EU, the pricing of prescription products 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 EU 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.

Moreover, efforts by governmental and other third-party payors, in the U.S. and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale, whether by us or a collaborator, of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Even if we receive marketing approval for any of our product candidates, they 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, the EMA or other regulatory authorities;
- availability of alternative treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies or those of our collaborators;
- our, or our collaborators', 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.

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 impact our ability to sell our product candidates profitably, if approved.

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 or a collaborator 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.

In March 2010, the Affordable Care Act ("ACA") was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. biopharmaceutical industry. The ACA 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. Among other things, it subjects biological products to potential competition by lower-cost biosimilars, expands the types of entities eligible for the 340B drug discount program, introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. 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 its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, including efforts to repeal or replace the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA.

In addition, other legislative and regulatory changes have been proposed and adopted in the U.S. since the ACA was enacted. For example:

- The U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. The reductions remain in effect through 2031.

- The U.S. American Taxpayer Relief Act of 2012 among other things, further reduced Medicare payments to several types of providers.

- The American Rescue Plan Act of 2021 eliminates the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024.

- Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation.

These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Additionally, there has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. There has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs.

Further, the government has issued regulations and guidance for states to build and submit importation plans for drugs from outside the U.S., pursuant to section 804 of the MMA. CMS has stated that drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If further implemented, importation of drugs from Canada could materially and adversely affect the price we receive for any of our product candidates.

Additionally, on November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed, and the Inflation Reduction Act of 2022 ("IRA") delayed implementation of the rule until January 1, 2032.

In addition, the IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to $ 2,000 which began in 2025; impose new manufacturer financial liability on certain drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation, and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general are not yet known.

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, or our collaborators, would 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.

Further, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals, if any, of our product candidates, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing conditions and other requirements.

Individual states in the U.S. have also become increasingly aggressive in passing legislation and implementing 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. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

In the EU, similar political, economic and regulatory developments may affect our, or our collaborators', ability to profitably commercialize our current or any future products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or Member State level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU Member States have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our, or our collaborators', ability to commercialize any products for which we obtain marketing approval. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

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. For example, the U.S. Supreme Court's June 2024 decision in *Loper Bright Enterprises v. Raimondo* overturned the longstanding *Chevron* doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The *Loper* decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the *Loper* decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. 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 we will be subject to extensive post-approval regulatory requirements and review.

If we obtain regulatory approval for any of our product candidates, we and any approved product candidates would be subject to extensive ongoing requirements and review 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. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the United States. 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 or 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, the FCPA and other similar laws generally prohibit us, our senior management, 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. If we were to pursue sales, marketing or distribution activities in the future, we may 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, the 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 UK and the U.S., and authorities in the EU, 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, and anti-money laundering 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, other anti-corruption laws, Trade Control laws or anti-money laundering 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, Trade Control laws or anti-money laundering 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 and were to pursue sale, marketing or distribution activities ourselves, we may 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 may market our product candidates ourselves 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 would be 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;
- differences in local business culture and practices, difference in customer attitudes and tendencies and general differences in culture and local trends;
- the potential need to recruit and work through local partners;
- reduced protection for or increased violation of intellectual property rights in some countries;
- inadequate 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 and anti-money laundering 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.

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 competent authorities of the EU Member States 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 other similar 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 U.S., 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 FCA, 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. These FCA lawsuits against pharmaceutical and medical device companies have led to substantial civil and criminal settlements, including elements such as fines or restitution, agreements to comply with burdensome reporting and compliance obligations, and exclusion from Medicare, Medicaid, and other federal and state healthcare programs. From time to time, legislation is drafted, introduced, passed in Congress and signed into law 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 the manner in which pharmaceutical products are regulated and marketed. 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 or in which we could choose to set up operations in the future, 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

Members of our Board and our principal shareholders and their affiliates have significant control over our company, which will limit other stakeholders' ability to influence corporate matters and could delay or prevent a change in corporate control.

The holdings of the members of our 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 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, which 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 board and our principal shareholders and their affiliates.

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 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. Moreover, 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 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. It is noteworthy that for 2024 and onwards, given the increased and exclusive focus on the RNA editing technology platform, the fact that we seek to hire and attract personnel in a narrower field puts a higher risk factor on our ability to attract personnel. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

We will need to maintain a good relationship with our employees to maintain our operations. A deterioration in our relationships with our employees could have an adverse impact on our business.

Maintaining good relationships with our employees and operating effectively and efficiently across our organization are crucial to our operations and our success. If we are unable to successfully maintain such relationships or manage the uncertainty as a result of the reduction in the number of our residual workforce, and the complexity of operations, our business may be adversely affected.

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, 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.

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

We are subject to a number of laws and regulations relating to privacy and data protection, including, in relation to the EU, the General Data Protection Regulation (EU) 2016/679 (the "EU GDPR") and, following the UK's withdrawal from the EU, the EU GDPR as incorporated into UK laws ("UK GDPR" and together with the EU GDPR, "GDPR"). As the regulatory focus on privacy issues continues to increase and worldwide laws and regulations concerning the handling of personal data expand and become more complex (including in relation to privacy, the use of artificial intelligence, the operation of digital platforms, and provision of digital services), we expect that potential risks related to data collection and use within the business may intensify. In addition, new laws or regulations governing privacy, security, the use of artificial intelligence, the provision of digital services, and data protection may be introduced which could apply in future. The nature and extent of such additions and changes in data protection laws or regulations, and the application to, or impact they may have on, the Company, is uncertain.

The data protection laws applicable to us impact our ability to collect, augment, analyze, use, transfer and share personal data. For example, the GDPR, among other obligations and requirements: (i) imposes requirements relating to having a legal basis or condition for processing personal data and, where applicable, how an organization can collect and rely upon consent obtained from an individual to process their personal data; (ii) imposes obligations in relation to the provision of information to individuals relating to the processing of their personal data; (iii) requires organizations to notify personal data breaches to competent data protection authorities and/or individuals; (iv) imposes additional requirements in relation to the processing of certain categories of data (i.e. "sensitive information" or special category data), which includes health data, data revealing racial or ethnic origin, and genetic data; (v) requiring data protection impact assessments for high risk processing; and (vi) taking certain measures when engaging third-party processors. The GDPR also grants individuals certain rights, subject to certain limitations, including the rights to request and access a copy of the personal data processed by an organization, to have inaccurate personal data rectified or completed if incomplete, to object to or restrict the processing of their personal data, and to request deletion of personal data.

Regulators can impose significant monetary fines for violations of laws and regulations relating to privacy and data protection. For example, non-compliance with certain obligations under the GDPR may result in monetary penalties of up to, the greater of, 4 per cent of the Company's worldwide turnover in the preceding financial year, or € 20.0 million (£ 17.5 million in the UK), whichever is higher. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. The GDPR, and other changes in laws or regulations associated with the enhanced protection of personal data, mean that the size of potential fines related to data protection and our costs of providing products and services, could result in changes to our business practices, and could prevent us from offering certain services in jurisdictions in which we operate. Although we have implemented contracts, policies and procedures designed to ensure compliance with applicable laws and regulations, there can be no assurance that our employees, contractors, partners, service providers or agents will not violate such laws and regulations or our contracts, policies and procedures. Additionally, public perception and standards related to the privacy of personal data can shift rapidly, in ways that may affect our reputation, the regulators' approaches to enforcement of existing laws, or influence regulators to enact regulations and laws that may limit our ability to handle personal data or provide certain products and services.

The GDPR, and other applicable data protection laws, also impose restrictions in relation to the international transfer of personal data. For example, in order to transfer data outside of the EEA to a non-adequate country, the GDPR requires us to enter into an appropriate transfer mechanism, and may require us to take additional steps to ensure an essentially equivalent level of data protection. The European Commission has issued standard contractual clauses for data transfers from controllers or processors in the EU (or otherwise subject to the GDPR) to controllers or processors established outside the EU. The new standard contractual clauses require exporters to assess the risk of a data transfer on a case-by-case basis, including an analysis of the laws in the destination country. The UK is not subject to the European Commission's new standard contractual clauses but has published a UK-specific transfer mechanism, which enables transfers from the UK. The UK-specific mechanism, the "International Data Transfer Agreement", requires a similar risk assessment of the transfer as the standard contractual clauses. Further, the EU and U.S. have adopted its adequacy decision for the EU-U.S. Data Privacy Framework ("Framework"), which entered into force on July 11, 2023. This Framework provides that the protection of personal data transferred between the EU and the U.S. is comparable to that offered in the EU. This provides a further avenue to ensuring transfers to the U.S. are carried out in line with GDPR. There has been an extension to the Framework to cover UK transfers to the U.S.. The Framework could be challenged like its predecessor frameworks. Implementing new or revised transfer mechanisms or ensuring an essentially equivalent protection may involve additional expense and potentially increased compliance risk. In the event a legislator, government, regulator or court imposes additional restrictions on international transfers, there may be operational interruption in the performance of services for customers and internal processing of employee information. Such restrictions may also increase our obligations in relation to carrying out international transfers of personal data, and incur additional expense and increased regulatory liabilities.

Our failure to comply with U.S. data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

There are numerous laws and legislative and regulatory initiatives at the U.S. federal and state levels as well addressing privacy and security concerns, and some state privacy laws apply more broadly than HIPAA and associated regulations. For example, the California Consumer Privacy Act ("CCPA"), creates individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal information about residents of California. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and became enforceable by the California Attorney General on July 1, 2020. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches that result in the loss of personal information. This private right of action may increase the likelihood of, and risks associated with, data breach litigation. While there is currently an exception for protected health information that is subject to HIPAA, and clinical trial regulations, as currently written, the CCPA may impact our business activities. There continues to be uncertainty surrounding the enforcement and implementation of the CCPA, exemplifying the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Further, as of January 1, 2023, the California Privacy Rights Act ("CPRA"), amended the CCPA and created additional obligations with respect to processing and storing personal information and sensitive personal information. The effects of the CCPA (as modified by the CPRA) are potentially significant and may require us to modify our data collection or processing practices and policies and to incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement and/or litigation.

Similar consumer privacy laws have passed or come into force in numerous U.S. states. Like the CCPA, these laws grant consumers rights in relation to their personal information and impose new obligations on regulated businesses, including, in some instances, broader data security requirements. In addition, federal and state legislators and regulators have signaled their intention to further regulate health and other sensitive information, and new and strengthened requirements relating to this information could impact our business. At the state level, some states have passed or proposed laws to specifically regulate health information. For example, Washington's My Health My Data Act, which comes into force in March 2024, requires regulated entities to obtain consent to collect health information, grants consumers certain rights, including to request deletion, and provides for robust enforcement mechanisms, including enforcement by the Washington state attorney-general and a private right of action for consumer claims. At the federal level, the FTC has used its authority over "unfair or deceptive acts or practices" to impose stringent requirements on the collection and disclosure of sensitive categories of personal information, including health information. Moreover, the FTC's expanded interpretation of a "breach" under its Health Breach Notification Rule could impose new disclosure obligations that would apply in the event of a qualifying breach.

We are increasingly dependent on information technology systems, and our systems and infrastructure face certain risks, including from cyber security incidents or compromises and data leakage, which in turn could lead to a determination that we have failed to comply with applicable data protection and cybersecurity regulations, resulting in a fine or regulatory enforcement action.

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, misuse, 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, misuse, and other events. Security threats, including cyber and other attacks are becoming increasingly sophisticated, frequent, and adaptive. For example, in February 2021 we experienced an incident in which personnel information was inadvertently made available to company employees broadly. In response, we made the required reports to regulatory authorities and took remedial measures to secure such information systems from unauthorized and unintentional access. 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 or adequately address breakdowns, breaches in our systems compromises or other 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. 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. Some cyber security incidents may be very difficult to prevent or adequately address.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security incidents, which could result in a material disruption of our product development programs, a determination that we have failed to comply with applicable data protection and cybersecurity regulations, resulting in a fine, 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, cyberattacks and unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The risk of cyber incidents could also be increased by cyberwarfare in connection with the ongoing conflict between Russia and Ukraine and the conflict in Israel, including potential proliferation of malware into systems unrelated to such conflicts. 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 recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and will rely on third parties to conduct future clinical trials, and similar events relating to their computer systems could also have similar consequences to our business. To the extent that any disruption or security incident were to result in unauthorized disclosure of, or access to, or accidental or unlawful loss, destruction, alteration of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including fines for failure to comply with applicable data protection and cybersecurity regulations, and the development of our product candidates could be delayed.

The use of new and evolving technologies, such as artificial intelligence ("AI"), in our offerings may present risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information, and personal data.

We continue to build and integrate AI into our offerings, and this innovation presents risks and challenges that could affect its adoption, and therefore our business. The use of certain artificial intelligence technology can give rise to intellectual property risks, including compromises to proprietary intellectual property and intellectual property infringement. Additionally, we expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area, such as for example in the U.S., the Colorado AI Act which will go into effect on February 1, 2026, and California's AB 2013, which requires generative AI developers to post information on their websites regarding the data used to train their AI systems. Additionally, in Europe the EU's Artificial Intelligence Act ("AI Act") — the world's first comprehensive AI law — entered into force on August 1, 2024 and, with some exceptions, will begin to apply as of August 2, 2026. This legislation imposes significant obligations on providers and deployers of high-risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. If we develop or deploy AI systems that are governed by the AI Act, we may be required to adopt higher standards of data quality, transparency, and human oversight, and adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements. The rapid evolution of AI will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that AI is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. Our vendors may in turn incorporate AI tools into their own offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information, and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

Our current operations are mainly concentrated in one location, 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 operational 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 relevant accounting standards, which may impact our reported financial situation and results;
- being 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 due to the location of our operations;
- restrictions imposed by local labor practices and laws of jurisdictions where we have employees on our business and operations, including unilateral cancellation or modification of contracts;
- rapid changes in global government, adverse market or macroeconomic conditions or market volatility resulting from global economic developments, political or civil unrest or instability, including due to war, international hostilities or terrorism (such as the ongoing conflict between Russia and Ukraine and the conflict in Israel), high inflation, future health 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.

If we were to experience any of the difficulties listed above, or any other difficulties, our international development activities and our overall financial condition may suffer and cause it to reduce or discontinue our international operations and market approval efforts.

Inadequate funding for the FDA, other government agencies, or comparable foreign regulatory authorities, or other disruptions to these agencies' operations, including policy, leadership and personnel changes could prevent new products 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.

Currently, federal agencies in the U.S. are operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted. 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 government agencies or comparable foreign regulatory authorities 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, other government agencies or comparable foreign regulatory authorities, including significant leadership, personnel and policy changes, 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 or other substantial disruption occurs, including as a result of reaching the debt ceiling, 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, government shutdown or other substantial disruption of other government agencies, such as the SEC, may also impact our business by delaying review of our public filings, which in turn could delay or frustrate our ability to access the public capital markets. Similar developments at regulators in other countries (including the EMA) could have similar impacts on our applications for marketing approval and on our business.

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, 2024, we had € 149,408,000 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 small amounts of interest income, if any. In 2022, some of our euro savings accounts required us to incur small amounts of interest expenses. In 2024 and 2023, we have generated interest income on our euro and U.S. dollar deposit accounts. 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, interest rates may be negative in the EU. 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 materialization of any of 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 our functional currency (i.e. 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" or "tax losses") in the Netherlands is currently limited and may be further limited. Under Dutch corporate income tax law, effective from January 1, 2022, tax losses may be carried forward indefinitely. However, the offset of losses will be limited in a given year against the first € 1.0 million of taxable profit. For taxable profit in excess of this amount, losses may only be offset up to 50% of this excess. As at December 31, 2024, we had a total of € 437.3 million tax loss carry-forwards available for offset against future taxable profits.

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, as well as 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.

The U.S. Congress, the Trump administration, or any new administration may make substantial changes to fiscal, tax, and other federal policies that may adversely affect our business.

In 2017, the U.S. Congress and the Trump administration made substantial changes to U.S. policies, which included comprehensive corporate and individual tax reform. In addition, the Trump administration called for significant changes to U.S. trade, healthcare, immigration and government regulatory policy. With the transition to the Biden administration in early 2021, changes to U. S. policy occurred and since the start of the Trump Administration in 2025, U.S. policy changes have been implemented at a rapid pace and additional changes are likely. Changes to U.S. policy implemented by the U.S. Congress, the Trump administration or any new administration have impacted and may in the future impact, among other things, the U.S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U.S. regulatory environment, inflation and other areas. Although we cannot predict the impact, if any, of these changes to our business, they could adversely affect our business. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them.

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 $ 0.56 per share at the close of the trading on May 11, 2022. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report, these factors include:

- the results of our preclinical studies and clinical trials;
- the presentation of data at industry conferences by us and/or our competitors;
- the responses to any of our INDs with the FDA and any of our clinical trial applications with the competent authorities of the EU Member States;
- any current or future preclinical studies 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;
- expiration or termination of licenses, research contracts or other collaboration agreements;
- the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;
- 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 U.S., the EU 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, including the impact of inflation and rising interest rates, and domestic or international political instability.

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. Historically, securities class action litigation has often been brought against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which could harm our business, operating results, or financial condition. 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 we are unable to maintain compliance with Nasdaq listing standards, our ordinary shares may be delisted from the Nasdaq Stock Market and you may face significant restrictions on the resale of your shares.

There can be no assurances that we will be able to maintain our Nasdaq listing in the future. For example, in May 2022, we received a notification from Nasdaq that the trading price of our ordinary shares did not meet the minimum bid price requirement of $ 1.00 per share for a period of 30 consecutive trading days. We were granted a 180-day compliance period to regain compliance by achieving a closing bid price of at least $ 1.00 per share for a minimum of 10 consecutive trading days. In October 2022, we transferred our listing from the Nasdaq Global Market to the Nasdaq Capital Market and received an additional 180-day compliance period, as contemplated by Nasdaq. On December 2, 2022, Nasdaq informed us that we had regained compliance with the minimum bid price rule. Nevertheless, share prices in biotech are volatile and there can be no assurances that we will be able to maintain our Nasdaq Capital Market listing in the future.

In the event we are unable to maintain compliance with the Nasdaq Capital Market listing standards and our ordinary shares are delisted from the exchange, it would, among other things, likely lead to a number of negative implications, including an adverse effect on the price of our ordinary shares, reduced liquidity in our ordinary shares, the loss of federal preemption of state securities laws, breach of covenants in agreements and greater difficulty in obtaining financing. In the event of a de-listing, we would take actions to restore our compliance with Nasdaq's listing requirements, but we can provide no assurance that any such action taken by us would allow our ordinary shares to become listed again, stabilize the market price or improve the liquidity of our ordinary shares, prevent our ordinary shares from dropping below the Nasdaq minimum bid price requirement in the future, or prevent future non-compliance with Nasdaq's listing requirements. If we cannot restore our compliance with Nasdaq's listing requirements, we would pursue eligibility for trading of these securities on other markets or exchanges, such as the OTCQB or OTCQX, which are unorganized, inter-dealer, over-the-counter markets which provides significantly less liquidity than the Nasdaq Capital Market or other national securities exchanges.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and trading price of our ordinary shares.

The global credit and financial markets have experienced extreme volatility and disruptions in the past several years, most recently due to the COVID-19 pandemic, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. We believe that the state of global economic conditions remain particularly volatile and uncertain, the impact of fiscal stimulus programs initiated by various governments in response to the pandemic and economic downturn and ongoing supply chain issues and inflationary pressures, but also due to recent and expected shifts in political, legislative and regulatory conditions concerning, among other matters, international trade and taxation, and that an uneven recovery or a renewed global downturn may negatively impact our ability to conduct clinical trials on the scale and timelines anticipated. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions, will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business or political environment or continued unpredictable and unstable market conditions. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflict, including the conflict between Russia and Ukraine and the conflict in Israel, terrorism or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the conflict in Ukraine, may also adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. If the current equity and credit markets deteriorate, it may make obtaining any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget. To the extent that our profitability and strategies are negatively affected by downturns or volatility in general economic conditions, our business and results of operations may be materially adversely affected.

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, or publish inaccurate or unfavorable research about our business, our share price would likely decline. In addition, 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 our ordinary shares subject to outstanding options, issuable upon vesting of outstanding restricted stock units, or reserved for future issuance under our equity incentive plans 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.

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

We may seek additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans 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.

In addition, such indebtedness also results in increased fixed payment obligations and 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. Also, 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.

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

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. As a result, capital appreciation, if any, of our ordinary shares will be the sole source of gain for our shareholders for the foreseeable future.

We have been a listed company since September 2014. Complying with all 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 substantial 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 ("DCGC") for example, are expected to result in ongoing increases in our legal, audit and financial compliance costs. The Exchange Act requires, among other things, that we file certain periodic reports with respect to our business and financial condition. We must also comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. Complying with Section 404 is 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, senior management 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 board is 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. 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.

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 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 2024 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 intend to provide the information necessary for U.S. holders to make a “qualified electing fund,” (“QEF”) election if we are treated as a PFIC for any taxable year.

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 both executive and non-executive members of our board under Dutch law are different than under the laws of some U.S. jurisdictions. In the performance of their duties, our board is 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.

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 U.S.; or

- a majority of our "executive officers" and a majority of our directors may not be U.S. citizens or residents, more than 50% of our assets cannot be located in the U.S. and our business must be administered principally outside the U.S..

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, would make some activities more time consuming and costly and could necessitate the hiring of additional accounting, financial and legal staff. 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 board.

We currently report our financial results under IFRS, which differ in certain significant respects 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 (members of) of our board.

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

- the authorization of a class of preferred shares that may be issued to a protection foundation to which we have granted a perpetual and repeatedly exercisable call option;
- a provision that our 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 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 board that has been approved by our board.

In addition, our board needs to act in the interest of our Company, 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 board is responsible for determining 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 board may also use its 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.

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 DCGC. The DCGC contains both principles and best practice provisions that regulate the internal affairs of the board and the relation between the 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 Capital 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.

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 board and senior management 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 the Company 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 the Company or any of our 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 ('*Wetboek van Burgerlijke Rechtsvordering*').

Based on the lack of a treaty as described above, U.S. investors may not be able to enforce against us or our 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.

Item 4: Information on the Company

A. History and Development of the Company

We are a biotechnology company dedicated to changing lives by developing RNA therapies for severe rare and common diseases. We focus on advancing our proprietary Axiomer RNA-editing platform technology.

We were 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 Nasdaq. They are currently trading on Nasdaq Capital Market under the ticker symbol "PRQR". As of December 31, 2024, we had raised € 518.0 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, private lenders and government institutions supporting our programs, including from FFB, RSRT 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 is registered with the Dutch Trade Register of the Chamber of Commerce ('*handelsregister van de Kamer van Koophandel')* under number 54600790. Our corporate seat is in Leiden, the Netherlands. The address of our headquarters and registered office is Zernikedreef 9, 2333 CK Leiden, the Netherlands, telephone number +31 88 166 7000. Our U.S. 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 Sarah Kiely, 245 Main Street, Cambridge, MA 02142, USA.

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 website is www.sec.gov. We maintain a corporate website at www.ProQR.com. Information found on, or accessible through, our website is not incorporated by reference into and should not be considered a part of this Annual Report, and the reference to our website in this Annual Report is an inactive textual reference only.

B. Business Overview

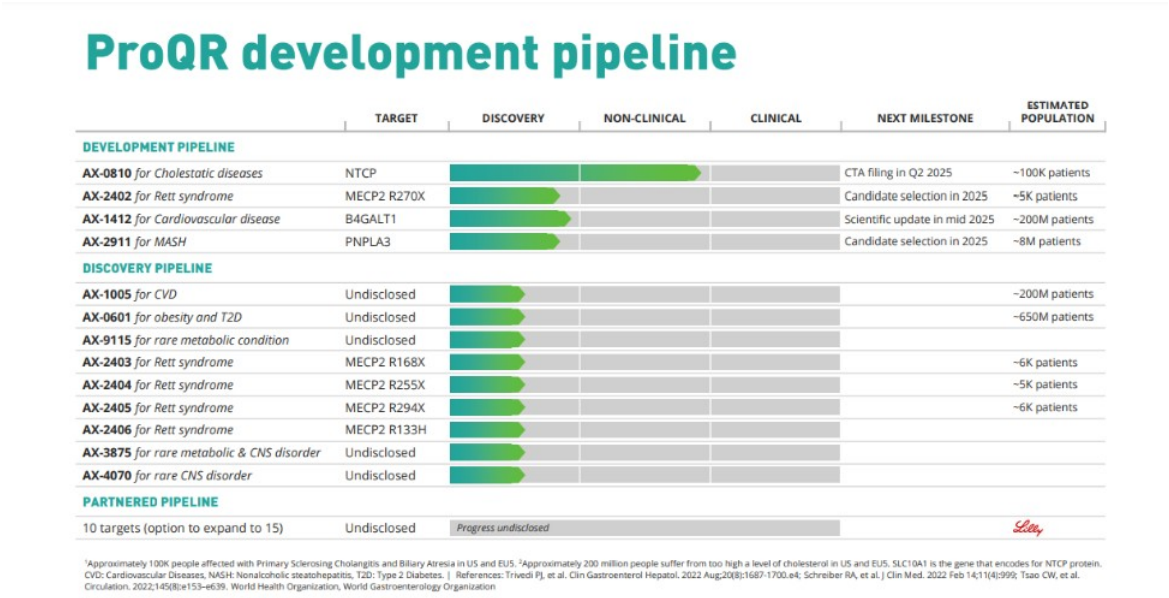
We are a biotechnology company at the forefront of RNA editing innovation, pioneering transformative solutions for diseases with significant unmet medical needs. To achieve this, we are advancing our proprietary Axiomer RNA-editing platform technology developed to harness ADAR to enable precise RNA editing. Our technology has the potential to create a new class of medicines with applicability to a broad range of therapeutic areas. Using our deep RNA expertise and our strong intellectual property position, we are advancing a platform to develop these RNA editing therapeutics, which we call EONs, for a variety of human diseases.

Axiomer uses EONs to mediate single nucleotide changes to RNA with high specificity and durability. Axiomer EONs are designed to recruit and direct endogenously expressed ADARs to change an Adenosine (A) to an Inosine (I) in the RNA – an Inosine is translated as a Guanosine (G). This approach can be used to correct an RNA with a disease-causing mutation back to a normal (wild type) RNA, modulate protein expression, or alter a protein so that it will have a new function that helps prevent or treat disease.

Since discovering the Axiomer RNA editing platform technology in 2014, we have established a leading intellectual property estate in the ADAR editing space, defined the design ground rules, and optimized chemistries for therapeutic use.

Our research and development strategy focuses on the use of our Axiomer platform to develop novel RNA editing therapeutics to address diseases with high unmet medical need. We are initially focused on diseases originating in the liver and in the CNS where research into human genetics has shown us that changing the RNA or correcting pathogenic mutations via A-to-I editing may lead to a benefit for patients. Our robust pipeline is strategically centered on addressing high unmet needs in liver and CNS diseases, leveraging validated biomarkers and well-defined clinical endpoints. The lead program we are advancing is AX-0810 for Cholestatic Diseases targeting NTCP. With funding from the RSRT, we are also advancing AX-2402 targeting Methyl CpG binding protein 2 ("MECP2") mutations for Rett Syndrome, a severe neurodevelopmental disorder. Other pipeline programs include AX-1412 targeting the B4GALT1 gene for Cardiovascular Diseases ("CVDs"), AX-2911 targeting PNPLA3 for Metabolic Dysfunction-Associated Steatohepatitis ("MASH"), as well as a number of additional earlier-stage pipeline programs.

In addition to advancing our wholly-owned pipeline programs, we entered into a global licensing and research collaboration with Lilly in September 2021 where our Axiomer RNA editing platform is being used to progress new drug targets for disorders toward clinical development and commercialization. Initially focused on five targets, the partnership was expanded to ten targets in December 2022, with an option for further expansion to fifteen targets.



We believe the platform has significant potential to yield many additional therapeutic candidates. Thus, we continuously evaluate further opportunities for beneficial collaborations or strategic partnerships to efficiently advance product candidates with the goal of bringing medicines to patients.

Our Strategy

We are advancing Axiomer as a platform to develop a new class of innovative medicines based on ADAR RNA editing, which we believe has the potential to treat a broad range of diseases that currently lack adequate treatment options. Our novel and proprietary RNA editing platform technology, known as Axiomer, use oligonucleotides to edit single nucleotides in the RNA. We believe the Axiomer technology may be applicable to thousands of disease-causing mutations by correcting RNA in genetic diseases. Beyond mutation correction, Axiomer also has the potential to address unmet medical needs in common conditions, by modulating protein expression or altering a protein so that it will have a new function to help prevent or treat diseases. We intend to continue to optimize our platform as we advance to clinical stage and beyond. Key elements of our strategy include:

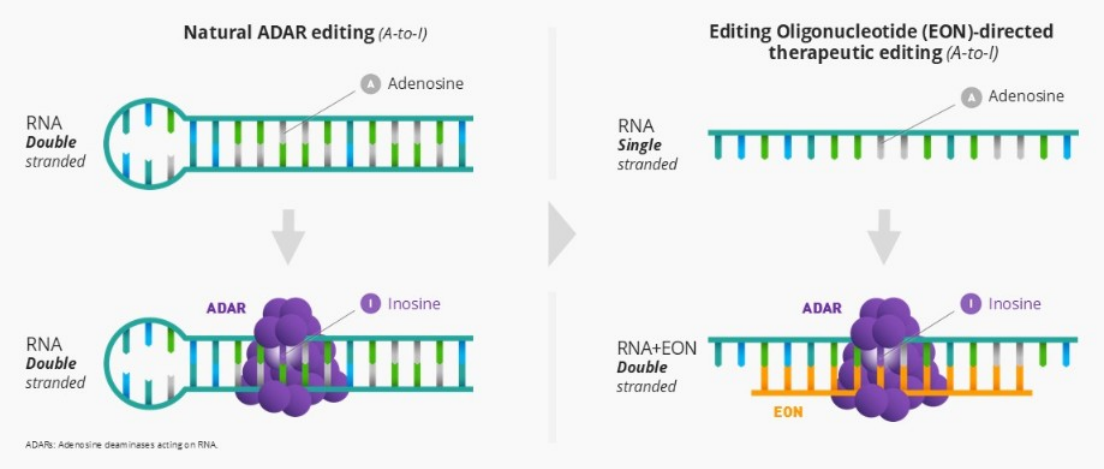
- Pipeline: We intend to use this platform to develop novel therapies initially for targets related to liver- and CNS-originating diseases, and beyond. With our Axiomer RNA-editing technology platform, we are advancing AX-0810 for Cholestatic Diseases targeting NTCP as our lead program, as well as AX-2402 targeting MECP2 for Rett Syndrome, AX-1412 for CVDs targeting B4GALT1, and AX-2911 targeting PNPLA3 for MASH as our other pipeline programs.
- Partnerships: We continue to validate and create value for this platform by selectively pursuing additional licensing, partnering, and other strategic relationships, such as our partnerships with Lilly, and the RSRT.

We seek to maximize the value of our pipeline by retaining development and commercialization rights to those product candidates, indications and geographies that we believe we can independently develop, seek approval for, and commercialize on our own. Beyond this, for other product candidates, such as those for more prevalent indications, and other geographies, we plan to selectively and opportunistically seek potential partnerships following early-stage clinical proof of concept.

Our Novel Axiomer RNA Editing Technology Platform

Antisense oligonucleotides, ("AONs"), have been used as therapeutics for decades. Our Axiomer RNA editing technology is based on oligonucleotides that are EONs, designed to recruit endogenous, naturally occurring ADAR enzymes as shown in Figure 1a, to make single adenosine-to-inosine (A-to-I) changes in the RNA in a highly specific and targeted manner, as shown in Figure 1b.

Figure 1a (left): RNA editing is a naturally occurring process whereby ADARs perform A to I editing.
Figure 1b (right): ProQR's Axiomer RNA editing technology platform uses EONs to recruit and direct endogenously expressed ADARs to edit an A to an I in the RNA, which is then translated as a G, allowing highly specific editing.



In vitro and *in vivo* work indicates that our EONs are generally applicable for the correction of RNA G-to-A mutations. The technology is also designed to modulate protein expression or alter proteins to provide a new function to help prevent or treat disease. With this applicability, we believe Axiomer has the potential to address hundreds of genetic and non-genetic diseases.

Across a range of targets, we have shown both in vitro and in vivo platform proof-of-concept for our Axiomer RNA editing technology platform, in cell models, organoids, and animal models, including relevant higher order species.

Our Pipeline Programs

AX-0810 for Cholestatic Diseases targeting NTCP

Cholestatic Diseases overview
Cholestatic Diseases are caused by a toxic buildup of bile acids in the liver due to bile duct dysfunction, which causes liver cell damage. The consequences of these disorders can be devastating and significantly impact a person's quality of life, including pruritus, dry skin, fatigue, pain, weight loss, and many others. Without treatment, the damage progresses through various stages, from fibrosis to cirrhosis, ultimately leading to liver failure and an increased risk of liver cancer. Liver transplants are often necessary for primary sclerosing cholangitis ("PSC") and biliary atresia ("BA"), two forms of Cholestatic Diseases with high unmet medical needs.

PSC is a condition that causes inflammation and is typically diagnosed in people aged 30 to 40, more commonly affecting men (66%). It is estimated that 80,000 people in North America and Europe have PSC, with a prevalence of 1 to 9 individuals per 100,000. This condition causes fibrosis and sclerosis of bile ducts, leading to a toxic buildup of bile acids in the liver.

BA is a pediatric condition that affects newborns, resulting from the absence or defect of bile ducts. This condition causes harmful bile acids to accumulate in the liver, leading to rapid progression to cirrhosis early in life. It is estimated that 20,000 individuals in North America and Europe have BA, with a prevalence of 1 in 10,000 to 15,000 births in the western world.

Limitations of the Current Treatment Landscape
Currently, there are no approved drugs for treating PSC and BA. For PSC, liver transplantation is the only treatment option with evidence to extend survival. However, PSC can return in 20 to 40% of patients who undergo liver transplantation, and the median survival without a transplant is only 21 years. Surgery in the first weeks of life for BA is the gold standard treatment. However, most patients who receive this surgery will still require a liver transplant early in life.

AX-0810 for Cholestatic Diseases targeting NTCP
The liver cells mainly obtain bile acids from the enterohepatic reuptake cycle. The process is primarily carried out by a transporter called NTCP, which takes bile acids from the portal circulation to the liver. Studies show that inhibiting NTCP can improve liver function by reducing the levels of toxic bile acids, improving liver damage markers (fibrosis, cholangiocyte proliferation, Alkaline phosphatase or ALP, alanine transaminase or ALT), and lowering inflammation biomarkers ("cytokines").

AX-0810, our Axiomer-targeted RNA editing oligonucleotide, aims to reduce the reuptake of bile acids in the liver by inhibiting NTCP function. Variants in NTCP that change its capacity to recycle bile acid into the liver naturally occur in some people without causing any symptoms associated with cholestasis. This finding suggests that our approach is safe and may reduce the accumulation of toxic bile acids in the liver. Moreover, such variants in NTCP also promote the elimination of bile acids from the body by increasing their excretion in the feces and urine, a process called sulfation of bile acids, which enhances their solubility and reduces their absorption in the intestines.

Populations in human genetics research with naturally occurring NTCP variants exhibit reduced bile acid uptake in the liver, supporting NTCP modulation as a therapeutic strategy. EON-mediated editing of NTCP introduces the Q68R variant, which disrupts sodium-binding within the NTCP channel, selectively reducing bile acids reuptake without affecting other NTCP function.

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Animal models, including humanized mice and non-human primates ("NHPs") have shown that NTCP modulation through EON-mediated editing leads to hepatoprotective effects, such as reduced bile acids accumulation and improved liver biomarkers, as shown in **Figure 2**.

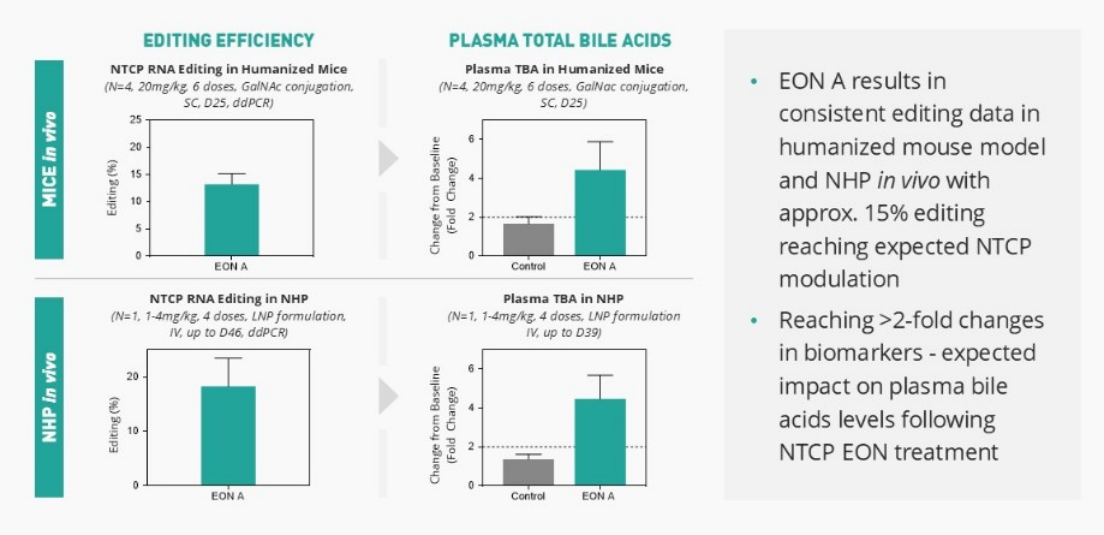

Figure 2. EON-mediated editing exhibits consistent editing of NTCP and favorable impact on biomarker in vivo.

As shown in **Figure 3**, *in vivo* studies demonstrate that NTCP modulation through EON-mediated editing results in an increase in conjugated bile acids within the plasma, confirming the specificity and efficacy of this therapeutic approach. Additionally, a bile acid challenge assay using Tauro-urso-deoxycholic acid ("TUDCA") in NHPs demonstrated reduced clearance of bile acids following treatment with Axiomer EON. This outcome, marked by a statistically significant decrease in bile acid elimination rates, underscores the ability of NTCP editing to modulate bile acid effectively.

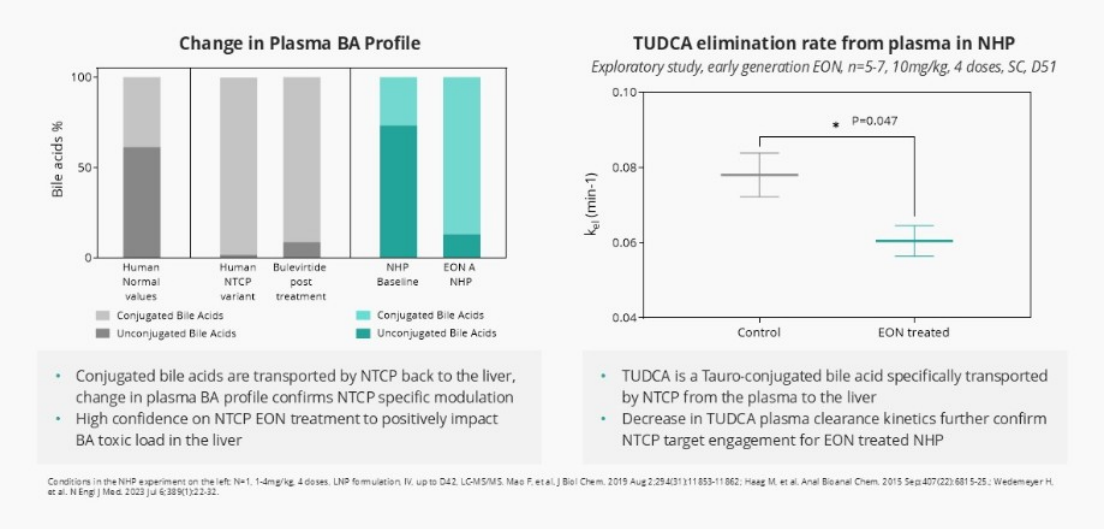

Figure 3. Proof of concept in NHP demonstrated via bile acid profile and TUDCA elimination.

We believe these findings have established a robust preclinical proof of concept for AX-0810, further supporting its clinical translation. AX-0810 has been optimized for enhanced potency and stability, with regulatory-enabling activities underway. A first-in-human clinical trial is scheduled for 2025, subject to regulatory authorization, featuring a placebo-controlled, single- and multiple-dose design across healthy volunteers. The study aims to measure a twofold increase in plasma bile acid levels and a favorable shift in bile acid profiles. We expect to share topline data from this trial in Q4 2025.

Based on its mechanism of action, we believe AX-0810 may have the potential to modify the course of Cholestatic Diseases, delay or prevent complications such as cirrhosis and liver failure, and alleviate associated symptoms. Furthermore, NTCP and bile acids play a pivotal role in a broad spectrum of diseases, providing substantial opportunities to extend beyond Cholestatic Diseases. For example, NTCP modulation may hold significant potential for addressing certain metabolic disorders such as obesity and CNS diseases, highlighting our approach as a potentially transformative solution across multiple therapeutic domains.

AX-2402 for Rett Syndrome targeting MECP2

Rett Syndrome overview
Rett Syndrome is a rare and debilitating neurodevelopmental disorder, affecting approximately 350,000 people worldwide, predominantly girls. Rett Syndrome is characterized by apparently normal psychomotor development during the first six to 18 months after birth, followed by a period of developmental stagnation, then a regression in language and motor skills, followed by long-term relative stability. During the phase of regression, affected patients develop repetitive, stereotypic hand movements that replace purposeful hand use. Additional symptoms include gait ataxia and apraxia, seizures, tremors, episodic apnea and/or hyperpnea, gastrointestinal issues, scoliosis and musculoskeletal problems, anxiety and sleep issues and bruxism.

Mutations in the MECP2 gene are the primary cause of the disorder. Located on the X chromosome, MECP2 encodes the methyl-CpG-binding protein 2, which plays a critical role in regulating gene expression and maintaining normal brain development and function. In individuals with Rett Syndrome, mutations in MECP2 disrupt the function of this protein, leading to abnormal gene expression patterns and impairments in neural circuitry.

Limitations of the Current Treatment Landscape
Currently, there are no approved treatments for Rett Syndrome. Traditional treatments involve multidisciplinary care, including physical therapy, occupational therapy, speech therapy, and medications to address specific symptoms such as seizures, breathing irregularities, and gastrointestinal issues. Supportive measures, such as nutritional management and assistive devices, also play a significant role in maintaining health and mobility. In recent years, however, the treatment landscape has evolved with promising advances in targeted therapies, including our RNA editing approach.

AX-2402 for Rett Syndrome targeting MECP2
AX-2402 is being developed for individuals with Rett syndrome who have the R270X mutation in MECP2 gene, and is based on ProQR's proprietary Axiomer RNA editing platform. The AX-2402 program utilizes EONs to correct the R270X nonsense mutation, restoring physiological MECP2 expression levels. We believe Axiomer EONs can target many mutations beyond R270X that collectively impact a large segment of the Rett population.

As the data show in **Figure 4**, preclinical data demonstrated 80% editing efficiency in patient-derived cells carrying the R270X mutation. Typically, the R270X mutation introduces a premature termination codon ("PTC"), which triggers nonsense-mediated decay ("NMD") and reduces MECP2 mRNA levels. Axiomer's editing approach recodes the PTC and also inhibits NMD, resulting in increased MECP2 RNA levels and increased R270W MECP2 protein levels.

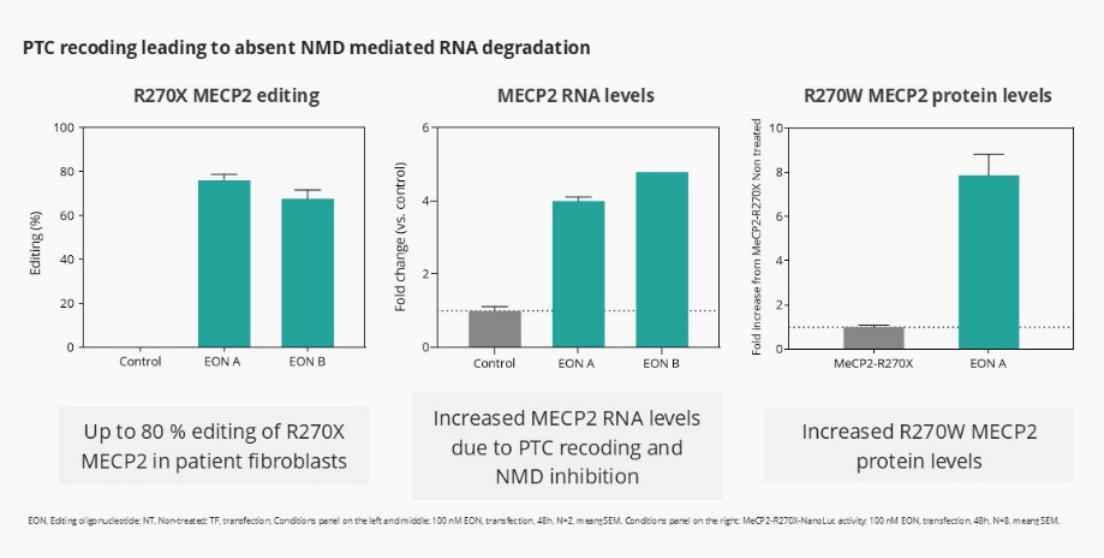

Figure 4. *In vitro* EON mediated editing of MECP2 in patient cells increases mRNA levels and restores protein expression supporting the potential of AX-2402 for Rett Syndrome.

In December 2024, we announced an expansion of our partnership with the RSRT. Building on the initial $ 1.0 million research grant announced in January 2024, the expanded partnership includes an additional $8.2 million in funding from the RSRT, for a total of $ 9.2 million. The funding will support the advancement of AX-2402 into clinical trials. Lead EON optimization is currently ongoing with the objective to select a clinical candidate for AX-2402 in 2025, and initiate clinical trial in 2026, with topline data readout anticipated in 2026.

AX-1412 for Cardiovascular Disease targeting B4GALT1

Cardiovascular Disease overview
CVDs are a group of health conditions that affect the heart and blood vessels, such as atherosclerosis which can lead to severe problems like heart attacks, heart failure, and stroke. The World Health Organization (“WHO”) has identified unhealthy diet, physical inactivity, tobacco use, and excessive alcohol consumption as major behavioral risk factors for heart disease and stroke, increasing intermediate risk factors including but not limited to high blood pressure, cholesterol, glucose levels, and obesity.

CVDs remain the leading cause of death globally, accounting for approximately 18 million deaths annually, or 32% of all global deaths, according to a report by the WHO in 2021. In the United States, the American Heart Association estimates that by 2035, more than 130 million adults will have some form of CVD.

Current Treatment Landscape and Limitations
CVD treatment involves taking medications to lower cholesterol and blood pressure levels. Current treatments including statins, ezetimibe, and PCSK9 inhibitors primarily are used to lower LDL cholesterol levels. Other treatments, such as ANGPTL3 inhibitors, decrease the residual risk of heart disease in patients with high LDL cholesterol levels. Despite advances in therapeutic options, a substantial unmet medical need persists. For example, less than 35% of Americans with high LDL cholesterol levels reach their target levels recommended by guidelines. CVD events still occur even when LDL cholesterol levels meet clinical goals. Many patients also struggle to continue taking their medications long-term, with less than 50% of patients taking their LDL-lowering medicines 2 years after a CVD event. Additionally, 5 to 10% of patients cannot tolerate high doses of statins, primarily due to muscle aches. This underscores the need for innovative approaches, such as our RNA editing therapeutic strategy.

AX-1412 for Cardiovascular Disease targeting B4GALT1
AX-1412 represents a potential targeted approach to RNA editing of B4GALT1 that leads to a promising strategy for protecting against CVDs by simultaneously lowering levels of LDL-c and fibrinogen. Recent gene-based analysis has shown that rare protective variants changing protein activity and predicted deleterious missense variants in B4GALT1 are associated with a decreased risk of coronary artery disease. Additionally, a particular missense variant (p.Asn352Ser) in the beta-1,4-galactosyltransferase 1 B4GALT1 gene is prevalent in the Amish population and associated with lower levels of LDL-c and CVDs, and a 36% reduction in coronary artery disease risk.

The beneficial effects of these genetic variations are due to the hypo-galactosylation of apolipoprotein B100 and fibrinogen, which are known to be independent drivers of an increased risk of CVDs, as well as immunoglobulin G and transferrin. However, it's important to note that studies have shown that B4GALT1 knockdown can lead to semi-lethality and severe developmental abnormalities in mice models and therefore we believe B4GALT1 inhibition is not a feasible therapeutic approach for this purpose.

Although there are several approaches to lowering the risks of CVDs, including reducing LDL-c and ApoB levels, reducing fibrinogen levels may offer additional benefits to patients with unmet medical needs in this large population. Fibrinogen reduction can be used either as a stand-alone therapy or an adjunct therapy to other treatments.

We are developing Axiomer targeted RNA EON AX-1412 to address CVD by editing B4GALT1. RNA editing to a protective variant of B4GALT1 can have positive effect on CVDs risk factors by leading to hypo-galactosylation of apolipoprotein B100 and fibrinogen. Based on its mechanism of action, we believe that AX-1412 is a novel and unique approach to address CVD by lowering LDL-C and fibrinogen levels ultimately leading to a reduced residual risk in CVDs.

Preclinical studies using an industry standard mouse model, which closely mimics human lipid metabolism, have demonstrated the ability of AX-1412 to edit B4GALT1, with biomarker improvements, including significant reductions in total cholesterol, LDL cholesterol, fibrinogen, and ApoB levels. While initial studies employed lipid nanoparticle (LNP) delivery systems, further work to optimize for GalNAc conjugated delivery is underway to align with the target product profile for CVD conditions. We expect to provide an update on GalNAc optimization of AX-1412 in mid-2025.

Assuming regulatory authorization to conduct clinical development, we intend to advance AX-1412 targeting B4GALT1 to early clinical proof of concept stage, then following successful demonstration of clinical proof of concept following an initial trial, we would seek to partner this program.

AX-2911 for Metabolic Dysfunction-Associated Steatohepatitis targeting PNPLA3

MASH overview

MASH is a progressive and highly prevalent liver disease that poses a severe global health challenge. Characterized by liver inflammation, fibrosis and fat accumulation, MASH can lead to life-threatening complications, including cirrhosis and hepatocellular carcinoma.

Current Treatment Landscape and Limitations

Despite its widespread impact, currently there are no approved treatment therapies specifically for MASH, and management primarily relies on lifestyle modifications such as weight loss, dietary changes, and exercise, alongside treatments for associated conditions like diabetes and dyslipidemia. Investigational therapies including FXR agonists, PPAR agonists, and antifibrotic agents, are in development, but have yet to achieve regulatory approval. This lack of effective treatments highlights the significant unmet medical need, reinforcing the importance of innovative approaches like AX-2911 to address the root causes of MASH.

AX-2911 for MASH targeting PNPLA3

The AX-2911 program uses the Axiomer editing platform to address MASH by targeting the PNPLA2 (patatin-like phospholipase domain containing 3) gene, which has been strongly implicated in the pathogenesis of MASH, particularly the I148M variant, which is present in 20-60% of affected individuals and disrupts lipid metabolism in the liver. By editing the PNPLA3 I148M variant to a 148V (valine) variant, AX-2911 aims to restore wild-type protein functionality and address the root cause of MASH.

Preclinical studies of AX-2911 have demonstrated restoration of normal lipid metabolism, over 50% editing efficiency, and reduction in lipid droplet size, providing validation of its therapeutic potential. We intend to commence development activities for AX-2911 in 2025, including to select a development candidate for this program and initiate clinical trial in 2026, with topline data readout anticipated in 2026.

Our Earlier-Stage/Discovery Programs

We have multiple other early-stage research programs ongoing that target additional diseases with our Axiomer EON approach, including AX-1005 for undisclosed targets in CVD, AX-0601 for obesity and Type 2 diabetes, AX-9115 for rare metabolic conditions, additional programs in Rett Syndrome, additional CNS programs, and multiple other unnamed targets and programs in our discovery pipeline.

Our Partnership Strategy

Our business strategy is to develop and ultimately commercialize a broad pipeline of RNA therapies based on our Axiomer RNA editing platform technology. We are initially focused on developing an internal pipeline and we believe there is broad applicability of the platform and as part of the strategy to advance Axiomer, we have entered into, and expect to enter into additional collaboration and licensing agreements as a means of obtaining funding and capabilities to advance programs based on Axiomer.

A global licensing and research collaboration with Lilly focuses on the discovery, development, and commercialization of potential new medicines for genetic disorders using our Axiomer RNA editing technology with a focus on CNS and PNS. The partnership, formed in 2021, initially focused on up to five targets. In December 2022, the partnership was expanded to up to ten targets, with an option for an additional five targets. Under the terms of the agreements, we received $ 125.0 million upfront from Lilly and would be paid an additional $ 50.0 million if Lilly exercises the option for five additional targets. We are also eligible to receive up to approximately $ 3.75 billion in milestones, as well as royalties on potential product sales.

In December 2024, we announced an expansion of our partnership with the RSRT. Building on the initial $ 1.0 million research grant announced in January 2024, the expanded partnership includes an additional $ 8.2 million in funding from the RSRT, for a total of $ 9.2 million. The funding will support the advancement of AX-2402 targeting MECP2 for Rett Syndrome into clinical trials.

We believe the Axiomer platform holds significant further potential for strategic transactions.

Ophthalmology Assets

In August 2022, we made the decision to exclusively focus our strategy on the advancement of our Axiomer RNA editing technology and to partner our ophthalmology programs. In December 2023, we announced that we had completed a transaction divesting the late stage ophthalmic assets sepofarsen and ultevursen to Théa who will continue the development of these therapies for patients with LCA10 and Usher Syndrome. Under the terms of the agreement, ProQR received an initial payment of € 8.0 million and may be eligible for up to € 165.0 million in further development, regulatory, and commercial earn-out payments upon related achieved milestones, as well as double-digit royalties based on commercial sales in the U.S. and EU. In December 2024, Sepul Bio, a business unit of Théa, announced the first clinical participant was dosed in LUNA, a Phase 2b clinical study of ultevursen for Usher Syndrome (Type 2a gene).

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 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 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.

Human Capital Resources

We believe in passion and commitment and have built a strong team of ProQRians from all walks of life and over 24 different nationalities, who are up to the challenge and committed to make a difference for the patients we serve. We actively create a caring atmosphere, 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 all 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 us 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, we 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, also known as CROs, are selected based on their expertise, quality and accreditations for laboratory animal care and welfare. CRO facilities are audited by us prior to contracting to ensure that the housing, husbandry and welfare of animals complies with the highest international standards. Personnel responsible for housing, husbandry and the care of animals must have received adequate and relevant documented education.

Manufacturing and Supply

We do not own or operate GxP manufacturing facilities to produce clinical or commercial drug product. Historically manufacture of drug substance and drug product for clinical use was outsourced to approved vendors under service agreements.

Currently, manufacture of small scale non-GxP drug substance and drug product batches to support the discovery and initial pre-clinical phase of the Axiomer platform are manufactured in our in-house laboratories. As the portfolio progresses, larger scale batches and those intended for clinical use will be manufactured at approved vendors under phase-appropriate service agreements.

Our vendor management strategy will ensure that we have sufficient capacity to meet the demands of the portfolio now and in the future. The contract manufacturing organizations selected to manufacture our product candidates under cGMP conditions are assessed and audited to ensure that they meet the extensive regulations in areas including technical expertise, facility and equipment management, documentation, data integrity, manufacturing processes and controls, personnel, quality control and quality assurance.

Intellectual Property

We strive to protect our technology platform 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 Axiomer Program

ProQR's Axiomer RNA editing technology platform uses EONs to recruit and direct endogenously expressed ADARs to edit an A to an I in the RNA, which is then translated as a G, allowing highly specific editing. Since 2014, when the first inventions were conceived at ProQR, we have been filing patent applications for intellectual property rights related to our Axiomer platform. Many of these claim EONs with specific features that allow them to guide recruitment of endogenous ADAR for the purpose of therapeutic RNA editing, without the need of ADAR overexpression or artificial ADAR recruitment systems. Further to that, we have grown a strong intellectual property position for EONs that can bring about RNA editing in RNA to yield a gain-of-function alteration or a loss-of-function alteration in a wide variety of therapeutic areas. We rely, and continue to rely, on intellectual property rights that are fully owned by us, or that have been co-filed with our research collaborators.

With regard to our Axiomer program, we filed the following international patent applications from 2015 to 20, several of which were continued in national and regional patent applications after the respective international phases.

PCT/EP2015/080347 – Granted in Australia (AU 2022201266), Brazil (BR 112017011510-7), Canada (CA 2,968,336), China (ZL 201580069286.1), Europe (EP 3234134 B1; opposition/appeal), Israel (IL 252386), India (IN 452659), Japan (JP 6718872), New Zealand (NZ 732182), South Africa (ZA 2017/03464) and the U.S. (US 10,676,737; US 11,781,134). Pending in Europe (divisional application) and the U.S. (continuation application). The term of any patents resulting from these applications would be expected to extend to at least 2035.

PCT/EP2017/065467 – Granted in Australia (AU 2017281497), Israel (IL 263332), Japan (JP 7074345), South Korea (KR 10-2418185) and the U.S. (US 10,988,763; US 11,649,454; US 12,018,257). Pending in Canada, China, Europe, New Zealand, and the U.S. (continuation application). The term of any patents resulting from these applications would be expected to extend to at least between 2037.

PCT/EP2017/071912 – Granted in China (CN 110352244 B), Europe (EP 3507366 B1; opposition/appeal), Japan (JP 2019-511856), New Zealand (NZ 751483), South Korea (KR 10-2501980), South Africa (ZA 2019/01016) and the U.S. (US 10,941,402; US 11,851,656; US 12,203,072). Allowed in Australia (pending opposition) and Israel. Pending in Canada, India, and the U.S. (continuation application). The term of any patents resulting from these applications would be expected to extend to at least between 2037.

PCT/EP2018/051202 – Granted in the U.S. (US 11,274,300). Pending in Europe. The term of a patent resulting from this application would be expected to extend to at least between 2038.

PCT/EP2019/062163 – Pending in Australia, Canada, Europe, Japan, New Zealand, and the U.S. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2039.

PCT/EP2020/051931 – Pending in Australia, Europe, New Zealand, and the U.S. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2040.

PCT/EP2020/053283 – Pending in Australia, Canada, Europe, Israel, New Zealand, and the U.S. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2040.

PCT/EP2020/059369 – Pending in Australia, Canada, China, Europe, Israel, Japan, New Zealand, and the U.S. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2040.

PCT/EP2020/060291 – Pending in Australia, Canada, Europe, Israel, New Zealand, and the U.S. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2040.

PCT/US2020/037580 – Granted in South Africa (ZA 2021/09497). Allowed in China. Pending in Australia, Canada, Europe, Israel, India, Japan, New Zealand, and the U.S. We filed this application together with The Regents of the University of California as a co-applicant. In the Axiomer program we are working together with Dr. Peter Beal of the University of California, Davis, CA, USA. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2040.

PCT/EP2020/087767 – Pending in Australia, Canada, Europe, Japan, and the U.S. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2040.

PCT/EP2021/070535 – Pending in Australia, Canada, Europe, Japan, and the U.S. The term of any patents resulting from these applications, if issued, would be expected to extend to at least 2041.

PCT/EP2023/053503 – Pending in Europe and the U.S. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2043.

PCT/EP2023/069612 – Pending in Australia, Canada, Europe, Japan, New Zealand, and the U.S. We filed this application together with The Regents of the University of California as a co-applicant. In the Axiomer program we are working together with Dr. Peter Beal of the University of California, Davis, CA, USA. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2043.

PCT/EP2023/069609 – Pending in Europe and the U.S. We filed this application together with The Regents of the University of California but all rights have been assigned to us. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2043.

PCT/EP2023/079290 – PCT pending. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2043.

PCT/EP2023/082797 – PCT pending. Co-pending in (non-PCT states) Taiwan and Argentina. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2043

PCT/EP2023/084865 – PCT pending. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2043

PCT/EP2023/083678 – PCT pending. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2043

PCT/EP2024/051278 – PCT pending. We filed this application together with the Freie Universität Berlin (FUB) as a co-applicant. In the Axiomer program we are working together with Dr. Alexander Weng of the FUB. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2044

PCT/EP2024/054190 – PCT pending. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2044.

PCT/US2024/021210 – PCT pending. Co-pending in (non-PCT states) Taiwan and Argentina. We filed this application together with Eli Lilly & Company as co-applicant, with whom we are working together under the Lilly licensing and research collaboration agreement, as amended in 2022. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2044.

PCT/EP2024/057800 – PCT pending. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2044.

PCT/EP2024/058159 – PCT pending. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2044.

PCT/EP2024/066520 – PCT pending. Co-pending in (non-PCT states) Taiwan and Argentina. The term of any patents resulting from this application, if issued, would be expected to extend to at least 2044.

Patent Rights Relating to Our Trident Program

With regard to our TRIDENT program, we filed an international patent application (PCT/US2019/024282) in 2019 directed to AONs that are applicable for nucleotide-specific pseudouridylation. A patent was granted in Israel (IL 277472), Japan (JP 7478923), South Africa (ZA 2020/05217), the U.S. (US 11,866,702), and in Europe (EP 3775210 B1). Applications are currently pending in Australia, Canada, China, India, New Zealand, and the U.S. (continuation application). In the TRIDENT program we are working together with Prof. Yi-Tao Yu at the University of Rochester, NY, USA. The term of any patents resulting from these applications would be expected to extend to at least 2039. In addition, two of our employees contributed to an invention with an application number PCT/US2024/025581 – PCT pending, with the University of Rochester as applicant.

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 Agreements

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 AONs 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 Trident program. The royalties payable under this license agreement are in the low single digits.

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

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA"), and its implementing regulations and other federal, state and local statutes and regulations. 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 GLP regulations;
- manufacture of the drug product in accordance with cGMP regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practice, or GCP, regulations to establish the safety and efficacy of the proposed drug for its intended use;
- preparation and submission to the FDA of a new drug application, or NDA;
- payment of user fees for FDA review 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.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

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 reporting, 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. 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. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated checkpoints based on access to certain data from the trial.

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 outside of clinical trials, known as expanded access or "compassionate use". There is no requirement for a company to provide expanded access to its investigational product. However, if a company decides to make its investigational product available for expanded access, FDA reviews each request for expanded access and determines if treatment may proceed. Under the FDCA, a sponsor of one or more investigational products for the treatment of a serious disease or condition is required to make publicly 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 holder 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.

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. Further, under the FDORA, the FDA may require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval for failure to conduct required post-approval studies with diligence, or to confirm a clinical benefit during post-marketing studies. 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 available 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.

Platform Technology Designation

Under FDORA, a platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA or BLA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA or BLA for a drug that uses or incorporates the platform technology. Designated platform technology status does not ensure that a drug will be developed more quickly or receive FDA approval. In addition, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

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 compared to available therapies. 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 ("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. Under the current statutory sunset provisions, FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has received rare pediatric disease designation for the drug or biologic by December 20, 2024. The FDA may not award any rare pediatric disease PRVs after September 30, 2026. It is possible the authority for FDA to award rare pediatric disease PRVs will be further extended by Congress, however.

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. 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. Manufacturers and other parties involved in the drug supply chain for prescription drugs and biologics must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stole and intentionally adulterated products or products that are otherwise unfit for distribution in the United States.

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 ("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 regulatory exclusivity or patent term. This six-month exclusivity, which runs from the end of other regulatory exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric clinical trial that fairly responds to 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 ("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 certain 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, ACA, 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 in the U.S. and applicable privacy legislation outside of the U.S., such as the GDPR in the EU and the UK. 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. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback statute is violated. Violations are subject to significant civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, a claim submitted for payment to any federal healthcare program that includes items or services that were made as a result of a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers, among others, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, and on November 20, 2020, the Office of Inspector General, or OIG, finalized further modifications to the federal Anti-Kickback Statute;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA and civil monetary penalty laws which 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. A claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the FCA. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring qui tam actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery or settlement. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes federal 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. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA fraud provisions without actual knowledge of the statute or specific intent to violate it;

- the federal transparency laws, including the provision of the ACA 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers (such as physician assistants and nurse practitioners), 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 on certain covered healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their respective business associates;

- Federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- 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; and

- the General Data Protection Regulation (EU) 2016/679 in the EU, which has been also been incorporated into UK's laws, which includes among other obligations and requirements on: (i) when and how an organization can collect and rely upon consent obtained from an individual to process their personal data; (ii) the provision of information to individuals relating to the processing of their personal data; (iii) how to notify personal data breaches to competent data protection authorities and/or individuals; and (iv) may include additional requirements in relation to the processing of certain categories of data (i.e. "sensitive information" or special category data), which includes health data, data revealing racial or ethnic origin, and genetic data.

Healthcare reform

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 impact our ability to sell our products profitably.

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 or a collaborator 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.

In March 2010, the ACA was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. biopharmaceutical industry. The ACA imposes a significant annual fee on companies that manufacture or import branded prescription drug products. It also contains provisions intended to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against healthcare fraud and abuse, establish transparency requirements for the healthcare and health insurance industries, and impose additional health policy reforms, any of which could negatively impact our business. Among other things, it subjects biological products to potential competition by lower-cost biosimilars, expands the types of entities eligible for the 340B drug discount program, introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. 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 its enactment, there have been judicial, Congressional and executive challenges to certain aspects of the ACA, including efforts to repeal or replace the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA.

In addition, other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted. For example:

- The U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. The reductions remain in effect through 2031.
- The U.S. American Taxpayer Relief Act of 2012 among other things, further reduced Medicare payments to several types of providers.
- The American Rescue Plan Act of 2021 eliminates the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024.
- Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation.

These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. There has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. Further, the government has issued regulations and guidance for states to build and submit importation plans for drugs from outside the United States, pursuant to section 804 of the MMA. CMS has stated that drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If further implemented, importation of drugs from Canada could materially and adversely affect the price we receive for any of our product candidates.

Additionally, on November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed, and the IRA delayed implementation of the rule until January 1, 2032.

In addition, the IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to $ 2,000 which began in 2025; impose new manufacturer financial liability on certain drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation, and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general are not yet known.

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, or our collaborators, would 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.

Regulation in the European Union

Product development, the regulatory approval process, and safety monitoring of medicinal products and their manufacturers in the EU 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 EU. In addition, medicinal products are subject to the extensive price and reimbursement regulations of the various EU Member States.

Clinical Trials Approval

As is the case in the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls.

In April 2014, the EU adopted the Clinical Trials Regulation (EU) No 536/2014 (Regulation), which replaced the previous Clinical Trials Directive 2001/20/EC (Directive) on January 31, 2022.

The Regulation overhauls the former system of approvals for clinical trials in the EU. Specifically, the Regulation, which is 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 EU. For instance, the Regulation provides for a streamlined application procedure using a single entry point (the Clinical Trials Information System) and strictly defined deadlines for the assessment of clinical trial applications.

Following the end of the Brexit transition period, the Medicines and Healthcare products Regulatory Agency (“MHRA”), the UK medicines regulator, continues to authorize clinical trials in the UK. The UK has implemented the now-repealed Clinical Trials Directive into national law through the Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended). The extent to which the regulation of clinical trials in the UK will mirror the EU Regulation in the long term is not yet certain, however on December 12, 2024, the UK government introduced a legislative proposal - the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2024 - that, if implemented, will replace the current regulatory framework for clinical trials in the UK. The legislative proposal aims to provide a more flexible regime to make it easier to conduct trials in the UK, increase the transparency of clinical trials conducted in the UK and make clinical trials more patient centered. The UK government has provided the legislative proposal to the UK Parliament for its review and approval. Once the legislative proposal is approved (with or without amendment), it will be adopted into UK law which is expected in early 2026.

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 the EMA. The scheme is open to medicines under development and for which the applicant intends to apply for a marketing authorization 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 and 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 applicant's ability to demonstrate that the medicine has 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 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 for Advanced Therapies ("CAT") for an advanced therapy, to provide continuous support and help to build knowledge ahead of a MAA;
- 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 EU regulatory system may be obtained through a centralized or national procedure. The centralized procedure results in the grant of a single marketing authorization that is valid for all—currently 27—EU Member States and in the additional Member States of the EEA (Iceland, Liechtenstein and Norway).

The UK ceased to be a Member State of the EU on January 31, 2020. Further information on the marketing authorization regime in the UK is included in the *Marketing Approval in the United Kingdom – Post-Brexit Regime* section below.

Pursuant to Regulation (EC) No. 726/2004, as amended, the centralized procedure is mandatory for certain types of products, including products designated as orphan medicinal products pursuant to Regulation (EC) No. 141/2000, medicines produced by biotechnological processes, advanced-therapy medicinal products (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 CHMP also has the discretion to permit other products to use the centralized procedure if they contain a new active substance, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

In the MAA, the applicant has to properly and sufficiently demonstrate the quality, safety and efficacy of the product. Under the centralized 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 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 an 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 asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. When an application is submitted for a marketing authorization in respect of a product which is expected to be of major public interest, particularly 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 EU. The marketing authorization may be subject to certain conditions, which may include, without limitation, the performance of post-authorization safety and/or efficacy studies.

EU 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, innovative medicinal products approved on the basis of a complete and independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU, during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted and authorized, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the EU market 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 ("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. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a compound is considered to be an innovative medicinal product, so that the innovator is able to gain the period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained a marketing authorization based on an MAA with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

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 an orphan medicinal product pursuant to Regulation (EC) No. 141/2000, as amended. Instead, medicinal products designated as orphan medicinal products that qualify for additional protections under Regulation (EC) No. 1901/2006 may receive 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 medicinal products.

Marketing Approval in the United Kingdom – Post-Brexit Regime

Now that the UK has left the EU, the MHRA is the UK's stand-alone medicines and medical devices regulator, taking any decisions and carrying out any functions which were previously carried out at the EU-level by the EMA.

The UK is no longer covered by the EU's procedures for the grant of marketing authorizations and a separate marketing authorization is required to market products in the UK.

On January 1, 2024, a new international recognition framework was put in place, under which the MHRA may have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators when considering an application for a UK marketing authorization. The MHRA also has the power to have regard to marketing authorizations approved in EU Member States through decentralized or mutual recognition (but not purely national procedures) procedures, with a view to granting marketing authorizations in the UK.

On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, and the medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changes the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA is responsible for approving all medicinal products destined for the UK market (Great Britain and Northern Ireland) and the EMA no longer has any role in approving medicinal products destined for Northern Ireland under the EU's centralized procedure. A single UK-wide marketing authorization will be granted by the MHRA for all novel medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. In addition, the new arrangements require all medicines placed on the UK market to be labelled "UK only", indicating they are not for sale in the EU.

Orphan Designation Regulation

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

- that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition;
- either (i) such condition affects no more than five in ten thousand persons in the EU when the application is made, or (ii) that it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in its development; and
- that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the product would be of a 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 product as an orphan medicinal product. An application for the designation of a product as an orphan medicinal product must be submitted at any stage of development of the product before filing of an MAA.

Orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following the grant of a marketing authorization. During this market exclusivity period, neither the EMA nor the European Commission nor any of the competent authorities in the EU Members States can accept an application or grant a marketing authorization for 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 product concerned, that the criteria for orphan 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 medicinal product if:

- the holder of the marketing authorization for the original orphan medicinal product has given its consent to the second applicant;
- the holder of the marketing authorization for the original orphan medicinal product is unable to supply sufficient quantities of the product; or

- the second applicant can establish in the application that the second product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior.

Regulation (EC) No. 847/2000 lays down definitions of the concept of 'clinical superiority'. Orphan designation does not shorten the duration of the regulatory review and approval process.

A separate process for orphan designation applies in the UK. Currently, the requirements for orphan designation in UK largely mirror those in the EU (save that they apply to the UK market only – e.g. if the prevalence of the condition is no more than five in ten thousand persons in UK). The main difference to the EU system is that there is no pre-marketing authorization orphan designation in Great Britain. Instead, the MHRA will make a decision on orphan status at the time it decides whether to approve the MAA.

As in the EU, medicinal products with orphan status will benefit from up to ten years of market exclusivity from the date of first approval of the product in the UK.

Manufacturing and Manufacturers' License

Pursuant to Directive (EU) 2017/1572, as transposed into the national laws of the Member States, the manufacturing of investigational medicinal products and approved medicinal products is subject to a separate manufacturer's license and must be conducted in strict compliance with GMP requirements, which mandate the methods, facilities, and controls used in manufacturing, processing, and packing of products to assure their safety and identity. Manufacturers must have at least one qualified person permanently and continuously at their disposal in the EU. The qualified person is ultimately responsible for certifying that each batch of finished product released onto the market has been manufactured in accordance with GMP and the specifications set out in the marketing authorization or investigational medicinal product dossier. GMP 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.

The provisions of Directive (EU) 2017/1572, as transposed in the UK, have generally been preserved in the UK following the end of the Brexit Transition Period (subject to applicable amendments to ensure its effective operation in the post-Brexit context). The UK-EU Trade and Cooperation Agreement also contains provisions relating to the mutual recognition of GMP inspections and documentation.

Advertising

In the EU and the UK, 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 of prescription only medicines. All prescription medicines advertising must be consistent with the product's approved summary of product 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.

Likewise, in the UK, a holder of a marketing authorization is subject to a number of ongoing obligations.

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 EU, 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 products is determined by guidelines established by the legislator or responsible national authority. The approach taken varies by EU 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 EU 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 products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products and some 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 medicinal products. Inclusion of orphan medicinal products in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any medicine. 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.

The UK also has its own pricing and reimbursement rules.

The aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval, and, in April 2024, the European Parliament proposed amendments to the legislative proposals. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

C. Organizational structure

At December 31, 2024, 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 V 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%); and
- ProQR Therapeutics I Inc. (United States, 100%).

ProQR Therapeutics N.V. is also the statutory director of Stichting Bewaarneming Aandelen ProQR ("ESOP Foundation") and has full control over this entity.

D. Property, Plants and Equipment

The Company leases office and laboratory facilities of 4,818 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, 2031 and may be renewed for subsequent 5-year terms. The Company also leases office space in the United States, at CIC Cambridge. The office space 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 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 IFRS as issued by the IASB which might differ in material respects from GAAP in the United States. In addition to historical financial information, the following discussion and analysis includes forward-looking statements that involve risks, uncertainties and assumptions. See "Cautionary Note Regarding Forward-Looking Statements." Our actual results and timing 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" and elsewhere in this Annual Report.

A. Operating Results

Overview

To date, we have financed our operations primarily through our initial public and follow-on offerings, and private placements of equity securities, convertible loans, licensing and research collaborations and to a lesser extent through funding from patient organizations and governmental bodies, such as Rijksdienst voor Ondernemend Nederland ("RVO").

In December 2022, the Company issued 9,381,586 shares to Lilly pursuant to the amended and restated licensing and research collaboration between the Company and Lilly, resulting in gross proceeds of € 14,122,000, with no significant transaction costs. In February 2023, ProQR also received an upfront payment of € 56,412,000.

In September 2024, the Company filed a shelf registration statement on Form F-3, 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 $ 300,000,000, the issuance and sale by the Company 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 (the "sales agreement") with Cantor Fitzgerald & Co. ("Cantor") in one or more at-the-market ("ATM") offerings. The Company will pay Cantor a commission equal to 3% of the gross proceeds of the sales price of all ordinary shares sold through Cantor as sales agent under the sale agreement. As of December 31, 2024, no shares have been issued pursuant to this ATM facility.

In October 2024, the Company consummated an underwritten public offering of 18,000,000 ordinary shares (the "Offering") at a public offering price of $ 3.50 per share (the "public offering price"). In addition, the Company granted the underwriters a 30-day option to purchase up to 2,700,000 additional ordinary shares at the public offering price, less underwriting discounts and commissions. The option was partially exercised on October 31, 2024, resulting in the issuance of 1,940,072 shares. The gross proceeds from the Offering and subsequent partial exercise of the underwriters' option, amounted to $ 69,790,000 (€ 64,600,000) while the transaction costs amounted to approximately € 4,365,000, resulting in net proceeds of approximately € 60,235,000.

Concurrently with the Offering, the Company entered into a share purchase agreement with Lilly in a separately negotiated transaction (the "concurrent private placement"), pursuant to which the Company agreed to offer and sell, and Lilly agreed to purchase, 3,523,538 ordinary shares at a price per share equal to the public offering price, for total gross proceeds of approximately $ 12,300,000, subject to a purchase price cap of $ 15,000,000, the consummation of the Offering and the satisfaction of other customary closing conditions. The proceeds of $ 12,300,000 million (€ 11,400,000) from the concurrent private placement were received on October 25, 2024. The ordinary shares purchased in the concurrent private placement are not subject to any underwriting discounts or commissions.

In December 2024, we announced an expansion of our research partnership with RSRT. Building on the initial $ 1.0 million research grant announced in January 2024, the expanded partnership includes an additional $ 8.2 million in funding from RSRT, for a total of $ 9.2 million. As part of the expanded partnership, the Company issued warrants to RSRT to purchase up to 2,144,772 ordinary shares at a fixed price of $ 3.73.

At December 31, 2024, we had cash and cash equivalents of € 149,408,000. In 2024, our revenues consist of non-refundable upfront fees and milestone payments in connection with collaboration and license agreements. 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, 2024, 2023 and 2022, we incurred net losses of € 27,763,000, € 27,735,000, and € 64,204,000, respectively. At December 31, 2024, we had an accumulated deficit of € 427,158,000. We expect to continue incurring losses for the foreseeable future as we invest in our Axiomer platform and continue our preclinical studies of our product candidates.

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 financial years beginning on or after January 1, 2024 that had a material impact on our financial statements.

A number of new standards, amendments to standards and interpretations are effective for annual periods beginning on January 1, 2024 and have not been applied in preparing these consolidated financial statements. None of these are 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.

Foreign Private Issuer Exemptions

As a foreign private issuer, we are not subject to the same requirements that are imposed upon U.S. domestic issuers by the 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 board will be required to notify the Dutch Authority for the Financial Markets ("AFM") of certain transactions they may undertake, including with respect to our ordinary shares, our senior management, 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

Revenue

Revenues to date have consisted principally of non-refundable upfront fees and research and development service fees in connection with collaboration and license agreements.

Other Income

Other income mainly consists of the net proceeds from the Company's divestment of its late-stage ophthalmic intellectual property assets, sepofarsen and ultevursen, to Théa, and grant income from government-related organizations and charities. (Government) Grants are recognized in other income in the same period in which the related research and development expenses are recognized.

Research and Development Expenses

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 (former) clinical activities and trials, including costs paid to CROs;
- costs for production of (pre-)clinical compounds and drug substances by contract manufacturers, including supporting studies such as stability studies and other analysis of the compounds;
- costs of related facilities, materials and equipment; and
- depreciation of tangible fixed assets used to develop our product candidates.

Our research and development expenses in 2024, 2023 and 2022 primarily related to the following key programs:

- Axiomer

  Research and development expenses relating to our Axiomer platform, including expenses relating to the work performed under our research and collaboration agreement with Lilly, primarily consist of salaries, costs for production of the preclinical compounds and costs paid to CROs for our preclinical studies. Other significant costs are our internal laboratory costs, including laboratory consumables and allocated housing expenses, as well as consultancy costs in support of our research and development activities for Axiomer.

- Sepofarsen for the treatment of LCA

  In 2022 and 2021, the research and development costs relating to sepofarsen primarily consisted of salaries and costs paid to CROs for clinical studies, including statistical analyses, and manufacturing of process performance qualification drug substance batches as well as (pre-)commercial drug product 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 support of our research and development activities. In 2023, costs related to sepofarsen were limited.

- Ultevursen for the treatment of Usher syndrome

  In 2022 and 2021, the research and development costs relating to ultevursen primarily consisted of salaries, costs paid to CROs for managing the clinical study, costs for statistical analyses and manufacturing of process performance qualification drug substance 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 support of our research and development activities. In 2023, costs related to ultevursen were limited.

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 increase as we continue our joint research projects with Lilly and our investments in the Axiomer platform, while progressing our internal pipeline targets towards clinical development.

Changes in internal or external variables with respect to the development of our Lilly collaboration program and the development of our Axiomer platform and resulting product candidates could result in a significant change in the costs and/or timing associated with the development of such product candidates. 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, or if we experience significant delays in enrollment in any future clinical trials, we could be required to expend significant additional financial resources and time on the completion of our development programs.

General and Administrative Expenses

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;
- cost of facilities, communication and office expenses;
- IT expenses; and
- depreciation of property, plant and equipment 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, board of 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 and restricted stock units at the grant date, and which are recognized over the course of 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. See Note 13(d) to the financial statements included elsewhere in this Annual Report for additional information on share-based compensation.

Financial Income and Expense

To date, our cash and cash equivalents have been deposited primarily in savings and short-term deposit accounts. Savings and deposit accounts generate interest income (or a limited amount of interest expenses in 2022). In 2024, 2023 and 2022 we held deposits in both euro and U.S. dollars.

Financial expenses primarily consist of interest expenses on convertible loans and government loans. Financial income and expense also includes foreign exchange gains or losses on our U.S. dollar denominated cash and cash equivalents and other foreign currency denominated monetary items.

Results related to derecognition of financial liabilities

Results related to derecognition of financial liabilities represent gains or losses arising from the extinguishment of convertible loans in 2023 and 2022.

Results related to financial liabilities measured at fair value through profit or loss

Results related to financial liabilities measured at fair value through profit or loss ("FVTPL") represent changes in the fair value of derivative financial instruments since their initial recognition. In 2024, 2023 and 2022, these derivative financial instruments consist of conversion options and warrants issued in connection with our convertible loans and partnership agreements. Following the extinguishment of convertible loans in the third quarter of 2022, the related conversion options have been derecognized. The warrants issued to the convertible loan issuers have not yet expired at December 31, 2024 and therefore have not been derecognized. The warrants related to partnership agreements were issued in 2024.

Income Tax

Due to the operating losses incurred since inception, the Company has no income tax provisions as at December 31, 2024. 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.

Results of Operations

Comparison of the periods ended December 31, 2024 and 2023

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

	Year ended December 31,		
	2024	2023	Change
		(€ in thousands)	
Revenue	18,905	6,514	12,391
Other income	640	3,011	(2,371)
Research and development costs	(36,356)	(25,148)	(11,208)
General and administrative costs	(13,661)	(16,236)	2,575
Operating result	**(30,472)**	**(31,859)**	**1,387**
Financial income	3,251	2,593	658
Financial expense	(1,084)	(1,458)	374
Results related to associates	—	—	—
Gain on disposal of subsidiary	—	92	(92)
Results related to derecognition of financial liabilities	—	1,866	(1,866)
Results related to financial liabilities measured at FVTPL	345	953	(608)
Corporate income taxes	197	78	119
Net loss	**(27,763)**	**(27,735)**	**(28)**

Revenue

In 2024, we realized revenue from our license and research collaboration agreement with Lilly amounting to € 18,905,000 (2023: € 6,514,000). The increase in Lilly revenue is due to new projects under the Lilly collaboration and milestones reached in 2024.

Other income

In 2024, other income consisted primarily of grant income from RSRT that focuses on utilizing Axiomer to develop EONs targeting an underlying genetic variant that causes Rett syndrome. No such income was recognized in 2023.

In 2023, other income consisted primarily of the net proceeds from the Company's divestment of its late-stage ophthalmic intellectual property assets, sepofarsen and ultevursen, to Théa. No such income was recognized in 2024.

Research and development costs

Research and development costs amounted to € 36,356,000 for the year ended December 31, 2024 compared to € 25,148,000 for the year ended December 31, 2023. These costs were primarily related to the development of our Axiomer platform, including costs incurred under the Lilly collaboration in 2024 and 2023, and investments in our own pipeline targets.

Our research and development expenses are highly dependent on the development phases of our product candidates.

The increase in research and development costs in the year ended December 31, 2024, compared to the year ended December 31, 2023, was due to higher outsourced research and development activities and higher employee benefits (including share-based compensation) in 2024 compared to 2023 related to our joint research projects with Lilly, increased investments in our own pipeline targets and our investments in the Axiomer platform. In addition, in 2024 there was higher allocation of general and administrative costs to research and development costs due to a higher number of employees working in research and development, as compared to 2023. The increase was partially offset by wind-down costs of CROs for the Phase 2/3 clinical trials for ultevursen in 2023 but not in 2024.

General and administrative costs

General and administrative costs amount to € 13,661,000 for the year ended December 31, 2024 and € 16,236,000 for the year ended December 31, 2023. The decrease in general and administrative costs in the year ended December 31, 2024 compared to the year ended December 31, 2023 is primarily attributable to higher allocation of general and administrative costs to research and development costs due to a higher number of employees working in research and development in 2024 as compared to 2023.

Financial income

We had financial income of € 3,251,000 for the year ended December 31, 2024, as compared to € 2,593,000 for the year ended December 31, 2023. The financial income mainly reflects interest income earned on cash and cash equivalents in 2024 and 2023.

Financial expenses

Financial expenses amounted to € 1,084,000 for the year ended December 31, 2024, as compared to € 1,458,000 for the year ended December 31, 2023. The decrease in 2024 compared to 2023 is mainly due to lower interest expenses in 2024 due to the partial repayment of the Innovation Credit loan from RVO in 2023.

Results related to derecognition of financial liabilities

In 2024, results related to derecognition of financial liabilities were nil (2023: € 1,866,000). In 2023, results related to the waiver agreements that ProQR's subsidiary Amylon Therapeutics B.V. ("Amylon") entered into with all of its lenders. Such lenders' loan agreements with Amylon are severed and any claims to repayment of any outstanding debt and accumulated interest are renounced.

Results related to financial liabilities measured at fair value through profit or loss

Results related to financial liabilities measured at FVTPL amounted to a gain of € 345,000 for the year ended December 31, 2024, as compared to a gain of € 953,000 for the year ended December 31, 2023. These results relate to fair value changes in our derivative financial instruments, consisting of issued warrants. The gains in 2024 and 2023 were due to the decrease in the fair value of warrants, mainly due to the decrease in ProQR's share price.

Comparison of the periods ended December 31, 2023 and 2022

Reference is made to our Annual Report on Form 20-F for the fiscal year ended December 31, 2023, filed with the SEC on March 13, 2024, for a comparison of the periods ended December 31, 2023 and 2022.

B. Liquidity and Capital Resources

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, convertible loans, licensing and research collaborations and to a lesser extent through funding from patient organizations and governmental bodies, such as RVO.

Cash and Funding Sources

The table below summarizes our main sources of financing for the years ended December 31, 2024, 2023 and 2022.

	Equity Capital	Lilly Upfront and Milestone Payments	Total
		(€ in thousands)	
Year ended December 31, 2022	14,122	—	14,122
Year ended December 31, 2023	—	56,412	56,412
Year ended December 31, 2024	71,635	5,096	76,731
Total	85,757	61,508	147,265

Equity capital
In 2024 our funding consisted of Offering of 18,000,000 ordinary shares and the respective option that resulted in additional issuance of 1,940,072 ordinary shares, at the public offering price of $ 3.50 per share. The gross proceeds from the Offering and subsequent partial exercise of the underwriters' option, amounted to $ 69,790,000 (€ 64,600,000) while the transaction costs amounted to approximately € 4,365,000, resulting in net proceeds of approximately € 60,235,000.

Concurrently with the Offering, we entered into the concurrent private placement with Lilly pursuant to which we agreed to offer and sell, and Lilly agreed to purchase, 3,523,538 ordinary shares at a price per share equal to the public offering price. The net proceeds from the concurrent private placement amount to approximately € 11,400,000.

We issued shares in 2022 and 2024. Our share issuances are set out in more detail in Note 13 (a) to the financial statements as included elsewhere in this Annual Report.

As at December 31, 2024 our outstanding shares totaled 105,212,527. The following items may result in future dilution for our shareholders:

- 1,054,010 treasury shares held by the Company, which can be used for all general purposes including option exercises under the equity incentive plan, as amended in May 2024;
- 1,444,379 treasury shares held by the ESOP foundation, which can be used for option exercises under the equity incentive plan, as amended in May 2024;
- 15,781,879 shares authorized for issuance for future grants under the equity incentive plan, as amended in May 2024;
- 679,628 warrants held by former convertible debt holders;
- 2,144,772 warrants held by RSRT.

If all of the above items were converted into shares at December 31, 2024, the number of outstanding shares would be 126,317,195.

Convertible loans and government borrowing
We received convertibles loans and government borrowing in 2021. Our convertible loans and government borrowings are set out in more detail in Note 14 to the financial statements as included elsewhere in this Annual Report.

Lilly upfront and milestone payments
In 2024, our sources of funding included the receipt of milestone payments amounting to $ 5,500,000 (€ 5,096,000) under the collaboration agreement with Lilly. In 2023, we received the upfront payments under the collaboration agreement with Lilly, which are reflected in changes in working capital. In 2022, we did not receive upfront payments from Lilly. For more details refer to Note 17 to the financial statements included elsewhere in this Annual Report.

Cash Flows

The table below summarizes our statement of cash flows for the years ended December 31, 2024 and 2023.

	Year ended December 31,		
	2024	2023	Change
		(€ in thousands)	
Net cash (used in) / generated by operating activities	(36,393)	21,548	(57,941)
Net cash (used in) / generated by investing activities	(4,073)	4,278	(8,351)
Net cash generated by / (used in) financing activities	70,276	(2,275)	72,551
Net increase / (decrease) in cash and cash equivalents	**29,810**	**23,551**	**6,260**
Currency effect cash and cash equivalents	673	599	74
Cash and cash equivalents at the beginning of the period	118,925	94,775	24,150
Cash and cash equivalents at the end of the period	**149,408**	**118,925**	**30,483**

Net cash used in operating activities amounted to € 36,393,000 in the year ended December 31, 2024, whereas net cash generated by operating activities amounted to € 21,548,000 in the year ended December 31, 2023. Total operating costs increased by € 8,633,000 in 2024 compared to 2023, which had a negative impact on net cash generated by operating activities In addition, the Company experienced a net positive cash flow from operating activities in 2023 mainly because of the receipt of the Lilly up-front payment of € 56,412,000 in February 2023.

Net cash used in investing activities in the year ended December 31, 2024 is mainly driven by purchases of laboratory equipment and other fixed assets of € 1,418,000. In addition, in 2024 ProQR paid the remaining portion of costs of € 2,655,000 related to the transaction with Théa. Net cash generated by investing activities in the year ended December 31, 2023 is mainly driven by the divestment of our late-stage ophthalmic intellectual property assets, sepofarsen and ultevursen, to Théa. Under the terms of the agreement, ProQR received an initial payment of € 8,000,000 and incurred cash outflows directly related to the transaction amounting to € 2,351,000 in 2023, leading to a net cash inflow from the Théa transaction of € 5,649,000 in 2023. This is partly offset by net investments in laboratory equipment and other fixed assets amounting to € 1,311,000, leading to net cash generated by investing activities of € 4,278,000 in 2023.

Net cash generated by financing activities amounted to € 70,276,000 in the year ended December 31, 2024 and consists of the net proceeds from the offering of € 60,235,000 and the share sale to Lilly of € 11,400,000. The cash inflows were offset by repayments of the lease liability for the Company's Leiden headquarters. In 2023, net cash used in financing activities included repayments of the lease liability for the Company's Leiden headquarters amounting to € 1,621,000 and the partial repayment amounting to € 1,008,000 of the Innovation Credit loan from RVO.

Reference is made to our Annual Report on Form 20-F for the fiscal year ended December 31, 2023, filed with the SEC on March 13, 2024, for a comparison of the periods ended December 31, 2023 and 2022.

For a description of our financial commitments, see below.

Funding Requirements

Our material cash requirements from known contractual and other obligations include contractual commitments to repay borrowings, lease liabilities, and trade and other payables. In 2025, such cash requirements include the following undiscounted amounts:

- Borrowings amounting to € 4,872,000
- Lease liabilities amounting to € 2,114,000
- Trade and other payables amounting to € 10,343,000

Beyond 2025, our cash requirements include the following undiscounted amounts:

- Lease liabilities amounting to € 12,682,000

We expect that our cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into mid-2027. 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 investments required to further develop our Axiomer platform and the results of current and potential future collaborations involving the Axiomer technology.
- 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;
- the amount of revenues, if any, we may derive from upfront, milestone or royalty payments resulting from licensing and research collaboration agreements.

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, 2024, 2023 and 2022:

	Year ended December 31,		
	2024	2023	2022
	(€ in thousands)		
Purchases of tangible fixed assets	1,203	1,371	708

Purchases of tangible fixed assets primarily consist of investments in laboratory equipment. Such investments decreased in 2024 compared to 2023 as the investments of the Company were focused on outsourced research and development activities instead of its in-house oligonucleotide manufacturing capacity.

Commitments

Our commitments consist of rent, patent license agreements, clinical support agreements, research and development commitments.

Refer to Notes 25 and 26 to the financial statements as included elsewhere in our Annual report and Item 4.B: "Business Overview" for more details on our commitments.

C. Research and Development

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, 2024 to December 31, 2024 that are reasonably likely to have a material adverse effect on the Company's net 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. 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. Significant estimates and judgements are disclosed in disclosure Note 2 *Basis of preparation* to the financial statements, under (e) Use of estimates and judgements.

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

Item 6: Directors, Senior Management and Employees

A. Directors and Senior Management

We have a one-tier governance structure with the board of directors as the ultimate decision-making body. Our board is supported by our senior management. Our management team is comprised of our executive directors together with our senior management ("Management Team"). Below is a summary of relevant information concerning our board members and senior management.

Board of Directors

The following table sets forth information with respect to each of our board members and their respective dates of birth. The terms of office of all our board members expire according to a rotation schedule drawn up by our board. The business address of our board members is our registered office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands.

Our board is currently composed of the following members:

Name	Date of Birth	Position	Member Since	Term Expires
James Shannon. M.D.	June 5, 1956	Non-executive director (Chairman)	June 21, 2016 and chairman since May 22, 2024	2026
Dinko Valerio, Ph.D.	August 3, 1956	Non-executive director	January 1, 2014	2026
Alison F. Lawton	September 26, 1961	Non-executive director	September 17, 2014	2026
Bart Filius	July 5, 1970	Non-executive director	May 21, 2019	2027
Begoña Carreño, Ph.D.	December 13, 1971	Non-executive director	May 18, 2023	2027
Theresa Heggie	November 17, 1960	Non-executive director	May 18, 2023	2027
Martin Maier, Ph.D.	October 31, 1965	Non-executive director	May 22, 2024	2028
Daniel de Boer	April 12, 1983	Chief Executive Officer and Executive director	February 21, 2012	2026
René Beukema	March 26, 1964	Chief Corporate Development Officer and General Counsel and Executive director	June 30, 2022	2026
Gerard Platenburg, Ph.D.	February 24, 1964	Chief Scientific Officer and Executive director	May 22, 2024	2028

All of our non-executive directors are independent under applicable Nasdaq standards and all of them are independent under the DCGC, with the exception of Ms. Theresa Heggie. Ms. Heggie was, prior to her appointment on our (former: supervisory) board in 2023, employed by ProQR as Chief Commercial Officer and Chief Operations Officer. Having been employed by the Company within three years prior to the date hereof, Ms. Heggie does not qualify as independent under applicable Nasdaq standards. Having been employed by the Company within five years prior to her appointment on our (former: supervisory) board, Ms. Heggie does not qualify as an independent under the DCGC. We do not intend to follow Nasdaq's requirements regarding Nasdaq Listing Rule 5605(b)(2), which mandates that independent directors must meet at regularly scheduled executive sessions where only independent directors are present.

The following sets forth biographical information regarding our board members. There are no family relationships among the members of our board.

James Shannon, M.D. has served on our board since June 2016 and has been Chair of our Scientific Advisory Board since 2020 and was elected Chair of our board in May 2024. Dr. Shannon has had an extensive career in drug development and pharma. From 2012 until his retirement in 2015, he 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 previously held board positions at several companies including Biotie, Circassia, Crucell, Endocyte and Cerimon Pharmaceuticals. More recently Dr. Shannon also served on the boards of Immodulon Therapeutics Limited and Horizon Therapeutics. Dr. Shannon currently serves as chairman of the boards at MannKind Corp., a public biopharmaceutical company, and Kyowa Kirin NA, a private biopharmaceutical company and subsidiary of Kyowa Kirin, and and holds board positions at myTomorrows, Xilio Therapeutics, a public clinical-stage biotechnology company, and Leyden Labaratories. He received his undergraduate and postgraduate degrees at Queen's University of Belfast and is a member of the Royal College of Physicians.

Dinko Valerio, Ph.D. is one of our founders and joined our board in 2014. Dr. Valerio chaired our board since its inception until May 2024. As a scientist and an experienced biotech entrepreneur Dr. Valerio is founder and former Chief Executive Officer of Crucell N.V., and one of the founders of its spinout, Galapagos Genomics. He was the founder and former general partner of Aescap Venture, a life sciences venture capital firm and co-founder and current board member of Leyden Laboratories. In 1992 Dr. Valerio was appointed professor of gene therapy at the University of Leiden, where he also received his Ph.D. with honors. Dr. Valerio was a visiting scientific specialist at Genentech, and a postdoctoral fellow at the Salk Institute.

Alison F. Lawton has served on our board since 2014. Ms. Lawton is an executive leader with more than 35 years of experience in biopharma. Most recently, she served as President and Chief Executive Officer of Kaleido Biosciences, Inc. from 2018 to 2020, and prior to that, as its President and Chief Operating Officer from 2017 to 2018. Ms. Lawton previously served as Chief Operating Officer at Aura Biosciences, from 2015 until 2017, and prior to that, as its consultant. Before that, Ms. Lawton served as Chief Operating Officer at OvaScience and as a biotech consultant for various companies, including as a part-time Chief Operating Officer consultant at X4 Pharmaceuticals from 2014 to 2026. Earlier in her career, Ms. Lawton worked at various positions of increasing responsibility at Genzyme, and subsequently at Sanofi-Aventis, including as head of Genzyme Biosurgery and Global Market Access. Ms. Lawton currently serves on the boards of directors of public pharmaceutical companies including X4 Pharmaceuticals and Dianthus Therapeutics, and on the board of directors of BlueRock Therapeutics, a private biotech company. She previously served on the boards of directors of Spyre Therapeutics, Verastem, CoLucid until its acquisition by Lilly and Cubist Pharmaceuticals until its acquisition by Merck & Co. She is past President and Chair of the board of Regulatory Affairs Professional Society and as a member of the FDA's Cellular, Tissue and Gene Therapies Advisory Committee. She earned her BSc in Pharmacology, with honors, from King's College London.

Bart Filius has served on our board since 2019. He is the former President and Chief Operating Officer of Galapagos, a position he held from 2021 to 2023. He joined Galapagos in 2014 as Chief Financial Officer and added the role of Chief Operating Officer in 2017. Prior to joining Galapagos, Mr. Filius held a variety of executive positions at Sanofi, where he was Vice President, Chief Financial Officer 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 currently holds a board position at Idorsia Ltd. Mr. Filius has an MBA degree from INSEAD and a bachelor's degree in Business from Nyenrode University.

Begoña Carreño, *Ph.D.* joined our board in 2023. Dr. Carreño is currently the Chief Business Development Officer at Aspeya Switzerland SA (formerly known as Vectura Fertin Pharma). Prior to this, she spent 18 years at Novartis Pharma AG in its Business Development and Licensing ("BD&L") group, her last role being World Wide BD&L Head in the Ophthalmology Franchise, based in Basel, Switzerland. Dr. Carreño has over 20 years Pharmaceutical Development experience. She is a seasoned and energetic BD&L professional that has led the BD&L efforts at Novartis across five different therapeutic franchises in the last 15 years. She has a proven track record in licensing deals, M&A as well as developing collaborations within cross functional, multi-cultural, matrix environment at global, regional and country level. Before joining Novartis, she was the Head of External Pharmaceutical projects at Almirall (Barcelona, Spain). Dr. Carreño holds a Ph.D. in Drug Delivery from the London School of Pharmacy (UK) and a BSc in Biochemistry from Keele University (UK).

Theresa Heggie was reappointed to our board in 2023. Previously, Ms. Heggie served as our Chief Operating Officer, after originally joining the Management Team in 2021 as our Chief Commercial Officer. Prior to joining us, she served as Chief Executive Officer of Freeline Therapeutics from 2020 to 2021. Previously, she held senior commercial and operating roles at Alnylam Pharmaceuticals as Senior Vice President, Head of CEMEA from 2017 to 2020. Before that, Ms. Heggie had roles at Bupa Group until 2016 and at Shire plc, where she built the EMEA rare disease business. Earlier in her career, Ms. Heggie held increasingly senior positions in the commercial organizations at Janssen Pharmaceuticals and Baxter Healthcare. She previously served as a member of the boards of directors at SOBI (Swedish Orphan Biovitrum AB) and Freeline Therapeutics, and currently serves on the board of BioCryst Pharamceuticals, a public pharmaceutical company. Ms. Heggie previously served on our board from 2019 to 2021. She earned her BSc from Cornell University.

Martin Maier Ph.D. joined our board in 2024. Dr. Maier currently serves as Senior Vice President, Oncology at Alnylam Pharmaceuticals. Dr. Maier joined Alnylam in 2006 and has contributed to the development of lipid nanoparticles and GalNAc conjugates, two clinically validated platforms for siRNA delivery, and the advancement of multiple therapeutic programs to development, which has resulted in the approval of five RNAi therapeutic to date. After receiving his Ph.D. in Organic Chemistry in 1997 at the University of Tübingen, Germany, Dr. Maier moved to the U.S. for his postdoctoral research at Ionis Pharmaceuticals, where he assumed a permanent position working on novel chemistries and delivery systems for AONs. Dr. Maier currently serves on various additional boards including the board of directors of the Oligonucleotide Therapeutics Society and the Scientific Advisory Board of the Gene and RNA Therapy Center Tübingen, Germany. During his 25 years of experience in the field of oligonucleotide therapeutics in both, ASO and

RNAi platforms, Dr. Maier authored more than 90 peer-reviewed scientific publications, reviews and book chapters and is the inventor on more than 40 issued patents.

Daniel de Boer is our Founder and has served as our Chief Executive Officer since our incorporation in 2012 and is an executive director of our Board. Mr. de Boer is a serial entrepreneur and passionate advocate for rare disease patients. After one of his children was diagnosed with a rare disease, he started ProQR to develop RNA therapies for rare diseases. Before founding ProQR, Mr. de Boer was founder and Chief Executive Officer of several technology companies.

René Beukema rejoined ProQR in 2022 having previously served as our Chief Corporate Development Officer and General Counsel from 2013 to 2018 and is an executive director of our Board. Mr. Beukema is a seasoned M&A and equity capital markets executive and an experienced corporate lawyer. From 2019 until June 2022, Mr. Beukema held the positions of Chief Corporate Development Officer and General Counsel at Frame Therapeutics, a neoantigen immune-oncology biotechnology company. He was instrumental in financing Frame Therapeutics and selling it to CureVac, a Nasdaq Listed biotechnology company. From 2021 to 2024 Mr. Beukema was a board member of Fibriant BV, a biotechnology company focused on the development of technology and products based on recombinant human fibrinogen and thrombin. Prior to his initial tenure at the Company, he served as General Counsel and Corporate Secretary of Crucell for twelve years, following his positions as Senior Legal Counsel at GE Capital / TIP Europe and Legal Counsel at TNT Express Worldwide. Mr. Beukema was also a venture partner of Aescap Venture, a life sciences venture capital firm from 2011 to 2012 and is co-founder of myTomorrows, a Dutch life sciences company. He is a founder of Tzu Cancer Therapeutics 8.V., a biotechnology company focused on developing advanced solutions to combat cancer. He holds a post-doctoral degree in corporate law from the University of Nijmegen in co-operation with the Dutch Association of In-house Counsel (‘*Nederlands Genootschap van Bedrijfsjuristen*’) and a master's degree in Dutch law from the University of Amsterdam.

Gerard Platenburg, Ph.D. is our co-founder and has served as our Chief Scientific Officer since 2022, following his tenure as our Chief Innovation Officer from 2014 to 2022, and joined our board as an executive director in May 2024. Dr. Platenburg has an extensive background in RNA modulation and orphan drug discovery and development and is currently in charge of our R&D. Dr. Platenburg has more than 25 years of senior managerial experience in growing biotech companies. Prior to joining our company, Dr. Platenburg worked at Isa Pharmaceuticals B.V. as its Chief Executive Officer. Dr. Platenburg co-founded Prosensa Holding N.V., growing it to become a well-known clinical stage RNA modulation company, and held various positions during his tenure including as its Chief Executive Officer and Chief Development Officer. Dr. Platenburg also worked at Pharming B.V. Dr. Platenburg is a passionate and driven pioneer of early-stage technologies. Dr. Platenburg has a master’s degree in Chemistry and Molecular Biology from Leiden University in 1987 and pursued a Ph.D. work at Leiden University.

Senior Management

The following table sets forth information with respect to each of the senior manager, their respective dates of birth and their positions as of the date of this Annual Report. The business address of our senior management is our registered office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands.

Name	Date of Birth	Position
Sheila Sponselee	May 22, 1984	Chief People & Operations Officer
Jurriaan Dekkers	March 17, 1976	Chief Financial Officer

Sheila Sponselee has served as our Chief People & Operations Officer since 2023. In this role she leads Human Resources, Recruitment, Information Technology, Facilities and the Project Management Office. Ms. Sponselee joined us in 2020 as VP of Human Resources and became VP, Head of People and Operations in 2022. Ms. Sponselee has more than 15 years of experience in human resources, recruitment, and operations across varied industries, including information technology and biopharma. Prior to joining us, Ms. Sponselee most recently led Human Resources at myTomorrows in the Netherlands from 2019 to 2020 and managed Human Resources at Korton Group B.V. from 2017 to 2019. She obtained her B.Sc. in Human Resource Management from the University of Applied Science and completed leadership programs at IMD Business School for Management and Leadership.

Jurriaan Dekkers has served as our Chief Financial Officer since 2022, where he leads the finance and procurement functions. He brings to the role more than 20 years of experience in finance, management and leadership roles in biopharma and healthcare companies, as well as in audit and consulting services. Prior to joining us, he most recently served as Chief Financial Officer at AstraZeneca in the Netherlands and Chief Executive Officer at Acerta Pharma (part of the AstraZeneca Group) from 2018 to 2022. Previously, Mr. Dekkers held various global and European finance roles at amongst others DaVita Medical Group, a US-listed international healthcare provider, from 2015 to 2018, and started his career at PwC. He is a Supervisory Board member at 'Stichting Kinderpostzegels' in the Netherlands. Mr. Dekkers holds a MSc. in Economics from the Erasmus University Rotterdam, the Netherlands, is a Certified Public Auditor (Register Accountant, "RA") graduate from the Erasmus University Rotterdam, and completed executive programs at IMD Business School and INSEAD Business School.

B. Compensation

Under Dutch law and our articles of association, the general meeting of shareholders must upon the proposal of our board adopt a compensation policy for the executive directors, which includes the outlines of the compensation of any executive directors who serve on our board and for the non-executive directors, setting forth the compensation components for non-executive board members. On June 30, 2022, the general meeting of shareholders adopted the current compensation policy of our company with respect to our board as well as with respect to our supervisory board, which was merged into one document "Board Compensation Policy" on May 22, 2024 when the Company adopted a one-tier governance structure. The non-executive members of the board determine the level and structure of the compensation of the executive board members in accordance with the Board Compensation Policy. Board members will be reimbursed for their expenses.

We incurred remuneration expenses in respect of our directors and senior management in an aggregate amount of approximately €5,321,000 for services provided during 2024, € 6,398,000 during 2023 and € 8,186,000 during 2022. For more information about compensation of the Board, see Note 27 (a) to the financial statements included elsewhere in this Annual Report.

Compensation of Non-Executive Directors

Under the current Board Compensation Policy, non-executive directors receive a board fee of € 34,000 per year and the chairperson receives a board fee of € 63,000 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 € 7,000 per year for service on that committee. The compensation, nominating and corporate governance committee chairperson receives € 12,000 per year for service on that committee, and each other member of the compensation, nominating and corporate governance committee receives € 5,500 per year for service on that committee. The chairperson of the research and development committee receives € 12,000 per year for service on that committee, and each other member of the research and development committee receives € 5,500 per year for service on that committee. In addition, non-executive directors of our board may be granted options with an underlying value of € 143,000 per year.

Compensation of Executive Directors

The Compensation of Executive Directors consists of annual base salary ("Annual Base Salary"), Short Term Incentive ("STI") (annual cash bonus), and Long-Term Incentive ("LTI") (Equity Incentive Plan). The compensation is based on the following principles:

- Flexibility: the compensation should provide flexibility to allow the Board, acting on the recommendation of the Compensation Committee, to reward the Executive Directors in a fair and equitable manner, including by awarding extraordinary awards ("Extraordinary Awards");

- This compensation should drive the right kind of management behavior, discourage unjustified risk taking and minimize any gaming opportunity;

- This compensation should enable paying for performance, taking into account not only the measurable financial performance of / or milestones achieved by the Company, but also, where appropriate, the efforts made by the Executive Directors, individually and as a whole, in managing the Company;
- Design of the compensation shall be based on current legislation applicable in the Netherlands;
- This compensation shall foster alignment of interests with our shareholders;
- The pension of the Executive Directors shall be based on the defined contribution system; and
- Pay differentials and position within the Company (internal pay ratios) shall also be taken into account and are considered and evaluated regularly.

The Executive Directors' compensation consists of the following key elements:

Compensation Component & Description	**Objective**
Annual Base Salary (fixed cash compensation based on level of responsibility and performance)	Compensate for performance of day-to-day activities
STI (reward paid in cash for performance in the preceding financial year, measured against financial, non-financial/personal targets and company milestones)	Compensate previous year's Company and individual performance Award opportunities in consideration for substantial contributions to the success of the Company and/or to promote and continued service Award for specific transactions of the Company
LTI	Retention of management talent Incentive to perform Alignment with shareholders' interests
Extraordinary Awards	Attract and retain management talent and/or award extraordinary circumstances, extraordinary performance or extraordinary Company results Enhanced alignment with shareholders' interests
Pension (defined contribution plan)	Provide competitive post-retirement benefits

Short-term incentive benefits include an annual bonus of € 394,000 for Mr. de Boer, an annual bonus of € 231,000 for Mr. Beukema and an annual bonus of € 185,000 for Dr. Platenburg. In accordance with our Board Compensation Policy, the annual bonus was determined by the board (non-executive board members only) and related to pre-determined quantified financial targets, non-financial/personal targets and/or company goals that were set by the board (non-executive board members only) prior to the start of 2024. Each year the non-financial targets and goals of the company are derived from our strategic and organizational priorities and also include qualitative targets that are relevant for the responsibilities of Mr. de Boer, Mr. Beukema and Dr. Platenburg. Moreover, the size of the annual share-based payments of Mr. de Boer, Mr. Beukema and Dr. Platenburg is determined by the board (non-executive board members only) based on contribution to the strategy of the Company, the Company's long-term development, individual performance and alignment of total compensation to the median of the compensation reference group selected in accordance with our Board Compensation Policy.

For further detail on compensation of members of our board and senior management, see Note 27 to the financial statements included elsewhere in this Annual Report.

C. Board Practices

Our board consists of executive directors ('*uitvoerend bestuurders'*) and non-executive directors ('*niet-uitvoerend bestuurders'*). All members of the board, non-executive and executive members alike, are collectively responsible for the management of the company.

Board – non-executive directors

The non-executive directors are responsible for the supervision of the activities of the executive directors and our company's general affairs and business. The non-executive directors are responsible for the quality of the performance of the board. Non-executive directors may, also at their own initiative, provide the executive directors with advice and may request any information from the executive directors that they deem appropriate. In performing its duties, the board is required to act in the interests of our company (including its stakeholders) and its associated business as a whole. Non-executive directors are not authorized to represent us in dealings with third parties.

Pursuant to Dutch law, non-executive members of the board must be natural persons. Under our articles of association, the number of non-executive board members is determined by our board itself. In our board rules we have established that the board should consist of at least two non-executive directors. Our articles of association provide that non-executive members of the board are appointed by the general meeting of shareholders upon a binding nomination by the 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 board may draw up a new binding nomination.

Our board rules provide that non-executive members of our board will serve for a maximum duration of two terms of four years, following which they may be re-appointed twice for a period of two years each time. Our articles of association provide that the non-executive board members must retire periodically in accordance with a rotation schedule adopted by the board. A non-executive board member who retires in accordance with the rotation schedule can be reappointed immediately. The board appoints a chairman from among its members.

Under our articles of association, the general meeting of shareholders may suspend or remove board members at any time. A resolution of our general meeting of shareholders to suspend or remove a board member may be passed by a simple majority of the votes cast, provided that the resolution is based on a proposal by our board. In the absence of a proposal by our board, a resolution of our general meeting of shareholders to suspend or remove a 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 board, each board member is entitled to cast one vote. A board member may grant a written proxy to another board member to represent him at a meeting of the board. All resolutions by our board are adopted by a simple majority of the votes cast unless our board rules provide otherwise or the board has otherwise adopted deviating voting procedures for certain decisions in writing. In case of a tie in any vote of the board, the chairman of the board shall have the casting vote. Our board may also adopt resolutions outside a meeting, provided that such resolutions are adopted in writing, all board members are familiar with the resolution to be passed and provided that no board member objects to such decision-making process.

Board – executive directors

Our executive board members are responsible for the day-to-day management of our operations under the supervision of the non-executive board members. Executive board members are required to:

- keep the non-executive board members informed in a timely manner in order to allow the board to carry out its responsibilities;
- consult with the non-executive board members on important matters; and
- submit certain important decisions to the board for its approval.

While the board as a whole bears collective responsibility for the company, our executive board members are tasked with the day-to-day operations of the company as set forth in our board rules. Our executive board members may perform all acts necessary or useful for achieving our corporate purposes within the limits of the delegation provided for our board rules and excluding those acts that are prohibited by law or by our articles of association. Executive board members are authorized to individually represent us in dealings with third parties. The executive board members may delegate this authority in whole or in part to employees of the company.

Under our articles of association, the number of board members is determined by the board, and pursuant to our board rules, there at least be 1 executive director appointed. The board elects a Chief Executive Officer from among the executive members of the board.

Members of the board are appointed by the general meeting of shareholders upon a binding nomination of the 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 board may draw up a new binding nomination.

Our board rules provide that, unless the resolution appointing an executive board member provides otherwise, executive members of our board will serve for a maximum term of four years. Our articles of association provide that the board members must retire periodically in accordance with a rotation schedule adopted by the board. Subject to such rotation schedule, an executive board member may be reappointed immediately for a term of not more than four years at a time.

Service Agreements

We have entered into service agreements with our Chief Executive Officer, Daniel de Boer, and with our Chief Corporate Development Officer and General Counsel, René Beukema, and with our Chief Scientific Officer, Gerard Platenburg. The service agreement with Mr. de Boer contains a termination notice period of two months, the service agreement with Mr. Beukema contains a termination notice period of one month and the service agreement with Dr. Platenburg contains a termination notice period of two months. The service agreements may be terminated in the event of an urgent reason (‘*dringende reden’*) at any time, without advance notice. The service agreements with Mr. de Boer, Mr. Beukema and Dr. Platenburg provide 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 agreements also contain certain restrictive covenants, including post termination non-competition and non-solicitation covenants, which survive for a period of 12 months post-termination.

Committees of the Board

During 2024, our board had an audit committee, a compensation, nominating and corporate governance committee, and a research and development committee, each of which has an adopted charter which is published on the Company's website. The board committees consisted solely of non-executive board members.

Audit Committee

Our audit committee consists of Bart Filius (chair), Alison F. Lawton and Begoña Carreño. 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 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 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 executive board directors, the senior management 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 board and the independent auditor(s);
- reviewing and approving all proposed related-party transactions;
- discussing the annual audited statutory financial statements with the executive board members;
- 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 executive board directors and the senior management; and
- attending to such other matters as are specifically delegated to our audit committee by our board from time to time.

Compensation, Nominating and Corporate Governance Committee

Our compensation, nominating and corporate governance committee consists of Theresa Heggie (chair), Dinko Valerio and James Shannon. Each member satisfies the independence requirements of the Nasdaq listing standards, and each member meets the criteria for independence set forth in best practice provision 2.1.8 of the DCGC, in each case, with the exception of Ms. Theresa Heggie. Ms. Heggie was, prior to her appointment to our (former: supervisory) board in 2023, employed by ProQR as Chief Commercial Officer and Chief Operations Officer from October 2021 to October 2022. Considering her employment by the Company within three years prior to the date hereof, Ms. Heggie does not qualify as independent under applicable Nasdaq standards. Having been employed by the Company within five years prior to her appointment on our (former: supervisory) board, Ms. Heggie does not qualify as independent under the DCGC. We do not intend to follow Nasdaq's requirements regarding the independence of all members of the compensation, nominating and corporate governance committee. Dutch law and the DCGC do not require that the compensation, nominating and

corporate governance committee be composed entirely of independent directors and only requires that a majority of the committee members are independent. In accordance with Dutch law and the DCGC, our compensation, nominating and corporate governance committee consists of a majority of members who qualify as independent under applicable Nasdaq standards and under the DCGC. With respect to compensation matters, the compensation, nominating and corporate governance committee assists our board in reviewing and approving or recommending our compensation structure, including all forms of compensation relating to our board members and our senior management. Executive Directors and senior management whose compensation is being discussed may not be present at compensation committee during such deliberation. With respect to nominating and corporate governance matters, the compensation, nominating and corporate governance committee assists our board in selecting individuals qualified to become our board members, in determining the composition of the board and its committees and our senior management and in developing and recommending a set of corporate governance guidelines applicable to the Company. Subject to and in accordance with the terms of the Board Compensation Policy approved by our general meeting of shareholders from time to time, as required by Dutch law, the compensation, nominating and corporate governance committee is responsible for, among other things:

- reviewing and making recommendations to the board with respect to compensation of our board members;
- reviewing and approving the compensation, including equity compensation, change-of-control benefits and severance arrangements, of our senior management (not part of our board) as it deems appropriate;
- overseeing the evaluation of our executive board members and our senior management;
- reviewing periodically and making recommendations to our board with respect to any incentive compensation and equity plans, programs or similar arrangements;
- exercising the rights of our 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 board from time to time;
- approving the compensation package for the senior management;
- monitoring the policy of the board on the selection criteria and appointment procedures for officers and senior management;
- recommending to the board persons to be nominated for election or re-election to the board and the board at any meeting of the shareholders;
- overseeing the board's annual review of its own performance and the performance of its committees; and
- considering, preparing, and recommending to the board a set of corporate governance guidelines.

Our board may also delegate certain tasks and powers under our Option Plan to the compensation, nominating and corporate governance committee.

Research and Development Committee

Our research and development committee consists of James Shannon (chair), Dinko Valerio, Martin Maier and Alison F. 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. The research and development committee assists the board in overseeing our product pipeline and research and development strategy. The research & development committee is responsible for, among other things:

- reviewing the company's research and development strategy, including the long-term strategy goals and objectives;
- reviewing and assessing quality of the research and development programs;
- reviewing the progress of the product pipeline, including a review and analysis of the progress and results of pre-clinical studies and clinical trials;
- reviewing and advising the board about strategic opportunities to enhance innovation and development;
- reviewing and assessing scientific activities critical to the success of the company's research and development strategy; and
- organizing and chairing meetings with the Company's scientific advisory board for supporting its review and assessment the company's research and development strategy.

Insurance and Indemnification of Board Members

Under Dutch law, 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 board members, (including in their former capacity as management board members and supervisory board members -as applicable- prior to 22 May 2024 when the general meeting of shareholders adopted the one-tier governance regime) (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 or she becomes involved, to the extent this relates to his or her 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 or her 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 board may stipulate additional terms, conditions and restrictions in relation to such indemnification.

D. Employees

As at December 31, 2024, we had a total of 166.1 employees (converted to FTE). Of these employees, 133.9 were engaged in research and development and 32.2 in general and administrative activities. For additional details we refer to Note 20 to the financial statements included elsewhere in this Annual Report. 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. For more information as to the risks associated with our workforce reduction, see Item 3.D: "Risk Factors".

E. Share Ownership

Refer to Item 7.A: "Major Shareholders" in this Annual Report.

F. Disclosure of a Registrant's Action to Recover Erroneously Awarded Compensation

Not applicable.

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, 2024 by:

- each of the members of our 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 105,212,527 ordinary shares outstanding as at December 31, 2024. 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, 2024, 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
Major Shareholders:		
Eli Lilly & Co. [1]	16,895,100	16.1 %
Van Herk [2]	11,461,995	10.9 %
Adage Capital Management, L.P. [3]	9,602,280	9.1 %
Board Members		
James Shannon [4]	252,169	0.2 %
Dinko Valerio [5]	907,243	0.9 %
Theresa Heggie [6]	339,199	0.3 %
Alison F. Lawton [7]	186,521	0.2 %
Bart Filius [8]	95,735	0.1 %
Begoña Carreño [9]	19,331	— %
Martin Maier [10]	875	— %
Daniel de Boer [11]	3,404,598	3.2 %
René Beukema [12]	1,418,051	1.3 %
Gerard Platenburg [13]	1,615,761	1.5 %
All board members as a group (10 persons) [14]	**8,239,483**	**7.7 %**

1 Information is based in part on a report on Schedule 13G/A filed by Eli Lilly and Company (“Lilly”), an Indiana corporation, on December 23, 2022. 9,381,586 shares were issued to Lilly in December 2022, as part of the Company’s amended and restated research and collaboration agreement with Lilly, and 3,523,538 shares were issued to Lilly in October 2024, as part of the Company’s concurrent private placement with Lilly. The address of Lilly is Lilly Corporate Center, Indianapolis, Indiana 46285.

2 Information is based on a report on Schedule 13G/A filed on February 14, 2025 by (i) Van Herk Investments B.V (“VHI”), with respect to Ordinary Shares beneficially owned by it, (ii) Van Herk Investments THI B.V. (“VHIT”), with respect to Ordinary Shares beneficially owned by VHI, (iii) Van Herk Private Equity Investments B.V. (“VHPI”), with respect to Ordinary Shares beneficially owned by VHI and VHIT, (iv) Stichting Administratiekantoor Penulata (“Penulata”), with respect to Ordinary Shares beneficially owned by VHI, VHIT and VHPI, (v) Van Herk Management Services B.V. (“VHMS”), with respect to Ordinary Shares beneficially owned by VHI, VHIT and VHPI, (vi) Onroerend Goed Beheer- en Beleggingsmaatschappij A. van Herk B.V. (“OGBBA”), with respect to Ordinary Shares beneficially owned by VHI, VHIT, VHPI and VHMS, (vii) A. van Herk Holding B.V. (Holdings), with respect to Ordinary Shares beneficially owned by VHI, VHIT, VHPI, VHMS and OGBBA, (viii) Stichting Administratiekantoor Abchrys (“Abchrys”), with respect to Ordinary Shares beneficially owned by VHI, VHIT, VHPI, VHMS, OGBBA and Holdings, and (ix) Adrianus van Herk (“Mr. van Herk”) with respect to Ordinary Shares beneficially owned by VHI, VHIT, VHPI, VHMS, OGBBA, Holdings, Penulata and Abchrys. Mr. van Herk is (i) an investor, (ii) the holder of all of the depositary receipts issued by Penulata and Abchrys, (iii) the sole board member of Penulata and Abchrys, and (iv) the sole managing director of VHMS, OGBBA and Holdings. Penulata holds substantially all of the issued and outstanding shares of VHPI. VHPI is the sole shareholder of VHIT. VHIT is the sole shareholder of VHI. Abchrys holds substantially all of the issued and outstanding shares of Holdings. Holdings is the sole shareholder of OGBBA. OGBBA is the sole shareholder of VHMS. VHMS is the sole managing director of VHI, VHIT and VHPI. The address of each of Mr. van Herk, VHI, VHIT, VHPI, Penulata, VHMS, OGBBA, Holdings and Abchrys is Lichtenauerlaan 30, 3062 ME Rotterdam, the Netherlands.

3 Information is based on a report on Schedule 13G filed on February 12, 2025, by (i) Adage Capital Management, L.P., ("ACM"), as the investment manager of Adage Capital Partners, L.P., ("ACP"), with respect to the ordinary shares, directly held by ACP, (ii) Robert Atchinson ("Mr. Atchinson"), as (1) managing member of Adage Capital Advisors, L.L.C., a limited liability company ("ACA"), managing member of Adage Capital Partners GP, L.L.C., a limited liability company ("ACPGP"), general partner of ACP and (2) managing member of Adage Capital Partners LLC, a Delaware limited liability company ("ACPLLC"), general partner of ACM, with respect to the Ordinary Shares directly held by ACP; and (iii) Phillip Gross ("Mr. Gross"), as (1) managing member of ACA, managing member of ACPGP and (2) managing member of ACPLLC, general partner of ACM, with respect to the Ordinary

Shares directly held by ACP. The total number of shares beneficially owned consists of 9,602,280 ordinary shares directly held by ACP. The address of the business office of each of the Reporting Persons is 200 Clarendon Street, 52nd Floor, Boston, Massachusetts 02116.

4 Consists of 61,538 ordinary shares and options to acquire 190,631 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

5 Consists of 725,692 ordinary shares and options to acquire 181,551 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024. 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 Keizersgracht 290A, 1016 EW, Amsterdam, the Netherlands.

6 Consists of 37,489 ordinary shares and options to acquire 301,710 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

7 Consists of options to acquire 186,521 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

8 Consists of options to acquire 95,735 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

9 Consists of options to acquire 19,331 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

10 Consists of options to acquire 875 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

11 Consists of options to acquire 3,404,598 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

12 Consists of 460,000 ordinary shares and options to acquire 958,051 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

13 Consists of 824,388 ordinary shares and options to acquire 791,373 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

14 Consists of 2,109,107 ordinary shares and options to acquire 6,130,376 ordinary shares that are currently exercisable or will be exercisable within 60 days after December 31, 2024.

Holdings by U.S. Shareholders

As at December 31, 2024, 99.98% 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, 2024, 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 27 to the financial statements included elsewhere in this Annual Report.

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 and incorporated herein by reference.

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, 2024, we believe no proceedings exists of which the outcome, if determined adversely, would 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 board determines. After reservation by the board of any profit, the remaining profit will be at the disposal of the general meeting of shareholders. The board is permitted, subject to certain requirements, to declare interim dividends without the approval of the general meeting of shareholders.

Distributions shall be payable in such currency as determined by our board. We intend that distributions, if any, shall be payable on such date as determined by our board. Our 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 Nasdaq. Our ordinary shares are currently trading on Nasdaq Capital 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 June 22, 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 February 27, 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. On June 10, 2021, the articles of association were amended to (i) combine the existing compensation committee and nominating and corporate governance committee into one committee, to be named the compensation, nominating and corporate governance committee, and to establish a new research and development committee, and (ii) to increase the authorized share capital. On May 23, 2024, the articles of association were amended to implement a one-tier governance structure of one board comprising executive and non-executive directors.

Our Company is registered with the Dutch Trade Register of the Chamber of Commerce (‘*handelsregister van de Kamer van Koophandel*’) 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, 2024, our authorized share capital is € 13,600,000, divided into 170,000,000 ordinary shares and 170,000,000 preferred shares, each with a nominal value of € 0.04. Under Dutch law, our authorized share capital is the maximum capital that we may issue without amending our articles of association Our ordinary shares are listed on the Nasdaq Capital Market under the symbol “PRQR.”

We have listed our ordinary shares in registered form and our shares are not certificated. We have appointed Equiniti Trust Company, LLC (formerly known as 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 Capital 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 at least 25% will be due upon issuance, and may also be issued against the Company's reserves if so requested by the protection 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 board. The sub-register shall be kept by our agent on behalf of the board. Our shareholders' register includes the names and addresses and other relevant details of all holders of registered shares, and shows 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 of usufruct ('*vruchtgebruik*') or a right of pledge ('*pandrecht*') in respect of any shares. Our registered ordinary shares are held through Depository Trust & Clearing Corporation ("DTCC") and therefore DTCC is 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 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 board. Our general meeting of shareholders may authorize our 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.

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 pre-emptive 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 pre-emptive 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 pre-emptive 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 board. Our general meeting of shareholders may authorize our board to restrict or exclude the pre-emptive rights in respect of newly issued ordinary shares. Such authorization for the 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 pre-emptive 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 pre-emptive rights or to designate our 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 22, 2024, our general meeting of shareholders adopted a resolution pursuant to which the board was delegated the authority for a period of 5 years from the date of the resolution of the general meeting of shareholders to, in accordance with applicable laws and Nasdaq listing rules: (a) issue ordinary shares up to 100% of the Company's authorized share capital for general purposes and issuances under Company's equity incentive or stock option plans with the proviso that the issuances under equity incentive or stock option plans are limited to 15% of the Company's issued share capital from time-to-time (minus any treasury shares); (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.

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 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.

On May 22, 2024, our general meeting of shareholders adopted a resolution pursuant to which the board was delegated the authority to perform acquisitions by the Company of (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 a resolution upon a proposal of our 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 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 can be held in Leiden, Amsterdam, Rotterdam, Schiphol Airport (municipality Haarlemmermeer), The Hague, 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 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 board has 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 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 board convene a shareholders' meeting and that the board has not 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 board. In addition, the agenda for a general meeting of shareholders may include such items as have been included therein by our 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 60th day before the day that the relevant general meeting of shareholders is to be 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 and 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 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 chairperson of the general meeting of shareholders may, in his or her 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 board. If the chairman of our board is absent and has not charged another person to chair the meeting in his place, the non-executive board members present at the meeting shall appoint one of themselves to be chairperson. If no non-executive board members are present at the general meeting of shareholders, the general meeting of shareholders will be chaired by our Chief Executive Officer or, if our Chief Executive Officer is absent, by another executive board member present at the meeting and, if none of them is present, the general meeting of shareholders shall appoint its own chairperson. The person who should chair the meeting may appoint another person in his or her stead.

The chairperson of the general meeting of shareholders may decide at his or her discretion to admit other persons to the meeting. The chairperson 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 chairperson 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 chairperson of the general meeting of shareholders is authorized to eject any person from the general meeting of shareholders if the chairperson 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 board members.

Voting rights may be exercised by shareholders or by a duly appointed proxy holder (the written proxy being acceptable to the chairperson 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 chairperson 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 chairperson of the general meeting of shareholders shall decide on the method of voting and may determine the voting procedure. The determination made by the chairperson of the general meeting of shareholders with regard to the results of a vote shall be decisive. However, where the accuracy of the chairperson'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 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 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 Board Liability

Pursuant to Dutch law, we are required to publish our annual accounts within eight days after adoption and ultimately within 12 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 five months by the general meeting of shareholders on account of special circumstances, our board will prepare the annual accounts. The annual accounts must be accompanied by an auditor's certificate, a report of the 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 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 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 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. Any amount remaining out of the profit is carried to reserve as the board determines. After reservation by the board of any profit, the remaining profit will be at the disposal of the general meeting of shareholders. The board is permitted, subject to certain requirements, to declare interim dividends without the approval of the general meeting of shareholders.

Distributions shall be payable in such currency as determined by our board. We intend that distributions, if any, shall be payable on such date as determined by our board. Our 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 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 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 in the amount of the nominal value of the preferred shares (to the extent paid-up) plus unpaid accrued dividends and deficits (if any) in preferred dividends, and (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 are currently 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.

Dutch 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) holds 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*') (the "Enterprise Chamber") 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 notice in a newspaper with a national circulation.

A shareholder that holds 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, and 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 (e.g. 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 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. 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 (‘*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 ('*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*') of a company resident in the Netherlands;

(iv) pension funds, investment institutions ('*fiscale beleggingsinstellingen*'), exempt investment institutions ('*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 EU, Norway, Liechtenstein, Iceland or any other state with which the Netherlands have agreed to exchange information in line with international standards;

(v) holders of ordinary shares that are entities that are resident of Aruba, Curaçao or St. Maarten and have a business enterprise which is carried on through a permanent establishment (vaste inrichting) or permanent representative (vaste vertegenwoordiger) located on Bonaire, Sint Eustatius or Saba to which the ordinary shares are attributable; and

(vi) holders of ordinary shares who are not considered the beneficial owner of the ordinary shares and/or the income and/or capital gains derived therefrom.

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 ('*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 taxation convention 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 ('*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) Conditional withholding tax on dividends

A Dutch conditional withholding tax applies to (deemed) dividend distributions made by us, to an affiliated (gelieerde) entity if such entity (i) is considered to be resident (gevestigd) in a jurisdiction that is listed in the yearly updated Dutch Regulation on low-taxing states and non-cooperative jurisdictions for tax purposes (Regeling laagbelastende staten en niet-coöperatieve rechtsgebieden voor belastingdoeleinden), or (ii) has a permanent establishment located in such jurisdiction to which the dividend is attributable, or (iii) is entitled to the dividend payable for the main purpose or one of the main purposes to avoid taxation of another person, or (iv) is not considered to be the recipient of the dividend in its jurisdiction of residence because such jurisdiction treats another (lower-tier) entity as the recipient of the dividend (hybrid mismatch), or (v) is not treated as resident anywhere (also a hybrid mismatch), or (vi) is a reverse hybrid whereby the jurisdiction of residence of a higher-tier beneficial owner (achterliggende gerechtigde) that has a qualifying interest (kwalificerend belang) in the reverse hybrid treats the reverse hybrid as tax transparent and that higher-tier beneficial owner would have been taxable based on one (or more) of the items in (i) – (v) above had the dividend been due to him directly, all within the meaning of the Dutch Withholding Tax Act 2021 (Wet bronbelasting 2021).

Dutch conditional withholding tax is levied at a rate equal to the highest Dutch corporate income tax rate (25.8% in 2025). The tax base for the Dutch conditional withholding tax on dividends is in line with the description of the term 'dividends' set forth above under "Taxation – Taxation in the Netherlands – (a) Dividend Withholding Tax". If a dividend is subject to both Dutch dividend withholding tax and conditional withholding tax, the amount of Dutch dividend withholding tax levied in respect of the dividend reduces the conditional withholding tax due in respect thereof.

(c) 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 49.50%), 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 (*'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 (*'normaal, actief vermogensbeheer'*) or derives benefits from the ordinary shares that are taxable as benefits from other activities (*'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 the holder's net investment asset base (*'rendementsgrondslag',* 'Box 3'). Box 3 is a taxation of the return on income from savings and (passive) investments. Taxation only occurs to the extent the fair market value of the assets reduced by the liabilities exceeds a threshold (*'heffingvrij vermogen'*) of € 57,000 (or € 114,000 in case of a fiscal partnership).

In short, the fair market value of the Box 3 assets per 1 January of each calendar year is deemed to yield income at a rate which depends on the type of asset: savings (0,92%), investments/other assets (6,04%) or debts (2,46%). This deemed income is then taxed at a flat rate of 36% (2024/2025). However, on 6 June 2024 the Dutch Supreme Court ruled that the current system of taxation in relation to an individual's savings and investments based on a 'deemed return' contravenes with Section 1 of the First Protocol to the European Convention on Human Rights in combination with Section 14 of the European Convention on Human Rights if the deemed return applicable to the savings and investments exceeds the actual return in the respective calendar year. In these rulings, the Dutch Supreme Court has also provided guidance for calculating the actual return. If the individual demonstrates that the actual return – calculated in accordance with the guidelines of the Dutch Supreme Court – is lower than the deemed return, only the actual return should be taxed under the regime for savings and investments.

The Dutch government envisages to implement new Box 3 legislation based on actual returns instead of deemed returns. However, it is announced that implementing such legislation is only feasible as of 2028 at the earliest.

(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 25.8% (a corporate income tax rate of 19% applies with respect to taxable profits up to € 200,000) (rate for 2025).

(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'*) 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 ('*normaal, actief vermogensbeheer'*) and does not derive benefits from the ordinary shares that are taxable as benefits from other activities ('*resultaat uit overige werkzaamheden*') in the Netherlands.

(d) 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.

(e) 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 disposing the ordinary shares.

(f) Residence

A shareholder will not become resident or deemed resident in the Netherlands for tax purposes by reason only of holding or disposing 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 (including S corporations), or persons that will hold our shares through such an entity;
- 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 (other than the Dutch tax considerations discussed above) 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 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 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 "PFIC 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 an ordinary share will be taxable to the U.S. holder as a dividend to the extent the distribution is made out 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 each such ordinary share. 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 all distributions will be reported as dividends, even if a 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 "PFIC 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 an ordinary share 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 in that ordinary share. Subject to the discussion under "PFIC 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 equal the cost of such ordinary share. Capital gain from the sale, exchange, or other taxable disposition of ordinary shares by 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 share 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.

(c) 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.

(d) PFIC considerations

If we are classified as a 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. We will inform our shareholders in our annual report on Form 20-F if we determine that we are a PFIC.

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 either: (i) at least 75% of its gross income is "passive income," referred to herein as the Income Test or (ii) at least 50% of the average quarterly value of its total gross assets (for which purpose, assuming we are treated as a publicly traded company pursuant to Section 1297(e)(3) of the Code, 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," Referred to herein as the Asset Test.

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. For purposes of the PFIC tests, gross income and gross assets of a corporation include its proportionate share of the gross income and gross assets of any other corporation of which it owns directly or indirectly at least 25% by value of the stock.

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 U.S. holder makes a purging election, which allows a shareholder to purge the continuing PFIC taint by either making a deemed sale election or, under certain conditions, a deemed dividend election. In addition, if we are classified as a PFIC, then a U.S. holder of our shares will be deemed to own, proportionately, shares we own of lower-tier corporations. If any such lower-tier corporation is a PFIC, then a U.S. holder will be treated as an (indirect) shareholder of that lower-tier PFIC.

Based on the average value of our gross assets and the composition of our income, we believe that we were not a PFIC during the 2024 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 on whether we will 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 unless you make one of the elections described below, a 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 applicable to you (other than income allocated to the current period or any taxable period before we became a PFIC, which would be subject to tax at the U.S. holder's regular ordinary income rate for the current year and would not be subject to the interest charge discussed below), and (c) the interest charge generally applicable to underpayments of tax had been imposed on the taxes deemed to have been payable in those years. In addition, dividend distributions made to you will not qualify for the lower rates of taxation applicable to long-term capital gains discussed above under "Distributions."

Certain elections exist that may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment (such as mark-to-market treatment) of the common shares. If a U.S. holder makes the mark-to-market election, the U.S. holder generally will recognize as ordinary income any excess of the fair market value of the ordinary shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ordinary shares over their fair market value at the end of the taxable year, but only to the extent of the net amount of income previously included as a result of the mark-to-market election 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 Capital 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.

Alternatively, you may avoid the general tax treatment for PFICs described above by electing to treat us as a QEF under Section 1295 of the Code, or QEF, for each of the taxable years during your holding period that we are a PFIC. If a QEF election is not in effect for the first taxable year in your holding period in which we are a PFIC, a QEF election generally can only be made if you elect to make an applicable deemed sale or deemed dividend election on the first day of your taxable year in which the PFIC becomes a QEF pursuant to the QEF election. The deemed gain or deemed dividend recognized with respect to such an election would be subject to the general tax treatment of PFICs discussed above. We intend to determine our PFIC status at the end of each taxable year and to satisfy any applicable record keeping and reporting requirements that apply to a QEF, and will endeavor to provide to you, for each taxable year that we determine we are a PFIC, a PFIC Annual Information Statement containing information necessary for you to make a QEF election with respect to us. We may elect to provide such information on our website.

If you make a QEF election with respect to a PFIC, you will be taxed currently on your pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is a PFIC, even if no distributions are received. Any distributions we make out of our earnings and profits that were previously included in your income under the QEF election would not be taxable to you. Your tax basis in your common shares would be increased by an amount equal to any income included under the QEF election and decreased by any amount distributed on the common shares that is not included in your income. In addition, you will recognize capital gain or loss on the disposition of your common shares in an amount equal to the difference between the amount realized and your adjusted tax basis in the common shares, each as determined in U.S. dollars. Once made, a QEF election remains in effect unless invalidated or terminated by the IRS or revoked by the shareholder. A QEF election can be revoked only with the consent of the IRS. You will not be currently taxed on the ordinary income and net capital gain of a PFIC with respect to which a QEF election was made for any taxable year of the non-U.S. corporation that such corporation does not satisfy the PFIC Income Test or Asset Test. You are urged to consult your own tax advisors regarding the availability of, and procedure for making, any deemed gain, deemed dividend or QEF election.

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 who are indirect shareholders of lower-tier PFICs, as discussed above.

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 PFIC or QEF) with respect to the company (and with respect to any lower-tier PFICs) 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.

(e) 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.

(f) 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 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 the information reporting requirements of the Exchange Act applicable to foreign private issuers and under those requirements will file reports with the SEC. Those reports may be inspected without charge on the websites described below. As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our senior management, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as United States companies whose securities are registered under the Exchange Act. Nevertheless, we will file with the SEC an Annual Report on Form 20-F containing financial statements that have been examined and reported on, with an opinion expressed by an independent registered public accounting firm.

We maintain a corporate website at *www.ProQR.com*. We intend to post our Annual Report on our website promptly following it being filed with the SEC. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

The SEC maintains a website (*www.sec.gov*) that contains reports, proxy and information statements and other information regarding registrants, such as ProQR, that file electronically with the SEC.

With respect to references made in this Annual Report to any contract or other document relating to ProQR, such references are not necessarily complete and you should refer to the exhibits attached or incorporated by reference to this Annual Report for copies of the actual contract or document

I. Subsidiary information

Not applicable.

J. Annual Report to Security Holders

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 (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). 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 do not engage in hedging transactions; we use natural hedging by utilizing primary instruments 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, 2024 our net position of financial instruments denominated in U.S. Dollars was a net asset of € 5,898,000 (2023: net liability of € 726,000). 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, 2024, we had a loan with a fixed interest rate, totaling € 4,582,000 (2023: several loans totaling € 4,292,000).

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, except with Lilly. 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 mid-2027. 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 and Chief Financial Officer, 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, 2024). 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, our Chief Executive Officer and Chief Financial Officer have concluded that these disclosure controls and procedures are effective as at December 31, 2024.

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 GAAP 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 GAAP, 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 GAAP. 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, 2024. Based on this assessment, management concluded that the Company's internal control over financial reporting was effective as at December 31, 2024.

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 Board of Directors
ProQR Therapeutics N.V.:

Opinion on Internal Control Over Financial Reporting

We have audited ProQR Therapeutics N.V. and subsidiaries' (the "Company") internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated statements of financial position of the Company as of December 31, 2024 and 2023, the related consolidated statements of profit or loss and comprehensive income, changes in equity, and cash flows for each of the years in the three-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements), and our report dated March 13, 2025 expressed an unqualified opinion on those consolidated financial statements.

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 of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included 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/ KPMG Accountants N.V.

Amstelveen, the Netherlands
March 13, 2025

D. Changes in Internal Control over Financial Reporting

During the year ended December 31, 2024, 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 16: [Reserved]

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 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 board members and our employees, including our Chief Executive Officer, Chief Financial Officer, 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 material 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 for our Board members or other executive officers, 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.

In addition to the Code of Business Conduct and Ethics we have adopted a whistleblower policy as contemplated in the DCGC, which is also posted on our company website at www.ProQR.com.

Item 16C: Principal Accountant Fees and Services

For the years ended December 31, 2024, 2023 and 2022, our independent public accounting firm is KPMG Accountants N.V., Amstelveen, the Netherlands, PCAOB Auditor ID 1012.

The information required is included in Note 28 to the financial statements included elsewhere in this Annual Report.

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 2024, 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

Not applicable.

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 do not intend to follow Nasdaq's requirements regarding the independence of all members of the compensation, nominating and corporate governance committee. Dutch law and the DCGC do not require that the compensation, nominating and corporate governance committee be composed entirely of independent directors and only requires a mere majority. In accordance with Dutch law and the DCGC, our compensation, nominating and corporate governance committee consists of a majority of members who qualify as independent under applicable Nasdaq standards and under the DCGC.

- We do not intend to follow Nasdaq's requirements regarding Nasdaq Listing Rule 5605(b)(2), which mandates that independent directors must meet at regularly scheduled executive sessions where only independent directors are present. In accordance with Dutch law and the DCGC, our directors may choose to meet in executive sessions at their discretion.

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 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 senior management, 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.

Item 16I: Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

Item 16J: Insider Trading Policies

We have adopted a Securities Trading Policy ("Securities Trading Policy"), which, among other things, governs the purchase, sale and other dispositions of our securities by our directors, executive officers and employees. Our Securities Trading Policy aims to promote compliance with applicable insider trading laws, rules and regulations, and the Nasdaq listing standards. A copy of our Securities Trading Policy is filed as an exhibit to this Annual Report.

Item 16K: Cybersecurity

ProQR uses, stores and processes data for and about our employees, partners and suppliers. We have implemented an information security management framework ("ISM") – which includes policies, operating procedures, and processes – that is designed to identify, assess, and mitigate risks from cybersecurity threats to this data and our systems.

Governance Related to Cybersecurity Risks

Our board has primary responsibility for overseeing our cybersecurity risk management program, as set forth in the ISM. Our board has tasked the Chief People & Operations Officer as the member of the executive committee with day-to-day management of the ISM. Assisting the Chief People & Operations Officer in managing the ISM is an ISM Committee of senior team members and advisors, which currently consists of the Chief People & Operations Officer and representatives from information technology, legal, and privacy.

Our IT Director has responsibility for managing and implementing the cybersecurity program and reports directly to the Chief People & Operations Officer, and has over 20 years of experience in the field of IT, including in network and systems security. We have also appointed an Information Security Officer to assist in managing our cybersecurity threat management program. Our Information Security Officer has broad experience in the IT field for over 30 years, including with respect to information security, internal audits, training and SOX compliance. Additionally, our Information Security Officer has a range of IT- and cybersecurity-related certifications issued by the Professional Evaluation and Certification Board.

Our audit committee, per the stipulations of our audit committee charter, oversees the ISM, including the assessment of data governance, security initiatives, significant existing and emerging cybersecurity risks, cybersecurity incidents, and any disclosure obligations arising from such incidents, as applicable.

Our audit committee convenes periodically to assess the company's applications of information and communication technology, including risks relating to cybersecurity, as appropriate. The Chief People & Operations Officer and ISM Committee report to our audit committee on relevant cybersecurity matters and associated risks as needed.

Cyber Risk Management and Strategy

Our cybersecurity risk management program is integrated within our business continuity planning and overall risk management. Under the guidance of the ISM Committee and the Information Security Officer, and with the support of our third-party information technology providers, our ISM addresses areas such as:

- Assessment and treatment of cyber and information security risks
- Assessment and treatment of information technology service continuity risks
- Assessment of cybersecurity risks related to certain third-party vendors, pursuant to our Vendor Management Policy

Additionally, we have an employee education program that is designed to raise awareness of cybersecurity threats to reduce our vulnerability to such threats as well as to encourage consideration of cybersecurity risks across functions. Further, we maintain an Incident Management Policy designed to assist us in identifying, responding to, and recovering from cybersecurity incidents.

As of the date of this report, we have not identified cybersecurity threats that have materially affected or are reasonably likely to materially affect the Company, including our business strategy, results of operations, or financial condition. However, we have from time to time, experienced threats and security incidents relating to our and our third-party vendors' information systems. For information regarding cybersecurity risks that may affect the Company, see Part I, Item 3.D: "Risk Factors—Risks Related to Our Organization, Structure and Operations" in this Annual Report.

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

The Exhibits listed in the Exhibit Index at the end of this Annual Report are filed as Exhibits to this Annual Report.

Index of Exhibits

Exhibit No.	Description
1.1*	Amended Articles of Association of the Registrant effective as of May 23, 2024
2.1	Registration Rights Agreement, dated as of December 29, 2021, by and between the Registrant and the parties named therein (incorporated by reference to Exhibit 10.3 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on December 30, 2021)
2.2	Form of Warrant Agreement issued to lenders identified therein (incorporated by reference to Exhibit 10.4 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on December 30, 2021)
4.1#*	ProQR Therapeutics N.V. Equity Incentive Plan
4.2#	Form of Management Services Agreement by and between the Registrant and Daniel 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)
4.3	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)
4.4*	Addendum to Form of Call Option Agreement by and between the Registrant and Stichting Continuity ProQR Therapeutics dated as of November 6, 2018
4.5*	Addendum to Form of Call Option Agreement by and between the Registrant and Stichting Continuity ProQR Therapeutics dated as of February 27, 2025
4.6*	Form of Indemnification Agreement for the Directors and Officers of the Registrant
4.7	English translation of Lease Agreement by and between the Registrant and The Netherlands Organisation for applied scientific research, 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)
4.8††	English translation of Lease Agreement by and between the Registrant and Leeds Investment I B.V., dated as of September 30, 2019 (incorporated by reference to Exhibit 4.7 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2019 (File No. 001-36622) filed on March 31, 2020)
4.9†	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)
4.10†	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)

Exhibit No.	Description
4.11†	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)
4.12†	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)
4.13††	Asset Purchase Agreement by and between the Registrant and Wings Therapeutics, Inc., dated as of May 22, 2019 (incorporated by reference to Exhibit 4.14 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2019 (File No. 001-36622) filed on March 31, 2020)
4.14††	Subscription Agreement by and between the Registrant and Wings Therapeutics, Inc., dated as of May 22, 2019 (incorporated by reference to Exhibit 4.15 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2019 (File No. 001-36622) filed on March 31, 2020)
4.15††	Supply and Services Agreement, by and between the Registrant and Nitto Denko Avecia Inc., dated as of July 12, 2019 (incorporated by reference to Exhibit 4.16 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2019 (File No. 001-36622) filed on March 31, 2020)
4.16*	Description of the Registrant's Securities
4.17†	Research and Collaboration Agreement, dated as of September 3, 2021, by and among the Registrant, Eli Lilly and Company and ProQR Therapeutics VIII B.V. (incorporated by reference to Exhibit 10.1 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on September 8, 2021)
4.18	Share Purchase Agreement, dated as of September 3, 2021, by and between the Registrant and Eli Lilly and Company (incorporated by reference to Exhibit 10.2 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on September 8, 2021)
4.19	Amended and Restated Research and Collaboration Agreement, dated as of December 21, 2022, by and among the Registrant, Eli Lilly and Company and ProQR Therapeutics VIII B.V. (incorporated by reference to Exhibit 10.1 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on December 23, 2022)
4.20	Share Purchase Agreement, dated as of December 21, 2022, by and between the Registrant and Eli Lilly and Company (incorporated by reference to Exhibit 10.2 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on December 23, 2022)
4.21	Controlled Equity OfferingSM Sales Agreement, dated November 4, 2021, by and between the Registrant and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form F-3 (File No. 333-260775) filed on November 4, 2021)

Exhibit No.	Description
4.22	Amended and Restated Asset Purchase Agreement, dated as of December 7, 2023, by and among ProQR Therapeutics N.V., ProQR Therapeutics I B.V., ProQR Therapeutics II B.V. and ProQR Therapeutics IV B.V. and Laboratoires Théa S.A.S. (incorporated by reference to Exhibit 10.1 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on December 8, 2023)
4.23	Share Purchase Agreement, dated as of October 22, 2024, by and between the Registrant and Eli Lilly and Company (incorporated by reference to Exhibit 10.1 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) filed on October 25, 2024)
8.1*	Subsidiaries of the Registrant
11.1*	ProQR Therapeutics N.V. Securities Trading Policy
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 KPMG Accountants N.V., Independent Registered Public Accounting Firm
97.1	ProQR Therapeutics N.V. Compensation Recovery Policy (incorporated by reference to Exhibit 97.1 to the Registrant's Annual Report on Form 20-F for the fiscal year ended December 31, 2023 (File No. 001-36622) filed on March 13, 2024)
101.INS*	XBRL Instance Document.
101.SCH*	XBRL Taxonomy Extension Schema Document.
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.
104*	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

* 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 13, 2025

PROQR THERAPEUTICS N.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: Chief Executive Officer

By: /s/ Jurriaan Dekkers

Name: Jurriaan Dekkers

Title: Chief Financial Officer

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Consolidated Financial Statements as at December 31, 2024 and 2023 and for the Years Ended December 31, 2024, December 31, 2023 and December 31, 2022

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors
ProQR Therapeutics N.V.:

Opinion on the Consolidated 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, 2024 and 2023, the related consolidated statements of profit or loss and comprehensive income, changes in equity, and cash flows for each of the years in the three-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

We also have 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, 2024, 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 13, 2025 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Allocation of the achievement of development milestones to the applicable performance obligation in the Eli Lilly Research and Collaboration Agreement

As disclosed in Note 17 of the financial statements, ProQR reached development milestones for certain targets under the Eli Lilly Research and Collaboration Agreement and attributed these development milestone amounts (EUR 5,096,000) to the single combined performance obligation of the contract.

We identified the allocation of the achievement of development milestones to the applicable performance obligation as a critical audit matter. This is due to the high degree of subjective and challenging auditor judgement required to determine whether the variable consideration for development milestones reached during the research and development activities is linked to the identified single combined performance obligation or to separate performance obligations.

The primary procedures we performed to address this critical audit matter included the following:

We obtained an understanding, evaluated the design and tested the operating effectiveness of the control over the Company's revenue recognition process for allocation of the achievement of development milestones to the identified performance obligation.

We evaluated whether the achieved development milestones were appropriately allocated to the applicable performance obligation in accordance with relevant accounting guidance by obtaining and reading the Eli Lilly and Company Research and Collaboration Agreement, evaluating its terms and conditions, and conducting inquiries with R&D personnel.

/s/ KPMG Accountants N.V.

We have served as the Company's auditor since 2020.

Amstelveen, The Netherlands
March 13, 2025

PROQR THERAPEUTICS N.V.

Consolidated Statement of Financial Position

		December 31, 2024	December 31, 2023
		(€ in thousands)	
Assets			
Property, plant and equipment	*7*	14,113	16,897
Investments in financial assets	*9*	—	—
Non-current assets		**14,113**	**16,897**
Other taxes	*10*	690	523
Prepayments and other receivables	*11*	3,747	1,538
Cash and cash equivalents	*12*	149,408	118,925
Current assets		**153,845**	**120,986**
Total assets		**167,958**	**137,883**
Shareholders' equity			
Share capital		4,308	3,370
Share premium		483,812	412,894
Reserves		27,598	25,976
Accumulated deficit		(427,158)	(400,850)
Equity attributable to owners of the Company	*13*	**88,560**	**41,390**
Non-controlling interests		—	—
Total equity		**88,560**	**41,390**
Liabilities			
Borrowings	*14*	—	4,292
Lease liabilities	*25*	11,067	13,828
Deferred income	*15*	29,429	44,170
Non-current liabilities		**40,496**	**62,290**
Borrowings	*14*	4,582	—
Lease liabilities	*25*	1,567	1,614
Derivative financial instruments	*14*	468	311
Trade payables		16	1,541
Social securities and other taxes		1,478	1,659
Deferred income	*15*	21,942	20,569
Other current liabilities	*16*	8,849	8,509
Current liabilities		**38,902**	**34,203**
Total liabilities		**79,398**	**96,493**
Total equity and liabilities		**167,958**	**137,883**

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

PROQR THERAPEUTICS N.V.

Consolidated Statement of Profit or Loss and Comprehensive Income

		Year Ended December 31,		
		2024	2023	2022
			(€ in thousands)	
Revenue	*17*	18,905	6,514	3,594
Other income	*18*	640	3,011	765
Research and development costs		(36,356)	(25,148)	(50,867)
General and administrative costs		(13,661)	(16,236)	(18,651)
Total operating costs	*19*	(50,017)	(41,384)	(69,518)
Operating result		**(30,472)**	**(31,859)**	**(65,159)**
Financial income	*21*	3,251	2,593	4,863
Financial expense	*21*	(1,084)	(1,458)	(5,127)
Results related to associates	*8*	—	—	(8)
Gain on disposal of associate	*9*	—	—	—
Gain on disposal of subsidiary	*14*	—	92	—
Results related to derecognition of financial liabilities	*14*	—	1,866	(1,390)
Results related to financial liabilities measured at FVTPL	*22*	345	953	2,713
Result before corporate income taxes		**(27,960)**	**(27,813)**	**(64,108)**
Corporate income taxes	*23*	197	78	(96)
Result for the year		**(27,763)**	**(27,735)**	**(64,204)**
Other comprehensive income				
Items that will never be reclassified to profit or loss				
Fair value loss on investment in financial asset designated as at FVTOCI		—	(621)	—
Items that are or may be reclassified to profit or loss				
Foreign operations – foreign currency translation differences		533	(395)	782
Total comprehensive loss		**(27,230)**	**(28,751)**	**(63,422)**
Result attributable to				
Owners of the Company		(27,763)	(28,119)	(64,424)
Non-controlling interests		—	384	220
		(27,763)	**(27,735)**	**(64,204)**
Total comprehensive loss attributable to				
Owners of the Company		(27,230)	(29,135)	(63,642)
Non-controlling interests		—	384	220
		(27,230)	**(28,751)**	**(63,422)**
Share information	*24*			
Weighted average number of shares outstanding		86,086,486	81,011,438	71,641,305
Earnings per share for result attributable to the equity holders of the Company (expressed in Euro per share)				
Basic and diluted loss per share		€ (0.32)	€ (0.35)	€ (0.90)

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

PROQR THERAPEUTICS N.V.
Consolidated Statement of Changes in Equity

	Attributable to Equity Holders of the Company								
	Share Capital	Share Premium	Equity Settled Employee Benefit Reserve	Option premium on convertible loans	Translation Reserve	Accumulated Deficit	Total	Non-controlling Interests	Total Equity
	(€ in thousands)	(€ in thousands)	(€ in thousands)	(€ in thousands)	(€ in thousands)	(€ in thousands)	(€ in thousands)	(€ in thousands)	(€ in thousands)
Balance at January 1, 2022	**2,995**	**398,309**	**28,443**	**1,426**	**430**	**(316,889)**	**114,714**	**(604)**	**114,110**
Result for the year	—	—	—	—	—	(64,424)	(64,424)	220	(64,204)
Other comprehensive income	—	—	—	—	782	—	782	—	782
Recognition of share-based payments	—	—	2,869	—	—	—	2,869	—	2,869
Issue of ordinary shares	375	14,197	—	—	—	—	14,572	—	14,572
Equity component of convertible loan	—	—	—	(1,426)	—	(56)	(1,482)	—	(1,482)
Shares options lapsed	—	—	(1,817)	—	—	1,817	—	—	—
Shares options exercised	—	34	(443)	—	—	443	34	—	34
Balance at December 31, 2022	**3,370**	**412,540**	**29,052**	**—**	**1,212**	**(379,109)**	**67,065**	**(384)**	**66,681**
Result for the year	—	—	—	—	—	(28,119)	(28,119)	384	(27,735)
Other comprehensive loss	—	—	—	—	(395)	(621)	(1,016)	—	(1,016)
Recognition of share-based payments	—	—	3,106	—	—	—	3,106	—	3,106
Shares options lapsed	—	—	(6,280)	—	—	6,280	—	—	—
Shares options exercised	—	354	(719)	—	—	719	354	—	354
Balance at December 31, 2023	**3,370**	**412,894**	**25,159**	**—**	**817**	**(400,850)**	**41,390**	**—**	**41,390**
Result for the year	—	—	—	—	—	(27,763)	(27,763)	—	(27,763)
Other comprehensive income	—	—	—	—	533	—	533	—	533
Recognition of share-based payments	—	—	2,544	—	—	—	2,544	—	2,544
Issue of ordinary shares	938	70,695	—	—	—	—	71,633	—	71,633
Shares options lapsed	—	—	(1,040)	—	—	1,040	—	—	—
Shares options exercised	—	223	(415)	—	—	415	223	—	223
Balance at December 31, 2024	**4,308**	**483,812**	**26,248**	**—**	**1,350**	**(427,158)**	**88,560**	**—**	**88,560**

The accompanying notes are an integral part of these consolidated financial statements. Specific reference is made to Note 13.

PROQR THERAPEUTICS N.V.
Consolidated Statement of Cash Flows

		Year Ended December 31,		
		2024	2023	2022
			(€ in thousands)	
Cash flow from operating activities				
Result for the year		(27,763)	(27,735)	(64,204)
Adjustments for:				
Other income	*18*	(640)	(3,011)	—
Depreciation	*7*	2,761	2,513	2,521
Results related to associates	*8*	—	—	8
Gain on disposal of associate	*9*	—	—	—
Results on derecognition of subsidiary		—	(131)	—
Share-based compensation	*13*	2,544	3,106	2,869
Financial income and expense	*21*	(2,167)	(1,135)	264
Results related to derecognition of financial liabilities	*14*	—	(1,866)	1,390
Results related to financial liabilities measured at FVTPL	*22*	(345)	(953)	(2,713)
Income tax (gains) / expenses	*23*	(197)	(78)	96
Changes in deferred income	*17*	(12,728)	(6,470)	(2,987)
Other changes in working capital		(536)	55,426	(2,004)
Cash (used in) / generated by operations		(39,071)	19,666	(64,760)
Corporate income tax received / (paid)		197	78	(96)
Interest received		3,251	2,593	106
Interest paid		(770)	(789)	(3,758)
Net cash (used in) / generated by operating activities		**(36,393)**	**21,548**	**(68,508)**
Cash flow from investing activities				
Purchases of property, plant and equipment		(1,418)	(1,371)	(708)
Proceeds from sale of property, plant and equipment		—	60	6
Proceeds from sale of intellectual property		—	7,940	—
Transaction costs on sale of intellectual property		(2,655)	(2,351)	—
Increase in short-term deposits		(17,000)	—	—
Decrease in short-term deposits		17,000	—	—
Net cash (used in) / generated by investing activities		**(4,073)**	**4,278**	**(702)**
Cash flow from financing activities				
Proceeds from issuance of shares, net of transaction costs	*13*	71,635	—	14,122
Proceeds from exercise of share options		223	354	34
Repayment of (convertible) loans	*14*	—	(1,008)	(43,372)
Repayment of lease liability	*25*	(1,582)	(1,621)	(1,674)
Net cash generated by / (used in) financing activities		**70,276**	**(2,275)**	**(30,890)**
Net increase / (decrease) in cash and cash equivalents		**29,810**	**23,551**	**(100,100)**
Currency effect cash and cash equivalents		673	599	7,351
Cash and cash equivalents at the beginning of the year	*12*	118,925	94,775	187,524
Cash and cash equivalents at the end of the year	***12***	**149,408**	**118,925**	**94,775**

The accompanying notes are an integral part of these consolidated 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 biotechnology company domiciled in the Netherlands that primarily focuses on the discovery and development of novel therapeutic medicines.

Since September 18, 2014, the Company's ordinary shares are listed on Nasdaq. They are currently trading at Nasdaq Capital 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 and is registered in the Trade Register at the Chamber of Commerce under number 54600790. The address of its headquarters and registered office is Zernikedreef 9, 2333 CK Leiden, the Netherlands.

At December 31, 2024, 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 V 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%)

ProQR Therapeutics N.V. is also statutory director of Stichting Bewaarneming Aandelen ProQR ("ESOP Foundation") and has full control over this entity.

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.

Revision of comparative figures

In the Company's application of IAS 21 *The Effects of Changes in Foreign Exchange Rates*, certain deferred income positions were incorrectly treated as monetary items in 2022. To correct for the effects of this error, which is immaterial for all affected prior periods, the comparative figures for the years ended December 31, 2022 have been revised as follows:

- In the Statement of profit or loss and other comprehensive income ("OCI") for the year ended December 31, 2022, revenue decreased by € 443,000 and financial income increased by € 1,130,000. Net loss for the year ended December 31, 2022 decreased by € 687,000.

- In the Statement of changes in equity, accumulated deficit at January 1, 2022 decreased by € 881,000.

- In the Statement of cash flows for the year ended December 31, 2022, in addition to the above revisions in result for the year and net financial income and expense, changes in working capital decreased by € 443,000. Net cash used in operating activities for the years ended December 31, 2022 was not affected by the revision.

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"). These consolidated financial statements were authorized for issue by the Company's Board of Directors ("Board or "board") and its Senior Management on March 13, 2025.

(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 board of ProQR has, upon preparing and finalizing the 2024 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. Management has not identified significant going concern risks.

The financial statements of the Company have been prepared on the basis of the going concern assumption 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 critical 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) Revenue recognition for the Eli Lilly and Company research and collaboration agreement

a. Identification of the performance obligation

Note 17 describes the Company's original research and collaboration agreement with Eli Lilly and Company ("Lilly"), and the amended and restated research and collaboration agreement (collectively, the "Collaboration agreement"). Under the Collaboration agreement, ProQR provides Lilly with a license (with a right to sub-license) to exploit compounds resulting from the collaboration and ProQR provides other promises such as the performance of R&D services. A significant amount of judgement is required to determine whether the license is distinct from the other promises in the contract. The license was concluded not to be distinct from the other promises in the contract based on the following considerations:

- the license has no stand-alone value to Lilly without the Company being involved in the research and development collaboration, and;
- there are significant interdependencies between the license and the research and development services to be provided by the Company.

Moreover, the compounds resulting from the collaboration do not represent a series of distinct services because they were not predetermined at the inception of the contract and can be terminated or replaced at the discretion of Lilly subject to the terms and conditions of the Collaboration agreement. In addition, the R&D services are the predominant factor within this contract until the handover of a compound to Lilly, rather than the individual targets. As such, the single combined performance obligation consists of multiple activities that are not distinct.

b. Determining the timing of satisfaction of performance obligations

Under the Collaboration agreement, the Company recognizes revenue over time, using an input method that estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services. As the Company's estimate of the total labor hours required is dependent on the evolution of the research and development activities, it may be subject to change. If the progression and/or outcome of certain research and development activities would be different from the assumptions that were made during the preparation of these financial statements, this could lead to material adjustments to the total estimated labor hours, which might result in a reallocation of revenue between current and future periods.

c. Determining the transaction price

The Company applied judgement to determine whether the equity investments made by Lilly in ProQR are part of the transaction price for the Collaboration agreement. The Company concluded that the differences between the prices that Lilly paid for the shares and the ProQR stock closing prices on the days of entering into the equity investment agreements arose because of the Company's existing obligations to deliver research and development services to Lilly under the terms of the Collaboration agreement. Therefore, the above differences between the closing share prices on the agreement effective dates and the equity investment prices paid by Lilly are considered to be part of the transaction price of the contract and are initially allocated to deferred revenue.

The contract also includes variable consideration, but no variable consideration was included in the initial transaction price at the inception, as it is not highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur. The Company includes such variable consideration in the transaction price when the uncertainty associated with the variable consideration is resolved.

Development milestone payments are variable considerations under the agreement. There are development milestones to be reached during the ProQR research program and development milestones to be reached, after the ProQR research program (during the R&D activities performed by Lilly).

The variable consideration for development milestone payments to be reached during the ProQR research program will be added to the transaction price of the identified single combined performance obligation once the variable constraint is resolved and revenue will be recognized based on the status of completion (satisfied part) of the single combined performance obligation.

The variable consideration for development milestones to be reached after the ProQR research program is linked to a separable right to use the license which comes into existence for each successful compound transferred to Lilly. This license is a separate performance obligation and will be recognized at a point in time when the development milestone for a license is achieved and the variable constraint is resolved.

As further described in Note 17, during 2024, the Company achieved development milestones during the ProQR research program under the agreement, which were added to the transaction price and recognized partially as revenue during 2024 based on the status of completion (satisfied part) of the single combined performance obligation.

The Collaboration agreement includes sales-based royalties, including commercial milestone payments based on the level of sales. The variable consideration for commercial milestones is linked to a separable right to use the license which comes into existence for each successful compound transferred to Lilly. This license is a separate performance obligation and will be recognized at a point in time when the commercial milestone for a license is achieved and the variable constraint is resolved. For sales-based royalties, the license is the predominant item to which the royalty relates. The sales-based royalties will be recognized after the handover of the compound to Lilly (after completion of the initial performance obligation) and once the respective sale level occurs.

Related revenue is recognized as the subsequent underlying sales occur at a point in time.

(ii) Research and development expenditures

Research expenditures are reflected in the income statement. Development expenses are currently also 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 the Company does 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

The following standards, amendments to standards and interpretations became effective for annual reporting periods beginning on or after January 1, 2024:

- IFRS 7 *Financial Instruments: Disclosure* and *IAS 7 Statement of Cash Flows:* Amendments for additional disclosure requirements for supplier finance arrangements.
- IFRS 16 *Leases:* Amendments relating to sale and leaseback transactions.
- IAS 1 *Presentation of Financial Statements*: Amendments to classification of liabilities as current or non-current, specifically those related to debt with covenants.

None of the new standards, amendments to standards and interpretations had a material impact on the Company’s financial statements. No changes in accounting policies occurred in 2024.

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

Non-controlling interests 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. Changes in the fair value of derivatives are generally recognized in profit or loss. If the Company is involved with hybrid contracts, the Company applies the following with regard to the embedded derivatives in the hybrid contract. Embedded derivatives are separated from the host contract and accounted for separately if the host contract is not a financial asset and the following criteria are met:

- the economic characteristics and risk of the embedded derivative are not closely related to the economic characteristics and risks of the host contract;
- a separate instrument with the same terms as the embedded derivative would meet the definition of a derivate; and
- the hybrid contract is not measured at fair value with changes in fair value recognized in profit or loss.

If an embedded derivative is separated from the hybrid contract, the host contract is accounted for in accordance with the determined policies for such a contract. The embedded derivative is accounted for in accordance with the Company's principles for the applicable derivatives.

(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 translated at the exchange rate prevailing at the date of the transaction.

(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) Revenue

Revenues to date have consisted principally of non-refundable upfront fees and research and development service fees in connection with collaboration and license agreements. The Company recognizes revenue when its customers obtain control of promised goods or services, in an amount that reflects the consideration that the Company expects to receive in exchange for those goods and services. Revenue is recognized for agreements that are in scope of IFRS 15 *Revenue from contracts with customers*, based on the following five steps:

(i) Identify the contract
The Company entered into collaboration and license agreements in which the Company licenses its intellectual property and/or provides research and development services. These arrangements include upfront payments, milestone payments based on clinical and regulatory criteria, research and development service fees and future sales-based milestones and sales-based royalties. In some cases, concurrently with the collaboration and license agreements, the Company enters into share purchase agreements with the customer. If this is the case, the Company analyzes whether the criteria to combine contracts, as set out by IFRS 15, are met.

(ii) Identify performance obligations
Contracts with customers can have one or more distinct performance obligations under IFRS 15. Identifying the performance obligations is based on an assessment of whether the promises in an agreement are capable of being distinct and are distinct from the other promises to transfer goods and/or services in the context of the contract. The Company assessed that there is one performance obligation in each of its material ongoing collaboration and license agreements, for the transfer of a license combined with performance of research and development services.

This is because the Company considers the two obligations cannot be distinct in the context of the contract as the licenses have no stand-alone value without the Company being involved in the research and development collaboration and that there is interdependence between the license and the research and development services to be provided.

(iii) Determine the transaction price
The Company's research and collaboration agreements include non-refundable upfront payments; equity components; milestone payments, the receipt of which is dependent upon the achievement of certain clinical, regulatory or commercial milestones; royalties on sales and research and development service fees. The transaction price excludes the amount of the part (or parts) of the contract that are initially measured in accordance with other Standards and allocate the amount of the transaction price that remains (if any) to each performance obligation.

a. Non-refundable upfront payments or license fees
If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable upfront fees allocated to this license at the point in time the license is transferred to the customer and the customer has the right to use the license.

For all its material ongoing research and collaboration agreements, the Company considers the performance obligations related to the transfer of the license as not distinct from the other promises to transfer goods and/or services; the Company uses judgement to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If over time, revenue is then recognized based on a pattern that best reflects the transfer of control of the service to the customer.

b. Milestone payments other than sales-based milestones
A milestone payment, being a variable consideration, is only included in the transaction price to the extent it is highly probable that a significant reversal in the amount of cumulative revenue recognition will not occur when the uncertainty associated with the variable consideration is subsequently resolved. The Company estimates the amount to be included in the transaction price upon achievement of the milestone event. The transaction price is then allocated to each performance obligation on a stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and, if necessary, adjusts the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and earnings in the period of adjustment.

c. Research and development service fees
The Company's collaboration and license agreements may include reimbursement for research and development services. R&D services are performed and satisfied over time because the customer simultaneously receives and consumes the benefits provided by us. Revenue associated with such R&D service fees is then recognized based on a pattern that best reflects the transfer of control of the service to the customer.

d. Sales based milestone payments and royalties

The Company's material collaboration and license agreements include sales-based royalties, including commercial milestone payments based on the level of sales. The Company concluded that the licenses are not the predominant items to which the royalties and commercial milestone payments relate. Related revenue will be recognized as the subsequent underlying sales occur.

(iv) Allocate the transaction price

An entity shall allocate the transaction price to each performance obligation identified in a contract on a relative stand-alone selling price basis. As the Company's collaboration and license agreements only contain one single performance obligation, the transaction price is entirely allocated to this single performance obligation.

(v) Recognize revenue

Revenue is recognized when the customer obtains control of the goods and/or services as provided in the research and collaboration agreements. Control can be transferred over time or at a point in time, which results in the recognition of revenue either over time or at a point in time.

The Company's research and collaboration agreements only contain one performance obligation, for which the Company's performance creates and subsequently enhances assets (e.g. exploitable compounds) that the customers control as the assets are created and/or enhanced. As such, the Company recognizes revenue over time.

The recognition of revenue over time is based on a pattern that best reflects the satisfaction of the related performance obligation, applying the input method. The input method estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services.

(e) Other income

Other income includes amounts earned from third parties and are recognized when earned in accordance with the substance and under the terms of the related agreements and when it is probable that the economic benefits associated with the transaction will flow to the 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.

(f) 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. This reduction of payroll taxes and social security contributions is classified under research and developments 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.

(g) 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.

(h) 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.

Deferred tax assets and liabilities are offset when there is a legally enforceable right to offset current tax assets against current tax liabilities and when they relate to income taxes levied by the same taxation authority and the Company intends to settle its current tax assets and liabilities on a net basis.

(i) 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. Right-of-use 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:

- buildings and leasehold improvements: 5-10 years
- laboratory equipment: 5 years
- other: 3-5 years

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

(j) Intangible assets

Expenditure on research activities is recognized as an expense in the period in which it is incurred. An internally-generated intangible asset arising from development (or from the development phase of an internal project) is recognized if, and only if, all of the following have been demonstrated:

- the technical feasibility of completing the intangible asset so that it will be available for use or sale;
- the intention to complete the intangible asset and use or sell it;
- the ability to use or sell the intangible asset;
- how the intangible asset will generate probable future economic benefits;
- the availability of adequate technical, financial and other resources to complete the development and to use
- or sell the intangible asset; and
- the ability to measure reliably the expenditure attributable to the intangible asset during its development.

The amount initially recognized for internally-generated intangible assets is the sum of the expenditure incurred from the date when the intangible asset first meets the recognition criteria listed above. Where no internally generated intangible asset can be recognized, development expenditures are recognized in the consolidated statements of profit and loss and other comprehensive income in the period in which they are incurred.

Due to uncertainties inherent to the development and registration with the relevant healthcare authorities of its products, the Company estimates that the conditions for capitalization are not met until the regulatory procedures required by such healthcare authorities have been finalized. The Company currently does not own products that have been approved by the relevant healthcare authorities and this has resulted in all development costs being recognized as an expense in the period in which they are incurred.

(k) 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.

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.

(l) 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.

The Company derecognizes a financial asset when the contractual rights to the cash flows from the asset expire, or the Company transfers the right to receive the contractual cash flows on the financial asset in a transaction in which substantially all the risks and rewards of ownership of the financial asset are transferred.

(m) 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 readily convertible to a known amount of cash and bear an insignificant risk of change in value.

(n) 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 Company 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 component parts of convertible loan notes issued by the Group are classified separately as financial liabilities and equity in accordance with the substance of the contractual arrangements and the definitions of a financial liability and an equity instrument. A conversion option that will be settled by the exchange of a fixed amount of cash or another financial asset for a fixed number of the Company's own equity instruments is an equity instrument. At the date of issue, the fair value of the liability component is estimated using the prevailing market interest rate for a similar non-convertible instrument. This amount is recorded as a liability on an amortized cost basis using the effective interest method until extinguished upon conversion or at the instrument's maturity date.

The conversion option classified as equity is determined by deducting the amount of the liability component from the fair value of the compound instrument as a whole. This is recognized and included in equity, net of income tax effects, and is not subsequently remeasured. In addition, the conversion option classified as equity will remain in equity until the conversion option is exercised, in which case, the balance recognized in equity will be transferred to share premium. Where the conversion option remains unexercised at the maturity date of the convertible loan note, the balance recognized in equity will be transferred to accumulated losses. No gain or loss is recognized in profit or loss upon conversion or expiration of the conversion option.

Transaction costs that relate to the issue of the convertible loan notes are allocated to the liability and equity components in proportion to the allocation of the gross proceeds. Transaction costs relating to the equity component are recognized directly in equity. Transaction costs relating to the liability component are included in the carrying amount of the liability component and are amortized over the lives of the convertible loan notes using the effective interest method.

Interest related to the financial liability is recognized in profit or loss.

Financial liabilities at fair value through profit or loss

Financial liabilities held for trading are classified as at FVTPL. A financial liability is classified as held for trading if it is a derivative (except for a derivative that is a financial guarantee contract or a designated and effective hedging instrument).

Financial liabilities at FVTPL are measured at fair value, with any gains or losses arising on changes in fair value recognized in profit or loss. The net gain or loss recognized is included in the 'results related to financial liabilities measured at FVTPL line item in profit or loss.

Fair value is determined in the manner described in Note 5.

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.

Offsetting

Financial assets and financial liabilities are offset and the net amount presented in the statement of financial position when, and only when, the Company currently has a legally enforceable right to set off the amounts and it intends either to settle them on a net basis or to realize the asset and settle the liability simultaneously.

(o) Leases

The Company assesses whether a contract is or contains a lease when it obtains the right to control the use of an identified asset for a period of time, in exchange for consideration. 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. In the cash flow statement, repayments of the principal portion of the lease liability are included in financing activities. Payments relating to the interest component of the lease liability are included in operating activities. Short-term lease payments and payments for leases of low-value assets are included in operating activities.

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.

(p) Non-current assets held for sale

Non-current assets (and disposal groups) classified as held for sale are measured at the lower of carrying amount and fair value less costs to sell.

Non-current assets and disposal groups are classified as held for sale if their carrying amount will be recovered through a sale transaction rather than through continuing use. This condition is regarded as met only when the sale is highly probable and the asset (or disposal group) is available for immediate sale in its present condition. Management must be committed to the sale which should be expected to qualify for recognition as a completed sale within one year from the date of classification.

When the Company is committed to a sale plan involving loss of control of a subsidiary, all of the assets and liabilities of that subsidiary are classified as held for sale when the criteria described above are met, regardless of whether the Company will retain a non-controlling interest in its former subsidiary after the sale. When the Company is committed to a sale plan involving disposal of an investment in an associate or, a portion of an investment in an associate, the investment, or the portion of the investment in the associate, that will be disposed of is classified as held for sale when the criteria described above are met. The Company then ceases to apply the equity method in relation to the portion that is classified as held for sale. Any retained portion of an investment in an associate that has not been classified as held for sale continues to be accounted for using the equity method.

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, 2025 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 the Company's cash balances are denominated in U.S. Dollars. This amount reflects the Company's current expectation of future expenditure in U.S. dollars.

At December 31, 2024 the Company's net position of financial instruments denominated in U.S. dollars was a net asset of € 5,898,000 (2023: net liability of € 726,000). 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 2024 and 2023 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, 2024 would have increased the Company's net loss by € 590,000 (2023: decreased by € 73,000). A 10% strengthening of the U.S. dollar against the functional currency of the Company would have an equal but opposite effect on the Company's 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 materials and services as well as external contracted research may vary over time. Currently, the commercial prices of any of the Company's future product candidates is uncertain. When product candidates approach the regulatory approval date or potential regulatory approval date, the uncertainty of potential sales prices decreases. The Company is not exposed to commodity price risk.

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

Cash flow and fair value interest rate risk

The Company's interest rate risk arises from current accounts and deposits and the sensitivity analysis below has been determined based on the exposure to interest rates on these short-term maturity primary financial instruments.

A 10% increase or decrease on actual interest rate is used when reporting interest rate risk internally to key management personnel and represents management's assessment of the reasonably possible change in interest rates.

As of December 31, 2024, if interest rates had been 10% higher, then pre-tax earnings for the year would have been € 324,000 higher, while if interest rates had been 10% lower, then pre-tax earnings for the year would have been € 324,000 lower.

The Company's exposure to interest rate risks on loans and leases is limited due to the use of fixed interest rates. The Company has a loan with a fixed interest rate, totaling € 4,582,000 at December 31, 2024 (2023: € 4,292,000). Details on the interest rates and maturities of these loans are provided in Note 14.

(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 outside of cash and cash equivalents. The Company's 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). As of December 31, 2024, the Company is in compliance with its cash management policy.

At December 31, 2024 and December 31, 2023, all of the Company's cash and cash equivalents were held at five large institutions, Rabobank, ABN Amro, BNP Paribas, Wells Fargo and JP Morgan. All institutions are highly rated (Moody's long-term debt ratings of Aa2, Aa3, A1, Aa2 and Aa2 for Rabobank, ABN Amro, BNP Paribas, Wells Fargo and JP Morgan 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:

	Within 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years
		(€ in thousands)		
At December 31, 2024				
Borrowings	4,872	—	—	—
Lease liabilities	2,114	2,306	6,917	3,459
Trade payables and other payables	10,343	—	—	—
Total	**17,329**	**2,306**	**6,917**	**3,459**
At December 31, 2023				
Borrowings	—	4,583	—	—
Lease liabilities	2,288	2,496	7,487	6,240
Trade payables and other payables	11,709	—	—	—
Total	**13,997**	**7,079**	**7,487**	**6,240**

The Company's future capital requirements and the period for which the Company's existing resources will support its operations may vary significantly from what the Company expects. The Company's 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 the Company's product candidates is highly uncertain, the Company is unable to estimate the actual funds it will require for development of its product candidates.

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).

Fair value of financial assets and liabilities that are measured at fair value on a recurring basis

Some of the Company's financial assets and liabilities are measured at fair value at the end of each reporting period. The following table gives information about how the fair values of these financial assets and liabilities are determined (in particular, the valuation technique and inputs used).

Financial liabilities	Valuation technique and key inputs	Significant unobservable inputs	Relationship and sensitivity of Significant unobservable inputs to fair value
Investment in Phoenicis Therapeutics, Inc	Market comparison technique: The valuation model is based on market multiples derived from quoted prices of companies comparable to the investee, adjusted for the effect of the non-marketability of the equity securities, and the result of the investee. The estimate is adjusted for the net debt of the investee.	Adjusted market-multiple	The estimated fair value would increase (decrease) if the adjusted market-multiple were higher (lower).
Investment in Yarrow Biotechnology, Inc.	Market comparison technique: The valuation model is based on market multiples derived from quoted prices of companies comparable to the investee, adjusted for the effect of the non-marketability of the equity securities, and the result of the investee. The estimate is adjusted for the net debt of the investee.	Adjusted market-multiple	The estimated fair value would increase (decrease) if the adjusted market-multiple were higher (lower).
Warrants and conversion options	Black-Scholes model. The following variables were taken into consideration: current underlying price of the Company's shares, options strike price, expected life, historical volatility of ProQR share returns over a period equal to the expected life, risk-free rate: based on the US Treasury yield curve rates per the valuation date (interpolated) for the expected life.	Not applicable	Not applicable

The investments in Phoenicis Therapeutics, Inc and Yarrow Biotechnology, Inc ("Yarrow") are measured using valuation methods based on so-called Level 3 inputs. Level 3 inputs are unobservable inputs. Changing one or more of the unobservable inputs to reflect reasonably possible alternative assumptions would not significantly change the fair value determined for Phoenicis Therapeutics, Inc and Yarrow.

Warrants are measured using valuation methods based on so-called Level 2 inputs. Level 2 inputs are inputs other than quoted prices that are observable for the liability, either directly or indirectly.

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.

Share options and restricted stock units ("RSUs") granted to employees and consultants are measured at the fair value of the equity instruments granted. The fair value of options 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.

6. Segment Information

The Company operates in one reportable segment, which comprises the discovery and development of innovative, RNA based therapeutics. The board is identified as the chief operating decision maker. The board reviews the operating results regularly to make decisions about resources and to assess overall performance.

Revenues are generated from external customers whose main registered offices are all geographically located in the United States. Substantially all non-current assets of the Company are located in the Netherlands. The amounts provided to the 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

	Buildings and leasehold improvements (€ in thousands)	Laboratory equipment (€ in thousands)	Other (€ in thousands)	Total (€ in thousands)
Balance at January 1, 2023				
Cost	22,863	4,912	1,339	29,114
Accumulated depreciation	(8,069)	(3,473)	(1,332)	(12,874)
Carrying amount	**14,794**	**1,439**	**7**	**16,240**
Additions	30	1,278	63	1,371
Depreciation	(1,951)	(546)	(16)	(2,513)
Effect of lease modification (Note 25)	1,859	—	—	1,859
Transfer	23	(30)	7	—
Disposals - cost	—	(252)	—	(252)
Accumulated depreciation on disposals	—	192	—	192
Movement for the period	**(39)**	**642**	**54**	**657**
Balance at December 31, 2023				
Cost	24,775	5,908	1,409	32,092
Accumulated depreciation	(10,020)	(3,827)	(1,348)	(15,195)
Carrying amount	**14,755**	**2,081**	**61**	**16,897**
Balance at January 1, 2024				
Cost	24,775	5,908	1,409	32,092
Accumulated depreciation	(10,020)	(3,827)	(1,348)	(15,195)
Carrying amount	**14,755**	**2,081**	**61**	**16,897**
Additions	244	916	43	1,203
Depreciation	(2,027)	(710)	(24)	(2,761)
Effect of lease modification (Note 25)	(1,226)	—	—	(1,226)
Transfer	—	—	—	—
Disposals - cost	—	—	—	—
Accumulated depreciation on disposals	—	—	—	—
Movement for the period	**(3,009)**	**206**	**19**	**(2,784)**
Balance at December 31, 2024				
Cost	23,793	6,824	1,452	32,069
Accumulated depreciation	(12,047)	(4,537)	(1,372)	(17,956)
Carrying amount	**11,746**	**2,287**	**80**	**14,113**

The depreciation charge for 2024 is included in research and development costs for an amount of € 2,331,000 (2023: € 1,994,000) and in general and administrative costs for an amount of € 430,000 (2023: € 519,000).

Buildings and leasehold improvements include a right-of-use asset relating to the lease of the Company's Leiden office and laboratory space, with a carrying amount of € 11,433,000 at December 31, 2024 (2023: € 14,524,000).

8. Investments in Associates

In May 2021, the Company obtained an 8% share in the common stock of Yarrow. ProQR's share in Yarrow subsequently changed to 5.1%. Although ProQR only owns 5.1% of Yarrow's shares, the Company had significant influence over Yarrow by virtue of its right to appoint one of Yarrow's three board members, as well as its participation in Yarrow's policy-making process, amongst other factors. As such, the Company's interest in Yarrow was initially recognized as an investment in associate.

In October 2023, Gerard Platenburg, Chief Scientific Officer at ProQR, ended his term on Yarrow's board of directors. From that moment onwards, ProQR no longer had significant influence over Yarrow. Yarrow was therefore derecognized as an associate and was accounted for as a financial asset, as disclosed in Note 9.

As the carrying amount of the Company's investment in Yarrow was € nil at December 31, 2022, ProQR did not recognize any further share of Yarrow's loss from continuing operations for the period from January through October 2023. The results related to associates amounting to € 8,000 for 2022 consisted of ProQR's share in the loss of Yarrow.

9. Investments in Financial Assets

Yarrow Biotechnology, Inc.

As disclosed in Note 8, Gerard Platenburg, Chief Scientific Officer at ProQR, ended his term on Yarrow's board of directors in October 2023. From then on, ProQR no longer had significant influence over Yarrow. Yarrow was therefore derecognized as an associate and was accounted for as a financial asset and measured at fair value.

ProQR holds a 5.1% interest in Yarrow. The Company elected to recognize subsequent changes in the fair value of its investment in Yarrow in Other Comprehensive Income. In October 2023, ProQR initially recognized its investment in the Yarrow financial asset at € nil. As at December 31, 2024, the fair value of the Yarrow financial asset amounted to € nil.

Phoenicis Therapeutics, Inc.

In May 2019, the Company acquired a non-controlling interest in Wings Therapeutics Inc. ("Wings") as part of the strategic spin out of its Dystrophic Epidermolysis Bullosa ("DEB") activities. In January 2021, Wings merged into Phoenicis Therapeutics Inc. ("Phoenicis") by means of a non-cash transaction. Consequently, Wings ceased to exist, and the related investment was derecognized. In 2021, a gain on disposal of associate was recognized amounting to € 514,000, which consisted of the € 621,000 fair value of Phoenicis equity instruments received by the Company, partly off-set by the derecognition of the carrying value of the Company's investment in Wings of € 107,000.

ProQR holds a 3.9% interest in Phoenicis. ProQR does not have significant influence in Phoenicis. The Company elected to recognize subsequent changes in the fair value of its investment in Phoenicis in Other Comprehensive Income. In September 2023, the investment was remeasured to nil, and ProQR recognized a fair value loss of € 621,000 in other comprehensive income. As at December 31, 2024 the fair value of the Phoenicis financial asset amounted to € nil (2023: € nil).

10. Other Taxes

	December 31, 2024	December 31, 2023
	(€ in thousands)	
Value added tax	690	523
	690	523

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

11. Prepayments and Other Receivables

	December 31, 2024	December 31, 2023
	(€ in thousands)	
Prepayments	2,410	793
Other receivables	835	745
Accrued income from Rett Syndrome Research Trust	502	—
	3,747	1,538

All receivables are considered short-term and due within one year. At December 31, 2024 and 2023, prepayments consisted principally of payments made by the Company for services not yet provided by vendors. At December 31, 2024 other receivables consisted principally of accrued grant income and deposits. The accrued grant income relating to Rett Syndrome Research Trust ("RSRT") includes the initial fair value of the warrants issued to RSRT that was accounted for as a reduction of the transaction price. The nature of the agreement with RSRT is described in Note 26. At December 31 2023, other receivables consisted principally of deposits.

12. Cash and Cash Equivalents

	December 31, 2024	December 31, 2023
	(€ in thousands)	
Cash at banks	74,199	59,775
Deposits	75,209	59,150
	149,408	118,925

The cash at banks is at full disposal of the Company. Deposits are fixed for at most 3 month periods at a time.

13. Shareholders' Equity

(a) Share capital

	Number of shares 2024	Number of shares 2023	Number of shares 2022
	Ordinary	Ordinary	Ordinary
Balance at January 1	84,248,384	84,246,967	74,865,381
Issued for cash	23,463,610	—	9,381,586
Issued for services	—	—	—
Exercise of share options / vesting of RSUs	(395,559)	537,513	144,688
Treasury shares issued (transferred)	394,481	(536,096)	(144,688)
Balance at December 31	**107,710,916**	**84,248,384**	**84,246,967**

The authorized share capital of the Company amounting to € 13,600,000 consists of 170,000,000 ordinary shares and 170,000,000 preference shares with a par value of € 0.04 per share. At December 31, 2024, 107,710,916 ordinary shares were issued. 105,212,527 ordinary shares were fully paid, and 2,498,389 ordinary shares were held by the Company as treasury shares (2023: 2,893,792).

In December 2022, the Company issued 9,381,586 shares to Lilly pursuant to the amended and restated licensing and research collaboration between the Company and Lilly (Note 17), resulting in gross proceeds of € 14,122,000, with no significant transaction costs.

In September 2024, the Company filed a shelf registration statement on Form F-3, 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 the Company 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 (the "sales agreement") with Cantor Fitzgerald & Co. ("Cantor") in one or more at-the-market ("ATM") offerings. The Company will pay Cantor a commission equal to 3% of the gross proceeds of the sales price of all ordinary shares sold through it as sales agent under the sale agreement. As of December 31, 2024, no shares have been issued pursuant to this ATM facility.

In October 2024, the Company consummated an underwritten public offering of 18,000,000 ordinary shares (the "Offering") at a public offering price of $ 3.50 per share (the "public offering price"). In addition, the Company granted the underwriters a 30-day option to purchase up to 2,700,000 additional ordinary shares at the public offering price, less underwriting discounts and commissions. The option was partially exercised on October 31, 2024, resulting in the issuance of 1,940,072 shares. The gross proceeds from the Offering and subsequent partial exercise of the underwriters' option, amounted to $ 69,790,000 (€ 64,600,000) while the transaction costs amounted to approximately € 4,365,000, resulting in net proceeds of approximately € 60,235,000.

Concurrently with the Offering, the Company entered into a share purchase agreement with Lilly in a separately negotiated transaction (the "concurrent private placement"), pursuant to which the Company agreed to offer and sell, and Lilly agreed to purchase, 3,523,538 ordinary shares at a price per share equal to the public offering price, for total gross proceeds of approximately $ 12,300,000, subject to a purchase price cap of $ 15,000,000, the consummation of the Offering and the satisfaction of other customary closing conditions. The proceeds of $ 12,300,000 million (€ 11,400,000) from the concurrent private placement were received on October 25, 2024. The ordinary shares purchased in the concurrent private placement are not subject to any underwriting discounts or commissions.

(b) Equity settled employee benefit reserve

The costs of share options and RSUs for employees, members of the 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-based compensation 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, the Company established a Dutch foundation named Stichting Bewaarneming Aandelen ProQR for holding shares in trust for employees, members of the Board of the Company and its group companies who from time to time could 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 and restricted stock units

The Company operates an equity-settled share-based compensation plan which was introduced in 2013. Options and RSUs may be granted to employees, members of the Board and consultants. The compensation expenses included in operating costs for this plan were € 2,544,000 in 2024 (2023: € 3,106,000), of which € 1,984,000 (2023: € 2,629,000) was recorded in general and administrative costs and € 560,000 (2023: € 477,000) 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 and RSUs. Typical vesting periods are:

- Four years, with 25% vesting after every year.
- Four years, in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date.
- Two years, with 25% vesting after every six months.

The options expire ten years after date of grant. Options granted under the stock option plan are granted at exercise prices which equal either the face value or the fair value of the ordinary shares of the Company at the date of the grant.

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 2024	Options granted in 2023	Options granted in 2022
Risk-free interest rate	3.903 %	3.960 %	2.570 %
Expected dividend yield	— %	— %	— %
Expected volatility	96.5 %	105.6 %	101.0 %
Expected life in years	5 years	5 years	5 years

The resulting weighted average grant date fair value of the options amounted to € 1.51 in 2024 (2023: € 2.14). The stock options granted have a 10-year life following the grant date and are assumed to be exercised seven years from date of grant for all awards.

The fair value of RSUs is determined at the grant date by using the Company's share price at the grant date. The resulting weighted average grant date fair value of the RSUs amounted to € 2.76 in 2023. No RSUs were granted in 2024.

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

	2024		2023		2022	
	Number of options	Average exercise price	Number of options	Average exercise price	Number of options	Average exercise price
Balance at January 1	11,186,240	€ 3.10	11,279,210	€ 3.66	7,643,143	€ 6.13
Granted	1,377,780	€ 1.94	1,793,449	€ 2.76	5,230,405	€ 0.89
Forfeited	(179,259)	€ 1.61	(276,272)	€ 4.62	(1,177,622)	€ 5.84
Exercised	(300,036)	€ 0.79	(337,746)	€ 1.07	(1,590)	€ 2.72
Expired	(412,933)	€ 4.05	(1,272,401)	€ 7.80	(415,126)	€ 7.94
Balance at December 31	**11,671,792**	**€ 3.38**	**11,186,240**	**€ 3.10**	**11,279,210**	**€ 3.66**
Exercisable at December 31	8,152,467		6,679,018		5,235,914	

The options outstanding at December 31, 2024 had an exercise price in the range of € 0.64 to € 21.06 (2023: € 0.60 to € 19.80) and a weighted-average contractual life of 6.3 years (2023: 6.8 years). The weighted-average share price at the date of exercise for share options exercised in 2024 was € 2.09 (2023: € 1.45).

Movements in the number of RSUs outstanding are as follows:

	2024 Number of RSUs	2023 Number of RSUs	2022 Number of RSUs
Balance at January 1	166,306	370,962	536,118
Granted	—	52,319	353,116
Forfeited	(17,775)	(66,881)	(371,102)
Released	(94,962)	(190,094)	(147,170)
Balance at December 31	**53,569**	**166,306**	**370,962**

Refer to Note 27 for the share-based compensation granted to senior management personnel.

14. Borrowings

	December 31, 2024	December 31, 2023
	(€ in thousands)	
Innovation credit	2,899	2,899
Accrued interest on innovation credit	1,683	1,393
Convertible loans	—	—
Accrued interest on convertible loans	—	—
Total borrowings	**4,582**	**4,292**
Current portion	4,582	—
Total non-current borrowings	**—**	**4,292**

Innovation credit ("Innovatiekrediet")

In December 2018, ProQR was awarded an Innovation credit for the sepofarsen program. Amounts were drawn under this facility from 2018 through 2022. The credit of € 3,907,000 was used to conduct the Phase 2/3 clinical study and efforts to obtain regulatory and ethical market approval (New Drug Applications ("NDA")/ Marketing Authorization Applications ("MAA")) of sepofarsen for LCA10. In the fourth quarter of 2023, ProQR made a partial repayment of the principal, amounting to € 1,008,000. The remaining amount payable of € 2,899,000 is recognized under current borrowings at December 31, 2024.

In December 2023, ProQR received a conditional waiver for the € 4,292,000 remaining balance of the Innovation credit including accrued interest. Consequently, the repayment of the total loan of € 4,292,000, including interest, will be waived if conditions are met, which will be reviewed annually. In January 2025, the conditional waiver for the total balance of € 4,582,000, including interest, was extended until December 31, 2025.

The amounts receivable relating to development & regulatory milestone payments under the Amended and Restated Asset Purchase Agreement with Laboratoires Théa S.A.S. ("Théa") are subject to a right of pledge for the benefit of the Rijksdienst voor Ondernemend Nederland ("RVO").

Convertible loans: Pontifax and Kreos

In July 2020, the Company entered into a convertible debt financing agreement with Pontifax Medison Debt Financing ("Pontifax"). Under the agreement, the Company had access to up to $ 30.0 million in convertible debt financing in three tranches of $ 10.0 million each that would mature over a 54-month period and had an interest-only period of 24 months. One tranche of $ 10.0 million (€ 8.4 million) was drawn down over the course of the agreement.

A second close of the convertible debt financing agreement was completed in August 2020 with Kreos Capital ("Kreos"). Under the second agreement, the Company had access to up to € 15.0 million in convertible debt financing in three tranches of € 5.0 million each that would mature over a 54-month period and had an interest-only period of 24 months. One tranche of € 5.0 million was drawn down over the course of the agreement.

In connection with the loan agreement, the Company issued to Pontifax and Kreos warrants to purchase up to an aggregate of 302,676 shares of its common stock at a fixed exercise price.

In December 2021, the Company amended its convertible debt financing agreement with the lenders. Under the amended agreement the Company drew down an additional $ 30.0 million (€ 26.5 million) that would mature over a 54-month period and had an interest-only period of 33 months. The amendment replaced the two undrawn tranches under the original convertible debt financing agreements.

In connection with the amended loan agreement, the Company issued to the lenders warrants to purchase up to an aggregate of 376,952 shares of its common stock at a fixed exercise price.

The convertible loans from Pontifax and Kreos bore an interest of 8.2% per annum.

In September 2022, ProQR extinguished its debt with Pontifax and Kreos by repaying all outstanding principal amounts. In addition, an early repayment penalty was incurred. The financial liability relating to Pontifax' conversion options was derecognized from derivative financial instruments. The option premium on convertible loans relating to Kreos' conversion options was derecognized from equity.

Pontifax' and Kreos' warrants remain in place until their five-year economic life expires. These warrants are accounted for as embedded derivatives and were recognized separately from the host contract as derivative financial liabilities at FVTPL.

Convertible loans: Amylon Therapeutics B.V.

Convertible loans amounting to € 2.3 million were issued to Amylon Therapeutics B.V. ("Amylon") in 2018 and 2019 and were interest-bearing at an average rate of 8% per annum. In 2022 and 2023, Amylon entered into waiver agreements with its lenders. Such lenders' loan agreements with Amylon are severed and any claims to repayment of any outstanding debt and accumulated interest are renounced. The total amount of convertible loans and accumulated interest waived under these agreements in 2023 is € 1,866,000 (2022: € 1,144,000). The resulting gains are recognized as a gain on derecognition of financial liabilities.

In the third quarter of 2023, Amylon was legally dissolved. The effect of the resulting derecognition of Amylon's remaining assets and liabilities is included in profit and loss as 'result on derecognition of subsidiary'.

The results related to the derecognition of financial liabilities, as described above, are as follows:

	2024	2023
	(€ in thousands)	
Gain on waiver of Amylon Therapeutics B.V. convertible loans	—	1,866
	—	**1,866**

Reconciliation of movements of liabilities to cash flows arising from financing activities

	Innovation credit	Convertible loans	Lease liability
		(€ in thousands)	
Balance at January 1, 2023	**4,943**	**1,828**	**15,200**
Changes from financing cash flows			
Repayments	(1,008)	—	(1,621)
The effect of changes in foreign exchange rates	—	—	—
Other changes			
Interest expense	357	38	—
Interest paid	—	—	—
Transaction costs	—	—	—
Repayments allocated to option premium on convertible loans (equity)	—	—	—
Repayments recognized as result on derecognition of financial liabilities	—	—	—
Effect of waived loan agreements	—	(1,866)	—
Effect of lease amendments	—	—	1,863
Balance at January 1, 2024	**4,292**	**—**	**15,442**
Changes from financing cash flows			
Repayments	—	—	(1,582)
The effect of changes in foreign exchange rates	—	—	—
Other changes			
Interest expense	290	—	—
Interest paid	—	—	—
Effect of waived loan agreements	—	—	—
Effect of lease amendments	—	—	(1,226)
Balance at December 31, 2024	**4,582**	**—**	**12,634**

15. Deferred Income

The following table summarizes details of deferred income at December 31, 2024 and December 31, 2023. The nature of the deferred income relating to Lilly is described in Note 17. The nature of the deferred income relating to RSRT is described in Note 26.

	December 31, 2024	December 31, 2023
	(€ in thousands)	
Payments from Eli Lilly and Company	50,930	64,739
Payments from Rett Syndrome Research Trust	441	—
Total deferred income	**51,371**	**64,739**
Current portion	(21,942)	(20,569)
Total non-current deferred income	**29,429**	**44,170**

The current portion of deferred income reflects the estimated value of the Company's work under the Lilly collaboration and RSRT grant that is expected to be performed within one year after the balance sheet date.

The table below analyzes ProQR's undiscounted deferred income release based on estimates for the measure of progress and allocated into relevant maturity groupings until the contractual maturity date:

	Within 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years
		(€ in thousands)		
At December 31, 2024				
Deferred Income	21,942	21,087	8,342	—
Total	**21,942**	**21,087**	**8,342**	**—**
At December 31, 2023				
Deferred Income	20,569	27,950	16,220	—
Total	**20,569**	**27,950**	**16,220**	**—**

16. Other Current Liabilities

At December 31, 2024, other current liabilities amount to € 8,849,000 (2023: € 8,509,000). At December 31, 2024 and December 31, 2023, other current liabilities consisted principally of accruals for services provided by vendors not yet billed, payroll related accruals and other miscellaneous liabilities.

17. Revenue

The following table summarizes details of revenue recognized in the years ended December 31, 2024, 2023 and 2022 by collaboration agreement and by category of revenue: upfront payments, other research and development service fees and equity consideration.

	2024	2023	2022
		(€ in thousands)	
Up-front payments			
Eli Lilly and Company	15,584	5,996	2,646
Yarrow Biotechnology, Inc.	—	—	191
Other R&D services			
Eli Lilly and Company	—	—	270
Yarrow Biotechnology, Inc.	—	—	118
Equity component			
Eli Lilly and Company	496	518	321
Yarrow Biotechnology, Inc.	—	—	48
Milestone payments			
Eli Lilly and Company	2,825	—	—
	18,905	**6,514**	**3,594**

The table below summarizes the changes in current and non-current deferred revenue for the years ended December 31, 2024 and 2023.

	Eli Lilly
	(€ in thousands)
Balance at January 1, 2023	**71,209**
Received or receivable	
Upfront payment	—
Equity component	—
Milestones achieved	—
Revenue recognition	
Upfront payment	(5,996)
Equity component	(518)
Milestones achieved	—
Foreign currency translation effects	44
Balance at January 1, 2024	**64,739**
Received or receivable	
Upfront payment	—
Equity component	—
Milestones achieved	5,096
Revenue recognition	
Upfront payment	(15,584)
Equity component	(496)
Milestones achieved	(2,825)
Foreign currency translation effects	—
Balance at December 31, 2024	**50,930**

Eli Lilly and Company collaboration

In September 2021, the Company entered into a global licensing and research collaboration with Lilly focused on the discovery, development, and commercialization of potential new medicines for genetic disorders in the liver and nervous system. ProQR and Lilly will use ProQR's proprietary Axiomer RNA editing platform to progress new drug targets toward clinical development and commercialization.

Under the terms of the agreement, ProQR received an upfront payment and equity consideration, and is eligible to receive milestone payments and royalties on the net sales of any resulting products. In September 2021, the Company issued 3,989,976 shares to Lilly, resulting in gross proceeds of $ 30,000,000 (€ 25,270,000). These shares were issued at a premium of $ 2,429,000 (€ 2,047,000), which was determined to be part of the transaction price and as such was initially recognized as deferred revenue. An up-front payment of $ 20,000,000 (€ 16,849,000) was received in October 2021.

In December 2022, the Company and Lilly amended their research and collaboration agreement described above, which expanded the collaboration. Under the amended and restated research and collaboration agreement, Lilly will gain access to additional targets in the central nervous system ("CNS") and peripheral nervous system ("PNS") with ProQR's Axiomer platform.

As described under Note 13, pursuant to the amended and restated agreement, the Company issued 9,381,586 shares to Lilly in December 2022, resulting in gross proceeds of $ 15,000,000 (€ 14,122,000). These shares were issued at a discount of $ 480,000 (€ 451,000), which is accounted for as a reduction of the transaction price. In February 2023, ProQR also received an upfront payment of $ 60,000,000 (€ 56,412,000). Lilly has the ability to exercise an option to further expand the partnership for a consideration of $ 50,000,000.

With regard to the original and amended and restated research and collaboration agreements with Lilly, the Company concluded as follows:

- The amended and restated research and collaboration agreement is accounted for as a separate contract under IFRS 15 given the group of promises to be delivered are distinct and are priced commensurate with stand-alone selling prices.

- For each of the agreements, the company identified one performance obligation under IFRS 15, for the transfer of a license combined with the performance of research and development activities. The Company concluded that the license is not capable of being distinct and is not distinct in the context of the contract. ProQR's services are evaluated as predominant at inception of the contract and the compounds resulting from the collaboration do not represent a series of distinct promises because they were not predetermined at the inception of the contract and can be terminated or replaced at the discretion of Lilly subject to the terms and conditions of the Collaboration agreement.

- The transaction price of the agreement includes fixed components, consisting of an up-front fee and an equity component (premium or discount). The agreement also contains variable parts, notably milestones, which are included in the transaction price to the extent that it is highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Development milestone payments to be reached during the ProQR research program will only be included to the extent that it is highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the milestones is subsequently resolved. Sales-based milestones and sales-based royalties will be included as the underlying sales occur.

- Initially, the Company recognizes revenue over time, using an input method that estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services.

After the handover of a compound to Lilly:

- The variable consideration for development milestones to be reached during the Lilly R&D activities is linked to a separable right to use the license which comes into existence for each successful compound transferred to Lilly. This license is a separate performance obligation and revenue will be recognized at a point in time when the development milestone for a license is achieved and the variable constraint is resolved.

- The variable consideration for commercial milestones is linked to a separable right to use the license which comes into existence for each successful compound transferred to Lilly. This license is a separate performance obligation and will be recognized at a point in time when the commercial milestone for a license is achieved and the variable constraint is resolved.

- For sales-based royalties, the license is the predominant item to which the royalty relates. The sales-based royalties will be recognized after the handover of the compound to Lilly (after completion of the initial performance obligation) and once the respective sale level occurs.

During the year ended December 31, 2024, the Company reached milestones amounting to $ 5,500,000 (€ 5,096,000) under the agreement, which were added to the transaction price and recognized partially as revenue during the year ended December 31, 2024.

Yarrow Biotechnology, Inc. collaboration

In May 2021, the Company entered into an exclusive worldwide license and discovery collaboration for an undisclosed target with Yarrow. Under the terms of the agreement, ProQR received an upfront payment, equity consideration and reimbursement for ongoing R&D services. ProQR was also eligible to receive milestone payments and royalties on the net sales of any resulting products. In May 2021, ProQR received an up-front payment of € 419,000 and 8% of the shares of Yarrow's common stock (see Note 8). In 2021, ProQR also received reimbursements for R&D services performed amounting to € 178,000.

With regard to its collaboration with Yarrow, the Company concluded as follows:

- There is one single performance obligation under IFRS 15, which is the transfer of a license combined with the performance of research and development activities. The Company concluded that the license is not capable of being distinct and is not distinct in the context of the contract.

- The transaction price of this agreement currently includes both fixed and variable components. The fixed part consists of an up-front fee and an equity component. The variable part consists of a cost reimbursement for research and development activities. The agreement also contains other variable parts, but those are not yet included in the transaction price. Milestone payments will only be included to the extent that it is highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the milestones is subsequently resolved. Sales-based milestones and sales-based royalties will be included as the underlying sales occur.

- The Company recognizes revenue over time, using an input method that estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services.

The Yarrow collaboration was terminated in the third quarter of 2022.

18. Other Income

	2024	2023	2022
		(€ in thousands)	
Net gain on divestment of intellectual property	—	2,931	—
Grant income	640	75	699
Other income	—	5	66
	640	**3,011**	**765**

In January 2024, the Company entered into an agreement with RSRT that focuses on the design and development of editing oligonucleotides ("EONs") using the Company's Axiomer technology platform targeting the transcription factor Methyl CpG binding protein 2 ("MECP2") and correcting mutations of interest. Under the agreement, RSRT awarded the Company up to € 1,015,000 as a research grant for the initial phase of the project that was received during 2024, out of which € 640,000 was recognized as Other income during 2024 and the remaining part recorded as Deferred income. As further described in Note 26, in December 2024, the Company expanded partnership with RSRT to include an additional $ 8,150,000 in funding from the RSRT to support the advancement of the selected candidates into clinical trials.

In December 2023, ProQR completed the divestment of its late-stage ophthalmic intellectual property assets, sepofarsen and ultevursen, to Théa. Under the terms of the agreement, ProQR received an initial payment of € 8,000,000. The Company incurred costs directly associated to the transaction amounting to € 5,069,000. The net gain on the divestment amounting to € 2,931,000 was recognized in other income. Costs directly associated to the transaction include the partial repayment of grant income received from Foundation Fighting Blindness ("FFB") for the development of ultevursen (€ 1,117,000), financial advisory fees (€ 2,715,000), incentive payments (€ 913,000), assignment and success fees (€ 260,000), and other costs (€ 64,000).

In February, 2018, the Company entered into a partnership agreement with FFB, under which FFB agreed to provide funding of $ 7,500,000 for the preclinical and clinical development of ultevursen for Usher syndrome type 2A targeting mutations in exon 13. FFB grant income amounted to € nil in 2023 compared to € 594,000 in 2022 and € 977,000 in 2021. Grant income in 2024, 2023 and 2022 further includes income from grants received from various institutions.

19. Operating Costs

Total operating costs include the following expenses by nature:

	2024	2023	2022
		(€ in thousands)	
Employee benefits	19,367	20,349	30,286
External R&D costs	12,838	4,809	19,824
Laboratory costs and other consumables	4,675	3,473	3,111
Advisory and legal costs	4,384	4,262	6,766
Insurance costs	918	1,458	1,895
Depreciation	2,761	2,513	2,521
Patent and license expenses	721	303	611
Other	4,353	4,217	4,504
	50,017	**41,384**	**69,518**

20. Employee Benefits

	2024	2023	2022
		(€ in thousands)	
Wages and salaries	13,438	13,797	23,441
Social security costs	2,367	2,480	2,661
Pension costs — defined contribution plans	1,018	966	1,315
Equity-settled share based payments	2,544	3,106	2,869
	19,367	**20,349**	**30,286**
Average number of employees for the period	163.0	144.0	163.0

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

	December 31, 2024	December 31, 2023	December 31, 2022
Research and Development	133.9	122.4	103.5
General and Administrative	32.2	34.2	26.7
Total number of employees (converted to FTE)	**166.1**	**156.6**	**130.2**

Of all employees 164.1 FTE are employed in the Netherlands (2023: 153.6 FTE).

Included in the wages and salaries for 2024 is a credit of € 1,888,000 (2023: € 1,170,000, 2022: € 792,000) with respect to WBSO subsidies.

21. Financial Income and Financial Expense

	2024	2023	2022
		(€ in thousands)	
Interest income:			
Current accounts and deposits	3,251	2,593	106
Interest costs:			
Current accounts and deposits	(74)	(31)	(406)
Lease liability	(713)	(774)	(793)
Loans and borrowings	(290)	(398)	(3,928)
Foreign exchange result:			
Net foreign exchange (loss) / benefit	(7)	(255)	4,757
	2,167	**1,135**	**(264)**

Financial income amounting to € 3,251,000 (2023: € 2,593,000, 2022: € 4,863,000) consists of interest income of € 3,251,000 (2023: € 2,593,000, 2022: € 106,000) for the year ended December 31, 2024. Further, 2022 consisted of a net foreign exchange benefit of € 4,757,000. Financial expenses amounting to € 1,084,000 (2023: € 1,458,000) consist of interest costs of € 1,077,000 (2023: € 1,203,000) and net foreign exchange costs of € 7,000 (2023: € 255,000). Financial expenses amounted to € 5,127,000 in 2022 and wholly consisted of interest costs.

22. Results related to financial liabilities measured at fair value through profit or loss

	2024	2023	2022
		(€ in thousands)	
Warrants to Rett Syndrome Research Trust	132	—	—
Warrants from convertible loans	213	953	2,713
	345	**953**	**2,713**

Results related to financial liabilities measured at FVTPL represent changes in the fair value of derivative financial instruments since their initial recognition. These derivative financial instruments consist of conversion options and warrants issued in connection with the Company's convertible loans, which are described in Note 14, and warrants issued in connection with the Company's partnership with RSRT, which is described in Note 26.

23. Income Taxes

The calculation of the tax charge is as follows:

	2024	2023	2022
		(€ in thousands)	
Consolidated result before corporate income taxes	(27,960)	(27,813)	(64,108)
Exclude: results related to associates	—	—	(8)
	(27,960)	**(27,813)**	**(64,100)**
Income tax based on domestic rate (25.8%)	7,214	7,176	16,538
Tax effect of:			
Different tax rates in foreign jurisdictions	—	(8)	10
(Non-deductible expenses) / non-taxable gains	(269)	(289)	133
Share- and loan-issue expenditures that are tax deductible	1,117	—	—
Change in unrecognized deductible temporary differences	(73)	(67)	(75)
Current year losses for which no deferred tax asset was recognized	(7,989)	(6,820)	(16,649)
True-up for prior year	197	86	(53)
Income tax benefit / (charge)	**197**	**78**	**(96)**
Effective tax rate	0.7 %	0.3 %	0.2 %

The Company recognizes deferred tax assets arising from unused tax losses, deductible temporary differences 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.

A deferred tax liability amounting to € 2,950,000 (2023: € 3,747,000) arises due to a taxable temporary difference associated with the Company's right-of-use asset for the lease of its Leiden headquarters. A deferred tax asset amounting to € 3,260,000 (2023: € 3,984,000) arises due to a deductible temporary difference associated with the corresponding lease liability. As these deferred tax positions relate to income taxes levied by the same taxation authority (namely that of the Netherlands), and there is a legally enforceable right to offset current tax assets against current tax liabilities, and the Company intends to settle its current tax assets and liabilities on a net basis, the deferred tax asset associated with the lease liability is offset against the deferred tax liability associated with the right-of-use asset. The remaining balance of the deferred tax asset is not recognized, as it is Management's judgment that there is no sufficient convincing evidence that sufficient taxable profit will be available against which the unused tax losses or unused tax credits can be utilized.

As per December 31, 2024, the Company has a total amount of € 437.3 million (2023: € 402.3 million, 2022: € 376.9 million) tax loss carry-forwards available for offset against future taxable profits, which may be carried forward indefinitely. However, the offset of losses will be limited in a given year against the first € 1.0 million of taxable profit. For taxable profit in excess of this amount, losses may only be offset up to 50% of this excess. In addition, as per December 31, 2024, the Company has a total of € 1.3 million (2023: € 2.3 million, 2022: € 3.3 million) of unused non-deductible interest expenses, which may be carried forward indefinitely. However, the offset will be limited in a given year against the higher of 20% of adjusted taxable profit or € 1.0 million of interest income.

24. Earnings Per Share

(a) Basic and diluted earnings per share

Basic earnings per share are calculated by dividing the result attributable to owners of the Company by the weighted average number of shares outstanding during the year.

	2024	2023	2022
Result attributable to owners of the Company (€ in thousands)	(27,763)	(28,119)	(64,424)
Weighted average number of shares outstanding	86,086,486	81,011,438	71,641,305
Basic (and diluted) earnings per share (€ per share)	**€ (0.32)**	**€ (0.35)**	**€ (0.90)**

(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.

25. Leases

The Company leases office and laboratory facilities of 4,818 square meters at Zernikedreef in Leiden, the Netherlands, where the Company's headquarters and its laboratories are located. The current lease agreement for these facilities terminates on June 30, 2031. The lease agreement contains no significant dismantling requirements.

The initial 10-year lease agreement for the Leiden office and laboratory facilities was accounted for as of commencement date July 1, 2020. This 10-year period was extended by 1 year to an 11-year period in December 2020. The lease contract may be extended for subsequent 5-year periods. As the Company is not reasonably certain to exercise these extension options, these are not included in the lease term.

The initially recognized lease liability and the corresponding right-of-use asset for this lease contract, on July 1, 2020, amounted to € 16,203,000 and € 16,332,000, respectively. A modification to reflect the additional 1 year lease period resulted in an increase in the carrying amounts of the lease liability and the right-of-use asset in 2020 of € 1,260,000.

Annually in June, the lease price is amended to reflect an indexation. In addition, based on the lease agreement the Company can in consultation with the owner amend a prepayment for non-lease component. During 2024 the Company reached an agreement to decrease the prepayment that resulted in remeasurement of the lease liability. This amendment did not qualify as a lease modification. As a result of the indexation and decrease of the prepayment in 2024, the lease liability was remeasured, resulting in an increase in the carrying amounts of the lease liability and the right-of-use asset of € 1,226,000 (2023: € 1,863,000 and 2022: € 592,000).

The following table summarizes the relevant disclosures in relation to the Company's leases in 2024, 2023 and 2022:

	2024 (€ in thousands)	2023 (€ in thousands)	2022 (€ in thousands)
Depreciation charge for right-of-use assets	1,867	1,833	1,737
Interest expense on lease liabilities	713	774	793
Expense relating to short-term leases	7	28	94
Total cash outflow for leases	2,302	2,423	2,701
Additions to right-of-use assets during the period	1,226	1,863	592

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 the Company's lease liability is included in Note 5 Financial Risk Management under (c) Liquidity risk. The total undiscounted commitment for lease agreements to which the Company had committed at December 31, 2024 amounts to € 14,795,000 (2023: € 18,511,000). 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.

26. Commitments and Contingencies

(a) Claims

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

(b) Patent license agreements

In October 2018, ProQR signed an agreement with Ionis Pharmaceuticals ("Ionis") 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. This license agreement was terminated effective January 2024.

In April 2014, the Company entered into a Patent License Agreement with Radboud University Medical Center ("Radboud") in the field of antisense oligonucleotide-based therapy for Leber congenital amaurosis ("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 certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of LCA. This license is assigned in full per December 2023 as part of the divestment of the product sepofarsen.

In June 2015, the Company 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 certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of Usher syndrome. This license was assigned in full per December 2023 as part of the divestment of the product ultevursen.

In January 2018, the Company entered into a license agreement with Inserm Transfert SA and Assistance-Publique-Hôpiteaux 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 ("AONs") for treating LCA and method of treatment claims relating to modulation of the splicing of the CEP290 gene product. This license agreement is assigned per December 2023 in connection with the sale of the ophthalmology products, sepofarsen and ultevursen. In consideration for the assignment, the Company has agreed to accept certain royalty obligations upon sepofarsen reaching certain regulatory milestones and net sales of products sold.

In January 2017, the Company entered into an agreement with the Leiden University Medical Center ("LUMC"), which gives the Company 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. This license was terminated per July 2023.

In February 2019, the Company entered into an agreement with the University of Rochester, New York, which gives the Company a world-wide, exclusive, royalty-bearing, sublicensable license in the field of AONs 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 September 2020, the Company entered into an agreement with Vico Therapeutics B.V., which gives the Company a world-wide, exclusive, royalty-bearing, sublicensable license in the field of the prophylactic and therapeutic use of antisense oligonucleotide for the treatment of Fuch's Endothelial Corneal Dystrophy caused by a trinucleotide repeat, under certain patent rights of Vico Therapeutics B.V. In partial consideration of the rights and licenses granted by the license agreement, the Company is required to make annual maintenance payments. Unless terminated earlier in accordance with the terms of the license agreement, the agreement will stay in effect until the expiration of all of the licensed patent rights. The license agreement may be terminated by either party in the event of an uncured breach by the breaching party. Vico Therapeutics B.V. may terminate the license agreement if the Company applies for an order or an order is made declaring the Company bankrupt or granting the Company suspension of payments, or a liquidator is appointed for the Company, or the Company is dissolved, liquidated, or ceases to carry on all or a substantial part of its business or a decision is taken to that effect, or in the event uncured payment defaults. The development of this candidate has been suspended per the strategic shift in focus as announced in August 2022.

(c) Clinical support agreements

In February 2018, the Company entered into an agreement with FFB, under which FFB has provided funding of $ 6,800,000 (€ 6,300,000) to advance ultevursen into the clinic.

Pursuant to the terms of the agreement, the Company was obligated to make certain repayments to FFB subject to development milestones. In December 2023, upon the occurrence of the sale of ultevursen to Théa, these payables were settled by means of a lump-sum payment in the amount of € 1,100,000 and a percentage of earn-out payments for milestones and sales to be received by the Company from Théa, ranging from 5-10%.

On January 4, 2024, the Company entered into an agreement with RSRT, under which RSRT committed funding in the amount of € 1,015,000 for research and development purposes related to Rett syndrome. On December 5, 2024, the Company and RSRT entered into a further agreement, under which the RSRT provides an additional award of up to $ 8,150,000 to support the development program to advance the Rett syndrome related program into clinical trials.

Pursuant to the terms of the agreement dated December 5, 2024, the Company is obligated to make a one-time milestone payment to RSRT of up to $ 40,750,000, payable in four equal annual installments following the first commercial sale of the product, the first of which is due within 60 days following the first commercial sale. The Company has also issued warrants with a term of 7 years to RSRT to purchase up to 2,144,772 ordinary shares at a fixed price of $ 3.73. These warrants will vest in full upon the occurrence of (i) product approval by the FDA or EMA, or (ii) a change of control transaction. Upon the occurrence of a change of control transaction, RSRT may elect to receive an amount of $ 16,300,000 in lieu of the warrants (which shall then immediately terminate), which amount shall be set-off against the aforementioned milestone payments, in four equal tranches. In case the Company licenses out the program, the Company shall pay 10% of the royalties received to RSRT, within 60 days of receipt of such licensing revenue. The warrants shall then lapse immediately. Either RSRT or ProQR may terminate the agreement for cause, which includes the Company's material failure to achieve certain milestones. The Company's payment obligations survive the termination of the agreement in case of termination by RSRT.

(d) Research and development commitments

The Company has research and development commitments, mainly with contract research organizations ("CRO's"), amounting to € 9,828,334 at December 31, 2024 (2023: € 8,893,000). Of these obligations an amount of € 9,542,784 is due in 2025, the remainder is due in 2 to 5 years.

27. Related-Party Transactions

Details of transactions between the Company and related parties are disclosed below.

(a) Compensation of the Board of Directors and senior management

In May 2024, the Company changed the governance structure from a two-tier to one-tier board with the previous members of the Supervisory Board appointed to the Board of Directors as Non-Executive Directors and the previous members of the Management Board appointed to the Board of Directors as Executive Directors. The Company's Board is supported by its senior management. Mr. Daniel de Boer, Mr. René Beukema and Dr. Gerard Platenburg (from May 2024 onwards) are the executive directors of the Company. Following the change in the governance, for 2024, the Company discloses the remuneration of the Board and senior management combined. The comparative information for 2023 and 2022 has been amended accordingly.

The remuneration of the Board of Directors and senior management in 2024 is set out in the table below:

	2024			
	Short term employee benefits	Post-employment benefits	Share-based payment	Total
	(€ in thousands)			
Non-Executive Directors				
Dinko Valerio, Ph.D.	56	—	51	107
Alison F. Lawton	48	—	51	99
James Shannon, M.D.	71	—	51	122
Bart Filius	49	—	51	100
Begoña Carreño, Ph.D.	42	—	35	77
Theresa Heggie	48	—	127	175
Martin Maier, Ph.D.*	26	—	—	26
Total Non-Executive Directors	340	—	366	706
Executive Directors				
Daniel de Boer**	939	27	864	1,830
René Beukema**	659	27	294	980
Gerard Platenburg, Ph.D.***	321	24	143	488
Total Executive Directors	1,919	78	1,301	3,298
Senior Management	946	48	323	1,317
	3,205	**126**	**1,990**	**5,321**

* Dr. Maier was elected to the Board of Directors on May 22, 2024. The remuneration set forth for Dr. Maier in the table above covers the period from May 22, 2024 to December 31, 2024.

** Short term employee benefits include bonuses for Mr. de Boer of € 394,000 and for Mr. Beukema of € 231,000 based on goals realized in 2024.

*** Dr. Platenburg was elected to the Board of Directors on May 22, 2024. Dr. Platenburg served as Chief Scientific Officer in 2024, 2023 and 2022. Until May 22, 2024, his renumeration was included as part of the Senior Management. Short term employee benefits include bonuses for Dr. Platenburg of € 185,000 based on goals realized in 2024, of which € 67,000 was included as part of the Senior Management.

The remuneration of the Board of Directors and senior management in 2023 is set out in the table below:

	2023			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	(€ in thousands)			
Non-Executive Directors				
Dinko Valerio, Ph.D.	74	—	76	150
Antoine Papiernik*	—	—	—	—
Alison F. Lawton	50	—	76	126
James Shannon, M.D.	56	—	76	132
Bart Filius	49	—	78	127
Begoña Carreño, Ph.D.**	50	—	34	84
Theresa Heggie***	30	—	241	271
Total Non-Executive Directors	309	—	581	890
Executive Directors				
Daniel de Boer****	1,167	27	1,245	2,439
René Beukema****	892	23	395	1,310
Total Executive Directors	2,059	50	1,640	3,749
Senior Management	1,145	52	562	1,759
	3,513	**102**	**2,783**	**6,398**

* Mr. Papiernik stepped down from the supervisory board on May 18, 2023. In 2023, Mr. Papiernik waived his compensation

** Dr. Carreño was elected to the supervisory board on May 18, 2023. The remuneration set forth for Dr. Carreño in the table above covers the period from May 18, 2023 to December 31, 2023.

*** Ms. Heggie was elected to the supervisory board on May 18, 2023. The remuneration set forth for Ms. Heggie in the table above covers the period from May 18, 2023 to December 31, 2023. Ms. Heggie's share-based payments include the effects of options and RSUs that were granted to her before her reappointment to the supervisory board on May 18, 2023.

**** Short term employee benefits include bonuses for Mr. de Boer of € 643,000 and for Mr. Beukema of € 481,000 based on goals realized in 2023.

The 2022 remuneration is set out in the table below:

	2022			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	(€ in thousands)			
Non-Executive Directors				
Dinko Valerio, Ph.D.	74	—	104	178
Antoine Papiernik*	—	—	—	—
Alison F. Lawton	52	—	104	156
James Shannon, M.D.	59	—	104	163
Bart Filius	49	—	104	153
Total Non-Executive Directors	234	—	416	650
Executive Directors				
Daniel de Boer**	1,295	24	1,145	2,464
René Beukema**	284	10	169	463
Total Executive Directors	1,579	34	1,314	2,927
Senior Management	3,980	123	506	4,609
	5,793	**157**	**2,236**	**8,186**

* In 2022, Mr. Papiernik waived his compensation

** Short term employee benefits include a bonus for Mr. Daniel de Boer of € 791,000 and for Mr. René Beukema of € 84,000 based on goals realized in 2022.

As at December 31, 2024:

- Dr. Valerio holds 725,692 ordinary shares in the Company, as well as 216,453 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Dr. Valerio was awarded 23,489 options to acquire ordinary shares at an exercise price of $ 1.98 per option. In 2023, Dr. Valerio was awarded 22,608 options to acquire ordinary shares at an exercise price of $ 3.41 per option. In 2022, Dr. Valerio was granted 23,931 options to acquire ordinary shares at an exercise price of $ 8.01 per option.

- Ms. Alison F. Lawton holds 221,423 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Ms. Lawton was granted 23,489 options to acquire ordinary shares at an exercise price of $ 1.98 per option. In 2023, Ms. Lawton was granted 22,608 options to acquire ordinary shares at an exercise price of $ 3.41 per option. In 2022, Ms. Lawton was granted 23,931 options to acquire ordinary shares at an exercise price of $ 8.01 per option.

- Dr. Shannon holds 61,538 ordinary shares in the Company and 225,533 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Dr. Shannon was granted 23,489 options to acquire ordinary shares at an exercise price of $ 1.98 per option. In 2023, Dr. Shannon was granted 22,608 options to acquire ordinary shares at an exercise price of $ 3.41 per option. In 2022, Mr. Shannon was granted 23,931 options to acquire ordinary shares at an exercise price of $ 8.01 per option.

- Mr. Filius holds 130,637 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Mr. Filius was granted 23,489 options to acquire ordinary shares at an exercise price of $ 1.98 per option. In 2023, Mr. Filius was granted 22,608 options to acquire ordinary shares at an exercise price of $ 3.41 per option. In 2022, Mr. Filius was granted 23,931 options to acquire ordinary shares at an exercise price of $ 8.01 per option.

- Dr. Carreño holds 49,957 options. These options vest in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Dr. Carreño was granted 23,489 options to acquire ordinary shares at an exercise price of $ 1.98 per option. In 2023, Dr. Carreño was granted 22,903 options to acquire ordinary shares at an exercise price of $ 3.41 per option. In 2022, Dr. Carreño was granted 3,565 options to acquire ordinary shares at an exercise price of $ 0.95 per option.

- Ms. Heggie holds 37,489 ordinary shares in the Company and 358,245 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Ms. Heggie was granted 23,489 options to acquire ordinary shares at an exercise price of $ 1.98 per option. In 2023, Ms. Heggie was granted 14,418 options to acquire ordinary shares at an exercise price of $ 1.74 per option. In 2022, Ms. Heggie was granted 159,150 options to acquire ordinary shares at an average exercise price of $ 0.84 per option.

- Dr. Maier holds 1,500 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Dr. Maier was granted 500 options to acquire ordinary shares at an exercise price of $ 1.98 per option.

- Mr. de Boer holds 4,435,067 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Mr. de Boer was awarded 479,171 options at an exercise price of $ 1.98 per option. In 2023, Mr. de Boer was awarded 442,182 options at an exercise price of $ 3.41 per option. In 2022, Mr. de Boer was awarded 1,650,051 options to acquire ordinary shares at an average exercise price of $ 0.76 per option.

- Mr. Beukema holds 460,000 ordinary shares in the Company as well as 1,506,493 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Mr. Beukema was awarded 143,175 options to acquire ordinary shares at an exercise price of $ 1.98 per option. In 2023, Mr. Beukema was awarded 132,123 options to acquire ordinary shares at an exercise price of $ 3.41 per option. In 2022, Mr. Beukema was awarded 1,000,000 options to acquire ordinary shares at an exercise price of $ 0.66 per option.

- Dr. Platenburg holds 824,338 ordinary shares in the Company as well as 990,909 options. These options either vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant, or in thirteen tranches where the first tranche vests at the first anniversary of the grant date, and the remaining options vest in twelve equal tranches of 6.25% each subsequent quarter until the fourth anniversary of the grant date. In 2024, Dr. Platenburg was awarded 164,715 options to acquire ordinary shares at an exercise price of $ 1.98 per option.

ProQR does not grant any loans, advance payments and guarantees to members of the Board of Directors.

(b) Transactions with Yarrow Biotechnology, Inc.

As described in Note 8. Investments in Associates, the Company, as of October 2023, no longer has significant influence over Yarrow. Yarrow is therefore, no longer considered a related party as of that point onwards. The Company did not have any transactions with Yarrow in the year ended December 31, 2024. Transactions with Yarrow for the years ended December 31, 2023 and 2022 are described in Note 17. Revenue.

28. Auditor fees

The fees for services provided by the Company's external auditors, KPMG Accountants N.V. for the years ended December 31, 2024, 2023 and 2022, are specified below for each of the financial years indicated:

	2024	2023	2022
		(€ in thousands)	
Audit fees	618	588	512
Audit-related fees	257	—	32
Tax fees	—	—	—
All other fees	—	—	—
	875	**588**	**544**

(1) Audit fees consist of aggregate fees for professional services provided in connection with the annual audit of the financial statements.

(2) Audit-related fees consist of procedures relating to share offerings, such as comfort letters, as well as consents and review of documents filed with the SEC.

(3) Tax fees consist of fees for professional services provided for tax compliance, advice, and planning and the nature of the services comprising these fees.

(4) All other fees consist of aggregate fees for services provided other than the services included above.

The Company's audit committee has adopted a policy governing the pre-approval of all audit and non-audit services performed by its external auditors, including audit services and audit-related services as described above, other than those for de minimis services which are approved by the audit committee prior to the completion of the audit, to ensure that the provision of such services does not impair the external auditors' independence from the Company and its management.

During fiscal years 2024, 2023 and 2022, no services were provided to the Company by KPMG Accountants N.V. other than in accordance with the pre-approval policies and procedures described above.

29. Subsequent events

No significant events occurred after the balance sheet date.

Exhibit 1.1

ARTICLES OF ASSOCIATION
DEFINITIONS AND INTERPRETATION
Article 1

1.1 In these articles of association the following definitions shall apply:

Article	An article of these articles of association.
Board	The Company's board of directors.
Board Rules	The internal rules applicable to the Board.
CEO	The Company's chief executive officer.
Class Meeting	The meeting of holders of shares of a certain class.
Company	The company to which these articles of association pertain.
DCC	The Dutch Civil Code.
Director	Refers to both an Executive Director and a Non-Executive Director
Executive Director	The member of the Board appointed as executive director.
General Meeting	The Company's general meeting of shareholders.
Group Company	An entity or company which is organisationally connected with the Company in an economic unit within the meaning of Section 2:24b DCC.
Indemnified Officer	A current or former member of the Board and a former member of the management board or supervisory board when the company had a two tier board system.
Meeting Rights	With respect to the Company, the rights attributed by law to the holders of depository receipts issued for shares with a company's cooperation, including the right to attend and address a General Meeting.
Non-Distributable Equity	The part of the Company's equity that is formed by the paid up and called up part of its capital and the reserves which it must maintain by law.
Non-Executive Director	The member of the Board appointed as non-executive director.
Person with Meeting Rights	A shareholder, a usufructuary or pledgee with voting rights.
Preferred Distribution	A distribution on the preferred shares for an amount equal to the Preferred Interest Rate calculated over the aggregate amount paid up on those preferred shares, whereby: a. any amount paid up on those preferred shares (including as a result of an issue of preferred shares) during the financial year (or the relevant part thereof) in respect of which the distribution is made shall only be

	taken into account proportionate to the number of days that elapsed during that financial year (or the relevant part thereof) after those preferred shares were paid up; b. any reduction of the aggregate amount paid-up on preferred shares during the financial year (or the relevant part thereof) in respect of which the distribution is made shall be taken into account proportionate to the number of days that elapsed during that financial year (or the relevant part thereof) until such reduction of the aggregate amount paid-up on preferred shares was effected; and c. if the distribution is made in respect of part of a financial year, the amount of the distribution shall be proportionate to the number of days that elapsed during that part of the financial year.
Preferred Interest Rate	The mathematical average, calculated over the financial year (or the relevant part thereof) in respect of which a distribution is made on preferred shares, of the EURIBOR interest rate for loans with a maturity of twelve months as published by Thomson Reuters, plus a margin not exceeding five hundred basis points (500bps) to be determined by the Board each time when preferred shares are issued without preferred shares already forming part of the Company's issued share capital.
Registration Date	The twenty-eighth day prior to the date of a General Meeting.
Simple Majority	More than half of the votes cast.
Subsidiary	A subsidiary within the meaning of Section 2:24a DCC, including: a. an entity in whose general meeting the Company or one or more of its Subsidiaries can exercise, whether or not by virtue of an agreement with other parties with voting rights, individually or collectively, more than half of the voting rights; and b. an entity of which the Company or one or more of its Subsidiaries are members or shareholders and can appoint or dismiss, whether or not by virtue of an agreement

	with other parties with voting rights, individually or collectively, more than half of the managing directors or of the supervisory directors, even if all parties with voting rights cast their votes.
Website	The Company's website.

1.2 References to "shares" or "shareholders" are to any class of shares or to the holders thereof, respectively.

1.3 References to statutory provisions are to those provisions as they are in force from time to time.

1.4 Terms that are defined in the singular have a corresponding meaning in the plural.

1.5 Words denoting a gender include each other gender.

1.6 The terms "written" and "in writing" include the use of electronic means of communication.

NAME AND SEAT
Article 2

2.1 The Company's name is ProQR Therapeutics N.V.

2.2 The Company has its corporate seat in Leiden.

OBJECTS
Article 3

The Company's objects are:

a. to develop, to bring to market and to exploit products and technologies in the field of biotechnology;

b. to research and develop (or to commission the research and development of) patents, know-how and intellectual and industrial property;

c. to make the Company's 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;

d. 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;

e. 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

f. to do anything which, in the widest sense, is connected with or may be conducive to the matters described above in this Article 3.

SHARES - AUTHORISED SHARE CAPITAL AND DEPOSITORY RECEIPTS
Article 4

4.1 The Company's authorised share capital amounts to thirteen million six hundred thousand euro (EUR 13,600,000).

4.2 The authorised share capital is divided into:

a. one hundred and seventy million (170,000,000) ordinary shares; and

b. one hundred and seventy million (170,000,000) preferred shares,

each having a nominal value of four eurocents (EUR 0.04).

4.2 The Board may resolve that one or more shares are divided into such number of fractional shares as may be determined by the Board. Unless specified differently, the provisions of these articles of association concerning shares and shareholders apply mutatis mutandis to fractional shares and the holders thereof, respectively.

4.3 The Company cannot cooperate with the issue of depository receipts for shares in its capital.

SHARES - FORM OF SHARES AND SHARE REGISTER
Article 5

5.1 All shares are registered shares, provided that the Board may resolve that one or more ordinary shares are bearer shares, represented by physical share certificates.

5.2 The Board is not required to comply with a request made by a shareholder to convert one or more of his registered shares into bearer shares or vice versa. If the Board resolves to grant such a request, the shareholder concerned shall be charged for the costs of such conversion.

5.3 Registered shares shall be numbered consecutively for each class of shares, starting from 1.

5.4 The Board shall keep a register setting out the names and addresses of all holders of registered shares and all holders of a usufruct or pledge in respect such shares. The register shall also set out any other particulars that must be included in the register pursuant to Section 2:85 DCC and further such other particulars as the Board deems prudent. Part of the register may be kept outside the Netherlands to comply with applicable local law or applicable stock exchange rules.

5.5 Shareholders, usufructuaries and pledgees whose particulars must be set out in the register shall provide the Board with the necessary particulars in a timely fashion. Any consequences of a failure to notify such particulars or to notify the correct particulars shall be borne by the relevant party.

5.6 All notifications may be sent to Persons with Meeting Rights in respect of registered shares at the addresses set out in the register.

5.7 If the Board has resolved that one or more ordinary shares are bearer shares, share certificates shall be issued for such bearer shares in such form as the Board may determine. Share certificates may represent one or more bearer shares. Each share certificate shall be signed by or on behalf of an Executive Director.

5.8 The holder of a bearer share that was lost may request the Company to provide a duplicate share certificate for such bearer share. The Company shall only provide such duplicate:

a. if the party making the request can demonstrate, to the satisfaction of the Board, that such party is indeed entitled to receive such duplicate; and

b. after having published the request on the Website for a period of four weeks without any objection to such request having been received by the Company within that period.

5.9 If an objection as referred to in Article 5.8 paragraph b. has been received by the Company in a timely fashion, the Company shall only provide the duplicate to the party who requested such duplicate after having been provided with a copy of a binding advice or court order to provide such duplicate, without the Company being

required to investigate the competence of the relevant arbitrators or court, as the case may be, or the validity of such binding advice or judgment, as the case may be.

5.10 Upon a duplicate of a share certificate for a bearer share having been provided by the Company, such duplicate shall replace the original share certificate and no rights can be derived from the share certificate thus replaced.

SHARES - ISSUE
Article 6

6.1 Shares can be issued pursuant to a resolution of the General Meeting or of another body authorised by the General Meeting for this purpose for a specified period not exceeding five years. When granting such authorisation, the number of shares that may be issued must be specified. The authorisation may be extended, in each case for a period not exceeding five years. Unless stipulated differently when granting the authorisation, the authorisation cannot be revoked. For as long as another body has been authorised to issue shares, the General Meeting shall not have this authority.

6.2 Article 6.1 applies mutatis mutandis to the granting of rights to subscribe for shares, but does not apply in respect of issuing shares to a party exercising a previously acquired right to subscribe for shares.

6.3 The Company may not subscribe for shares in its own capital.

SHARES - PRE-EMPTION RIGHTS
Article 7

7.1 Upon an issue of shares, each holder of ordinary shares shall have a pre-emption right in proportion to the aggregate nominal value of his ordinary shares. Preferred shares do not carry pre-emption rights.

7.2 In deviation of Article 7.1, holders of ordinary shares do not have pre-emption rights in respect of an issue of:

a. preferred shares;

b. ordinary shares against non-cash contribution; or

c. ordinary shares to employees of the Company or of a Group Company.

7.3 The Company shall announce an issue with pre-emption rights and the period during which those rights can be exercised in the State Gazette and in a daily newspaper with national distribution, unless all shares are registered shares and the announcement is sent in writing to all shareholders at the addresses submitted by them.

7.4 Pre-emption rights may be exercised for a period of at least two weeks after the date of announcement in the State Gazette or after the announcement was sent to the shareholders.

7.5 Pre-emption rights may be limited or excluded by a resolution of the General Meeting or of the body authorised pursuant to Article 6.1, if that body was authorised by the General Meeting for this purpose for a specified period not exceeding five years. The authorisation may be extended, in each case for a period not exceeding five years. Unless stipulated differently when granting the authorisation, the authorisation cannot be revoked. For as long as another body has been authorised to limit or exclude pre-emption rights, the General Meeting shall

not have this authority.

7.6 A resolution of the General Meeting to limit or exclude pre-emption rights, or to grant an authorisation as referred to in Article 7.5, shall require a majority of at least two thirds of the votes cast if less than half of the issued share capital is represented at the General Meeting.

7.7 The preceding provisions of this Article 7 apply mutatis mutandis to the granting of rights to subscribe for shares, but do not apply in respect of issuing shares to a party exercising a previously acquired right to subscribe for shares.

SHARES - PAYMENT
Article 8

8.1 Without prejudice to Article 8.2, the nominal value of a share and, if the share is subscribed for at a higher price, the difference between these amounts must be paid up upon subscription for that share. However, it may be stipulated that part of the nominal value of a preferred share, not exceeding three quarters thereof, need not be paid up until the Company has called for payment. The Company shall observe a reasonable notice period of at least one month with respect to any such call for payment.

8.2 Parties who professionally place shares for their own account may be allowed by virtue of an agreement to pay up less than the nominal value of the shares subscribed for by them, provided that at least ninety-four percent (94%) of this amount is paid up in cash ultimately upon subscription for those shares.

8.3 Shares must be paid up in cash, except to the extent that payment by means of a contribution in another form has been agreed.

8.4 Payment in a currency that is not a unit of the euro is only permitted with the Company's consent. Where such a payment is made, the payment obligation is satisfied for the amount in euro for which the paid amount can be freely exchanged. The date of the payment determines the exchange rate. The previous sentence does not prejudice the last sentence of Section 2:80a(3) DCC.

8.5 The Board is authorised to enter into legal acts relating to non-cash contributions and the other legal acts referred to in Section 2:94 of the Dutch Civil Code without the prior approval of the General Meeting.

SHARES - FINANCIAL ASSISTANCE
Article 9

9.1 The Company may not provide security, give a price guarantee, warrant performance in any other way or commit itself jointly and severally or otherwise with or for others with a view to the subscription for or acquisition of shares or depository receipts for shares in its capital by others. This prohibition applies equally to Subsidiaries.

9.2 The Company and its Subsidiaries may not provide loans with a view to the subscription for or acquisition of shares or depository receipts for shares in the Company's capital by others, unless the Board resolves to do so and the relevant statutory requirements of Section 2:98c DCC are observed.

9.3 The preceding provisions of this Article 9 do not apply if shares or depository receipts for shares are subscribed for or acquired by or for employees of the

Company or of a Group Company.

SHARES - OWN SHARES
Article 10

10.1 The acquisition by the Company of shares in its own capital which have not been fully paid up shall be null and void.

10.2 The Company may only acquire fully paid up shares in its own capital for no consideration or if and to the extent that the General Meeting has authorised the Board for this purpose and all other relevant statutory requirements of Section 2:98 DCC are observed.

10.3 An authorisation as referred to in Article 10.2 remains valid for no longer than eighteen months. When granting such authorisation, the General Meeting shall determine the number of shares that may be acquired, how they may be acquired and within which range the acquisition price must be. An authorisation shall not be required for the Company to acquire ordinary shares in its own capital in order to transfer them to employees of the Company or of a Group Company pursuant to an arrangement applicable to them, provided that these ordinary shares are included on the price list of a stock exchange.

10.4 The Company may acquire shares in its own capital for cash consideration or for consideration satisfied in the form of assets. In the case of a consideration being satisfied in the form of assets, the value thereof, as determined by the Board, must be within the range stipulated by the General Meeting as referred to in Article 10.3.

10.5 Articles 10.1 through 10.3 do not apply to shares acquired by the Company by universal succession.

10.6 In this Article 10, references to shares include depository receipts for shares.

SHARES - REDUCTION OF ISSUED SHARE CAPITAL
Article 11

11.1 The General Meeting can resolve to reduce the Company's issued share capital by cancelling shares or by reducing the nominal value of shares by virtue of an amendment to these articles of association. The resolution must designate the shares to which the resolution relates and it must provide for the implementation of the resolution.

11.2 A resolution to cancel shares may only relate to:

a. shares held by the Company itself or in respect of which the Company holds the depository receipts; or

b. all preferred shares, with repayment of the amounts paid up in respect thereof and provided that, to the extent allowed under Articles 34.1 and 35.2, a distribution is made on those preferred shares, in proportion to the amounts paid up on those preferred shares, immediately prior to such cancellation becoming effective, which distribution shall consist of:

i. the total of all Preferred Distributions (or parts thereof) in relation to financial years prior to the financial year in which the cancellation occurs, to the extent that these have not yet been paid as described in Article 35.1; and

ii. the Preferred Distribution calculated in respect of the part of the

financial year in which the cancellation occurs, for the number of days that have elapsed during such part of the financial year.

11.3 A resolution of the General Meeting to reduce the Company's issued share capital shall require a majority of at least two thirds of the votes cast if less than half of the issued share capital is represented at the General Meeting.

11.4 If a resolution of the General Meeting to reduce the Company's issued share capital relates to preferred shares, such resolution shall always require the prior or simultaneous approval of the Class Meeting of preferred shares.

SHARES - TRANSFER REQUIREMENTS
Article 12

12.1 Except as otherwise provided or allowed by Dutch law, the transfer of a share shall require a deed to that effect and unless the Company itself is a party to the transaction, acknowledgement of the transfer by the Company.

12.2 The acknowledgement shall be set out in the deed or shall be made in such other manner as prescribed by law.

SHARES - USUFRUCT AND PLEDGE
Article 13

13.1 Ordinary shares can be encumbered with a usufruct or pledge. Preferred shares can be encumbered with a usufruct, but cannot be pledged. The voting rights attached to preferred shares which are subject to a usufruct, cannot vest in the usufructuary concerned.

13.2 The voting rights attached to an ordinary share which is subject to a usufruct or pledge vest in the shareholder concerned.

13.3 In deviation of Article 13.2, the holder of a usufruct or pledge on ordinary shares shall have the voting rights attached thereto if this was provided when the usufruct or pledge was created.

13.4 Usufructuaries and pledgees without voting rights shall not have Meeting Rights.

TRANSFER RESTRICTIONS
Article 14

14.1 A transfer of preferred shares shall require the prior approval of the Board. A shareholder wishing to transfer one or more preferred shares must first request the Board to grant such approval. For the avoidance of doubt, a transfer of ordinary shares is not subject to transfer restrictions under these articles of association.

14.2 The transfer of preferred shares to which the request for approval relates must take place within three months after the approval of the Board has been granted or is deemed to have been granted pursuant to Article 14.3.

14.3 The approval of the Board shall be deemed to have been granted:

a. if no resolution granting or denying the approval has been passed by the Board within three months after the Company has received the request for approval; or

b. if the Board, when denying the approval, does not notify the requesting shareholder of the identity of one or more potential acquirers willing to purchase the preferred shares to which the request for approval relates.

14.4 If the Board denies the approval and notifies the requesting shareholder of the

identity of one or more potential acquirers, the requesting shareholder shall notify the Board within two weeks after having received such notice whether:

a. he withdraws his request for approval, in which case the requesting shareholder cannot transfer the preferred shares concerned; or

b. he accepts the potential acquirer(s), in which case the requesting shareholder shall promptly enter into negotiations with the potential acquirer(s) regarding the price to be paid for the preferred shares concerned.

14.5 If the negotiations referred to in Article 14.4 paragraph b. have resulted in an agreement within two weeks after the end of the period referred to in Article 14.4, the preferred shares concerned shall be transferred for the agreed price within three months after such agreement having been reached. However, if the negotiations referred to in Article 14.4 paragraph b. have not resulted in an agreement within two weeks after the end of the period referred to in Article 14.4:

a. the requesting shareholder shall promptly notify the Board thereof; and

b. the price to be paid for the preferred shares concerned shall be equal to the value thereof, as determined by one or more independent experts to be appointed by the requesting shareholder and the potential acquirer(s) by mutual agreement.

14.6 If no agreement is reached on the appointment of the independent expert(s) as referred to in Article 14.5 paragraph b. within two weeks after the end of the period referred to in Article 14.5:

a. the requesting shareholder shall promptly notify the Board thereof; and

b. the requesting shareholder shall promptly request the president of the district court in whose district the Company has its corporate seat to appoint three independent experts to determine the value of the preferred shares concerned.

14.7 If and when the value of the preferred shares concerned has been determined by the independent expert(s), irrespective of whether he/they were appointed by mutual agreement or by the president of the relevant district court, the requesting shareholder shall promptly notify the Board of the value so determined.

14.8 Promptly following the receipt of a notice as referred to in Article 14.7, the Board shall request the/each potential acquirer whether he wishes to withdraw from the sale procedure and, if so, to send notice thereof to the Board within two weeks, failing which he shall be assumed not to have withdrawn from the sale procedure.

14.9 If no potential acquirer withdraws from the sale procedure in accordance with Article 14.8, the preferred shares concerned shall be transferred for the price determined by the independent expert(s) within three months after the end of the period referred to in Article 14.8. However, if any potential acquirer withdraws from the sale procedure in accordance with Article 14.8, the Board:

a. shall promptly inform the requesting shareholder and the other potential acquirer(s), if any, thereof; and

b. shall give the opportunity to each other potential acquirer, if any, to declare to the Board and the requesting shareholder, within two weeks, his willingness to acquire the preferred shares that have become available as a

result of the withdrawal, for the price determined by the independent expert(s).

14.10 If it appears that all preferred shares concerned can be transferred for a price determined by the independent expert(s), as a result of one or more other potential acquirers having declared his/their willingness to acquire preferred shares that have become available as a result of a withdrawal as described in Article 14.9 paragraph b., such transfer shall take place within three months after the end of the period referred to in Article 14.9 paragraph b. However, if it appears that not all preferred shares concerned can be transferred for a price determined by the independent expert(s) as a result of a withdrawal by one or more potential acquirers:

a. the Board shall promptly notify the requesting shareholder thereof; and

b. the requesting shareholder shall be free to transfer all of the preferred shares to which the request for approval relates, provided that the transfer takes place within three months after having received the notice referred to in paragraph a.

14.11 The Company may only be a potential acquirer under this Article 14 with the consent of the requesting shareholder.

14.12 All notices given pursuant to this Article 14 shall be provided in writing.

14.13 The preceding provisions of this Article 14 do not apply if:

a. a shareholder is under a statutory obligation to transfer his preferred shares to a previous holder thereof; or

b. a shareholder transfers preferred shares to the Company, except in the case that the Company acts as a potential acquirer pursuant to Article 14.11.

14.14 In this Article 14 rights to subscribe for preferred shares shall be equated with preferred shares.

BOARD – COMPOSITION AND APPOINTMENT
Article 15

15.1 The total number of Directors, as well as the number of Executive Directors and Non-Executive Directors, is determined by the Board. Only individuals can be Non-Executive Directors.

15.2 Each Director shall retire in accordance with a rotation schedule to be included in the Board Rules. A retiring Director can be reappointed immediately, subject to such rotation schedule.

15.3 Directors will be appointed by the General Meeting of Shareholders. Directors will be appointed either as an Executive Director or as a Non-Executive Director.

15.4 The Board will nominate a candidate for each vacant seat.

15.5 A nomination by the Board will be binding. However, the General Meeting of Shareholders may deprive the nomination of its binding character by a resolution passed with a two-third majority of the votes cast representing more than half of the issued share capital. If the binding nomination is not deprived of its binding character, the person nominated will be deemed appointed. If the nomination is deprived of its binding character, the Board will be allowed to make a new binding nomination.

15.6 At a General Meeting of Shareholders, votes in respect of the appointment of a

Director can only be cast for candidates named in the agenda of the meeting or explanatory notes thereto.

15.7 A nomination to appoint a Director will state the candidate's age and the positions he holds or has held, insofar as these are relevant for the performance of the duties of a Director. The nomination must state the reasons on which they are based.

15.8 A nomination will also state the candidate's term of office. The term of office of Directors may not exceed a maximum period of four years at a time. A Director who ceases office in accordance with the previous provisions is immediately eligible for reappointment.

15.9 Each Director may be suspended or removed by the General Meeting of Shareholders at any time. A resolution of the General Meeting of Shareholders to suspend or remove a Director other than pursuant to a proposal by the Board requires a two-third majority of the votes cast representing more than half of the issued share capital. An Executive Director may also be suspended by the Board. A suspension by the Board may at any time be discontinued by the General Meeting of Shareholders.

15.10 Any suspension may be extended one or more times, but may not last longer than three months in the aggregate. If, at the end of that period, no decision has been taken on termination of the suspension or on removal, the suspension will end.

REMUNERATION OF DIRECTORS
Article 16

16.1 The Company must have a policy with respect to the remuneration of Directors. This policy is determined by the General Meeting; the Board will make a proposal to that end. The Executive Directors may not participate in the discussion and decision-making process of the Board on this.

16.2 The authority to establish remuneration and other terms of service for Directors is vested in the Board, with due observance of the remuneration policy referred to in Article 16.1 and applicable provisions of law. The Executive Directors may not participate in the discussion and decision-making process of the Board with respect to the remuneration of Executive Directors.

16.3 The Board shall submit to the General Meeting of Shareholders for approval plans to issue Ordinary Shares or to grant rights to subscribe for Ordinary Shares to Directors. The plans shall at least indicate the number of Ordinary Shares and the rights to subscribe for Ordinary Shares that may be allotted to Directors and the criteria that shall apply to the allotment or any change thereto.

16.4 The absence of approvals required pursuant to Article 16.3 will not affect the authority of the Board or its members to represent the Company.

16.5 Directors are entitled to an indemnity from the Company and D&O insurance, in accordance with Article 24.

BOARD – GENERAL DUTIES.
Article 17

17.1 The Board is charged with the management of the Company. In performing their duties, Directors shall be guided by the interests of the Company and of the business connected with it.

17.2 The Board shall draw up Board Rules concerning the organisation, decision-making and other internal matters of the Board, with due observance of these articles of association. In performing their duties, the Directors shall observe and comply with the Board Rules.

BOARD – ALLOCATION OF DUTIES
Article 18

18.1 The duty of the Non-Executive Directors is to supervise the performance of duties by the Executive Directors as well as the general course of affairs of the Company and the business connected with it. The Non-Executive Directors are also charged with the duties assigned to them pursuant to the law and these Articles of Association.

18.2 The Board shall elect a Non-Executive Director to be the chairman of the Board. The Board may remove the chairman of the Board, in the sense that the Non-Executive Director so removed shall subsequently continue his term of office as a Non-Executive Director without having the title of chairman of the Board.

18.3 An Executive Director, designated by the Board, will be the CEO. The Board may grant other titles to Directors.

18.4 The specific duties of the CEO and other Directors, if any, will be laid down by the Board in writing.

18.5 To the extent permitted by Dutch law, the Board may assign and delegate such duties and powers to individual Directors and/or committees. This may also include a delegation of resolution-making power, provided this is laid down in writing. A Director to whom and a committee to which powers of the Board are delegated, must comply with the rules set in relation thereto by the Board.

18.6 The Board may appoint a company secretary and is authorised to replace him at any time. The company secretary holds the duties and powers vested in him pursuant to these Articles of Association or a resolution of the Board. In absence of the company secretary, his duties and powers are exercised by his deputy, if designated by the chairman of the Board.

BOARD - REPRESENTATION
Article 19

19.1 The Board is authorised to represent the Company. Each Executive Director is also solely authorised to represent the Company.

19.2 The Company may appoint officers with general or limited power of representation. Each of these officers may represent the Company subject to the limitations relating to his power.

BOARD – MEETINGS AND DECISION-MAKING
Article 20

20.1 The Board meets as often as deemed desirable by the chairman of the Board. The meeting is chaired by the chairman of the Board or in his absence the vice-chairman. Minutes of the proceedings at the meeting must be kept.

20.2 Board resolutions are adopted by absolute majority of the votes cast. Each Director has one vote. Where there is a tie in any vote of the Board, the chairman of the Board shall have a casting vote. The Board may designate types of resolutions which are

subject to requirements deviating from the foregoing. These types of resolutions and the nature of the deviation must be clearly specified and laid down in writing.

20.3 Decisions taken at a meeting of the Board will only be valid if the majority of the Directors is present or represented at the meeting. The Board may designate types of resolutions which are subject to requirements deviating from the foregoing. These types of resolutions and the nature of the deviation must be clearly specified and laid down in writing.

20.4 Meetings of the Board may be held by means of an assembly of the Directors in person in a formal meeting or by conference call, video conference or by any other means of communication, provided that all Directors participating in such meeting are able to communicate with each other simultaneously. Participation in a meeting held in any of the above ways shall constitute presence at such meeting.

20.5 For adoption of a resolution other than at a meeting, it is required that the proposal is submitted to all Directors, none of them has objected to the relevant manner of adopting resolutions and such majority of the Directors as required pursuant to Article 20.2 has expressly consented to the relevant manner of adopting resolutions.

20.6 Third parties may rely on a written declaration by the chairman of the Board, each Executive Director or the company secretary concerning resolutions adopted by the Board or a committee thereof. Where it concerns a resolution adopted by a committee, third parties may also rely on a written declaration by the chairman of such committee.

20.7 In Board meetings and with respect to the adoption of Board resolutions, a Board member may be represented only by another Board member, authorized in writing.

20.8 The Board may establish additional rules regarding its working methods and decision-making process.

BOARD – CONFLICTS OF INTERESTS
Article 21

21.1 A Director having a conflict of interests as referred to in Article 21.2 or an interest which may have the appearance of such a conflict of interests (both a **(potential) conflict of interests**) must declare the nature and extent of that interest to the other Directors.

21.2 A Director may not participate in deliberating or decision-making within the Board, if with respect to the matter concerned he has a direct or indirect personal interest that conflicts with the interests of the Company and the business connected with it. This prohibition does not apply if the conflict of interests exists for all Directors and the Board shall maintain its power.

21.3 A conflict of interests as referred to in Article 21.2 only exists if in the situation at hand the Director must be deemed to be unable to serve the interests of the Company and the business connected with it with the required level of integrity and objectivity. If a transaction is proposed in which apart from the Company also an affiliate of the Company has an interest, then the mere fact that a Director holds any office or other function with the affiliate concerned or another affiliate, whether or not it is remunerated, does not mean that a conflict of interests as referred to in Article 21.2 exists.

21.4 The Director who in connection with a (potential) conflict of interests does not exercise certain duties and powers will insofar be regarded as a Director who is unable to perform his duties (*belet*).

21.5 A (potential) conflict of interests does not affect the authority concerning representation of the Company set forth in Article 19.1.

BOARD – VACANCIES AND INABILITY TO ACT
Article 22

22.1 For each vacant seat on the Board, the Board can determine that it will be temporarily occupied by a person (a stand-in) designated by the Board. Persons that can be designated as such include former Directors (irrespective of the reason why they are no longer Directors).

22.2 If and as long as one or more seats on the Board are vacant, the management of the Company will be temporarily entrusted to the person or persons who (whether as a stand-in or not) do occupy a seat in the Board.

22.3 If the seats of one or more Directors are vacant, the Board may temporarily entrust duties and powers of the vacant seat to another Director.

22.4 When determining to which extent Board members are present or represented, consent to a manner of adopting resolutions, or vote, stand-ins will be counted-in and no account will be taken of vacant seats for which no stand-in has been designated.

22.5 For the purpose of this Article 22, the seat of a Director who is unable to perform his duties (*belet*) will be treated as a vacant seat.

BOARD – APPROVAL BOARD RESOLUTIONS
Article 23

23.1 The Board requires the approval of the General Meeting for resolutions entailing a significant change in the identity or character of the Company or its business, in any case concerning:

a. the transfer of (nearly) the entire business of the Company to a third party;

b. entering into or terminating a long term cooperation between the Company or a subsidiary (*dochtermaatschappij*) and another legal entity or company or as a fully liable partner in a limited partnership or general partnership, if such cooperation or termination is of fundamental importance for the Company;

c. acquiring or disposing of a participation in the capital of a company if the value of such participation is at least one third of the sum of the assets of the Company according to its balance sheet and explanatory notes or, if the Company prepares a consolidated balance sheet, its consolidated balance sheet and explanatory notes according to the last adopted annual accounts of the Company, by the Company or a subsidiary (*dochtermaatschappij*).

23.2 The absence of approvals required pursuant to Article 23.1 will not affect the authority of the Board or its members to represent the Company.

INDEMNITY
Article 24

24.1 The Company shall indemnify each of its Indemnified Officers against:

a. any financial losses or damages incurred by such Indemnified Officer; and

b. any expense reasonably paid or incurred by such Indemnified Officer 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 or former position with the Company, in each case to the fullest extent permitted by applicable law.

24.2 No indemnification shall be given to an Indemnified Officer:

a. if a Dutch court has established, without possibility for appeal, that the acts or omissions of such Indemnified Officer that led to the financial losses, damages, suit, claim, action or legal proceedings as described in Article 24.1 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).

24.3 The Board may stipulate additional terms, conditions and restrictions in relation to the indemnification referred to in Article 24.1.

GENERAL MEETINGS – CONVENING AND HOLDING GENERAL MEETINGS
Article 25

25.1 Annually, at least one General Meeting must be held. This annual General Meeting shall be held within six months after the end of the Company's financial year.

25.2 A General Meeting shall also be held:

a. within three months after the 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; and

b. whenever the Board so decides.

25.3 General Meetings must be held in the place where the Company has its corporate seat in Amsterdam, Rotterdam, Schiphol Airport (municipality Haarlemmermeer), The Hague, Oegstgeest, Leidschendam, Katwijk, Noordwijk or Wassenaar.

25.4 If the Board have failed to ensure that a General Meeting as referred to in Articles 25.1 or 25.2 paragraph a. is held in a timely fashion, each Person with Meeting Rights may be authorised by the court in preliminary relief proceedings to convene the General Meeting.

25.5 One or more Persons with Meeting Rights who collectively represent at least ten percent (10%) of the Company's issued share capital may request the Board in writing to convene a General Meeting, setting out in detail the matters to be discussed. If the Board has not taken the steps necessary to ensure that the General Meeting could be held within the relevant statutory period after the request, the requesting Person(s) with Meeting Rights may be authorised, at his/their request, by the court in preliminary relief proceedings to convene a General Meeting.

25.6 Any matter of which the discussion has been requested in writing by one or more Persons with Meeting Rights who, individually or collectively, represent at least three percent (3%) of the Company's issued share capital shall be included in the

convening notice or announced in the same manner, if the Company has received the substantiated request or a proposal for a resolution no later than on the sixtieth day prior to that of the General Meeting.

25.7 A General Meeting must be convened with due observance of the relevant statutory minimum convening period.

25.8 All Persons with Meeting Rights must be convened for a General Meeting:

a. by means of an announcement published on the Website, where it shall remain directly and permanently available until the General Meeting; and

b. if so required under applicable law, in a daily newspaper with national distribution.

25.9 The holders of registered shares may be convened for a General Meeting by means of letters sent to the addresses of those shareholders in accordance with Article 5.6. The previous sentence does not prejudice the possibility of sending a convening notice by electronic means in accordance with Section 2:113(4) DCC.

GENERAL MEETING - PROCEDURAL RULES
Article 26

26.1 The General Meeting shall be chaired as follows, and in the following order of priority:

a. if there is a chairman of the Board and he is present at the General Meeting, by the chairman of the Board;

b. by another Non-Executive Director present at the General Meeting chosen by the Non-Executive Directors present at the General Meeting;

c. if there is a CEO and he is present at the General Meeting, by the CEO;

d. by another Executive Director present at the General Meeting chosen by the Executive Directors present at the General Meeting; or

e. by another person appointed by the General Meeting.

The person who should chair the General Meeting pursuant to paragraphs a. through d. may appoint another person to chair the General Meeting instead of him.

26.2 The chairman of the General Meeting shall appoint another person present at the General Meeting to act as secretary and to minute the proceedings at the General Meeting. Where an official report of the proceedings is drawn up by a civil law notary, no minutes need to be taken. Every member of the Board may instruct a civil law notary to draw up such an official report at the Company's expense.

26.3 The chairman of the General Meeting shall decide whether persons other than:

a. Persons with Meeting Rights; and

b. others with a statutory right to attend the General Meeting,

shall be admitted to the General Meeting.

26.4 The holder of a written proxy representing a Person with Meeting Rights at a General Meeting shall only be admitted to the General Meeting if the proxy is determined to be acceptable by the chairman of the General Meeting.

26.5 The Company may direct that any person, before entering a General Meeting, identify himself by means of a valid passport or driver's license and to be submitted to such security restrictions or arrangements as the Company may consider to be appropriate under the given circumstances. Persons who do not comply with these

requirements or restrictions may be refused entry to the General Meeting.

26.6 The chairman of the General Meeting has the right to eject any person from the General Meeting if he considers that person to disrupt the orderly proceedings at the General Meeting. In case of ejection, the chairman of the General Meeting may temporarily adjourn the meeting.

26.7 The General Meeting may be conducted in the English language, if so determined by the chairman of the General Meeting.

26.8 The chairman of the General Meeting may limit the amount of time that individuals present at the General Meeting are allowed to take in addressing the General Meeting and the number of questions they are allowed to raise, with a view to ensuring the orderly proceedings at the General Meeting.

GENERAL MEETING - EXERCISE OF MEETING AND VOTING RIGHTS
Article 27

27.1 Each Person with Meeting Rights has the right to attend, address and, if applicable, vote at a General Meeting, whether in person or represented by the holder of a written proxy. Holders of fractional shares of a certain class, if any, together constituting the nominal value of a share of that class, shall exercise these rights collectively, whether through one of them or through the holder of a written proxy.

27.2 The Board may decide that each Person with Meeting Rights is entitled, whether in person or represented by the holder of a written proxy, to participate in, address and, if applicable, vote at the General Meeting by electronic means of communication. For the purpose of applying the preceding sentence it must be possible, by electronic means of communication, for the Person with Meeting Rights to be identified, to observe in real time the proceedings at the General Meeting and, if applicable, to vote. The Board may impose conditions on the use of the electronic means of communication, provided that these conditions are reasonable and necessary for the identification of the Person with Meeting Rights and the reliability and security of the communication. Such conditions must be announced in the convening notice.

27.3 The Board can also decide that votes cast through electronic means of communication or by means of a letter prior to a General Meeting are considered to be votes that are cast during the General Meeting. These votes shall not be cast prior to the Registration Date.

27.4 For the purpose of Articles 27.1 through 27.3, those who have voting rights and/or Meeting Rights on the Registration Date and are recorded as such in a register designated by the Board shall be considered to have voting rights and/or Meeting Rights, as the case may be, irrespective of whoever is entitled to the shares at the time of the General Meeting. Subject to mandatory Dutch law, the Board is free to determine, when convening a General Meeting, whether the previous sentence applies.

27.5 As a prerequisite for a Person with Meeting Rights to exercise his Meeting Rights and, if applicable, his voting rights at a General Meeting, that Person with Meeting Rights must notify the Company in writing of his identity and his intention to attend the General Meeting. This notice must be sent after the Registration Date and must be received by the Company ultimately on the seventh day prior to the General

Meeting. Persons with Meeting Rights that have not complied with this requirement may be refused entry to the General Meeting.

GENERAL MEETING - DECISION-MAKING
Article 28

28.1 Each share, irrespective of which class it concerns, shall give the right to cast one vote at General Meetings. For this purpose, fractional shares of a certain class, if any, collectively constituting the nominal value of a share of that class shall be considered to be equivalent to a share of that class.

28.2 No vote may be cast at a General Meeting in respect of a share belonging to the Company or a Subsidiary or in respect of a share for which any of them holds the depository receipts. Usufructuaries and pledgees of shares belonging to the Company or its Subsidiaries are not, however, precluded from exercising their voting rights if the usufruct or pledge was created before the relevant share belonged to the Company or Subsidiary. Neither the Company nor a Subsidiary may vote shares in respect of which it holds a usufruct or a pledge.

28.3 Unless a greater majority is required by law or by these articles of association, all resolutions of the General Meeting shall be passed by Simple Majority.

28.4 Invalid votes, blank votes and abstentions shall not be counted as votes cast. Shares in respect of which an invalid or blank vote has been cast and shares in respect of which an abstention has been made shall be taken into account when determining the part of the issued share capital that is present or represented at a General Meeting.

28.5 Where there is a tie in any vote of the General Meeting, no resolution shall have been passed.

28.6 The chairman of the General Meeting shall decide on the method of voting and may determine the voting procedure at General Meetings.

28.7 The determination made by the chairman of the General Meeting 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 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 General Meeting so requires. The legal consequences of the original vote shall lapse as a result of the new vote.

28.8 The Board shall keep a record of the resolutions passed. The record shall be available at the Company's office for inspection by Persons with Meeting Rights. Each of them shall, upon request, be provided with a copy of or extract from the record, at no more than the cost price.

28.9 The members of the Board shall, in that capacity, have an advisory vote at General Meetings.

GENERAL MEETING - RESOLUTIONS REQUIRING A PRIOR PROPOSAL
Article 29

The following resolutions can only be resolved upon by the General Meeting at the proposal of the Board:

a. the issue of shares or the granting of rights to subscribe for shares;

b. the limitation or exclusion of pre-emption rights;

c. the granting of an authorisation as referred to in Articles 6.1, 7.5 or 10.2;

d. the reduction of the Company's issued share capital;

e. the granting of an approval as referred to in Article 23.1;

f. a distribution to the holders of ordinary shares;

g. the determination that all or part of a distribution, instead of being made in cash, shall be made in the form of shares in the Company's capital or in the form of assets;

h. the amendment of these articles of association;

i. the entering into of a merger or demerger;

j. the instruction of the Board to apply for the Company's bankruptcy; and

k. the Company's dissolution.

CLASS MEETINGS
Article 30

30.1 A Class Meeting shall be held whenever a resolution of that Class Meeting is required by Dutch law or under these articles of association or whenever the Board so decides.

30.2 Without prejudice to Article 30.1, for Class Meetings of ordinary shares, the provisions concerning the convening, drawing up of agendas for, holding of and decision-making at General Meetings shall apply mutatis mutandis.

30.3 For Class Meetings of preferred shares, the following shall apply:

a. Articles 25.9, 26.2, 28.1, 28.2 and 28.4 through 28.9 apply mutatis mutandis;

b. a Class Meeting of preferred shares must be convened no later than on the eighth day prior to that of the meeting;

c. a Class Meeting of preferred shares shall appoint its own chairman;

d. all resolutions of a Class Meeting of preferred shares shall be passed by Simple Majority; and

e. where the rules laid down by these articles of association in relation to the convening, location of or drawing up of agendas for Class Meetings of preferred shares have not been complied with, legally valid resolutions may still be passed by the Class Meeting of preferred shares by a unanimous vote at a meeting at which all preferred shares are represented.

30.4 Holders of preferred shares may pass resolutions in writing instead of at a meeting. However, such resolutions may only be passed by a unanimous vote of all holders of preferred shares. The votes may also be cast electronically.

REPORTING – FINANCIAL YEAR, ANNUAL ACCOUNTS AND REPORT OF THE BOARD
Article 31

31.1 The Company's financial year shall coincide with the calendar year.

31.2 Annually, within the relevant statutory period, the Board shall prepare the annual accounts and the report of the Board and deposit them at the Company's office for inspection by the shareholders.

31.3 The annual accounts shall be signed by the members of the Board. If any of their signatures is missing, this shall be mentioned, stating the reasons.

31.4 The Company shall ensure that the annual accounts, the report of the Board and the

particulars to be added pursuant to Section 2:392(1) DCC shall be available at its offices as from the convening of the General Meeting at which they are to be discussed. Persons with Meeting Rights are entitled to inspect such documents at that location and to obtain a copy at no cost.

31.5 The annual accounts shall be adopted by the General Meeting.

REPORTING - AUDIT
Article 32

32.1 The General Meeting shall instruct an auditor as referred to in Section 2:393 DCC to audit the annual accounts. Where the General Meeting fails to instruct an auditor, the Board shall be authorised to do so.

32.2 The instruction may be revoked by the General Meeting and by the body that has granted the instruction. The instruction can only be revoked for well-founded reasons; a difference of opinion regarding the reporting or auditing methods shall not constitute such a reason.

DISTRIBUTIONS - RESERVES
Article 33

33.1 The Company may maintain any reserve attached exclusively to the ordinary shares as the Board deems to be appropriate.

33.2 The Company shall not attach any reserve to the preferred shares.

DISTRIBUTIONS - ENTITLEMENT AND RESTRICTIONS
Article 34

34.1 A distribution can only be made to the extent that the Company's equity exceeds the Non-Distributable Equity.

34.2 The preferred shares do not carry any entitlement to distributions other than as described in Articles 11.2, 35.1 and 36.3.

34.3 The parties entitled to a distribution shall be the shareholders, usufructuaries and pledgees, as the case may be, as at a date to be determined by the Board for that purpose. This date shall not be earlier than the date on which the distribution was announced.

34.4 Subject to the other provisions of this Article 34, the General Meeting may resolve to make a distribution from the Company's reserves.

34.5 The General Meeting may resolve that all or part of such distribution, instead of being made in cash, shall be made in the form of shares in the Company's capital or in the form of assets.

34.6 The Board may resolve to make interim distributions, provided that it appears from interim accounts to be prepared in accordance with Section 2:105(4) DCC that the requirement referred to in Article 34.1 has been met, and taking into account the priority of distributions under Article 35.1.

34.7 The Board may resolve to charge amounts to be paid up on shares against the Company's reserves, irrespective of whether those shares are issued to existing shareholders.

34.8 A distribution shall be payable in such currency and on such date as determined by the Board.

34.9 A claim for payment of a distribution shall lapse after five years have expired after

the distribution was declared.

34.10 For the purpose of calculating any distribution as referred to in this Article 34, shares held by the Company in its own capital shall not be taken into account. No distribution as referred to in this Article 34 shall be made to the Company in respect of shares held by it.

DISTRIBUTIONS - PROFITS
Article 35

35.1 Subject to Article 34.1, the profits shown in the Company's annual accounts in respect of a financial year shall be appropriated as follows, and in the following order of priority:

a. to the extent that any preferred shares have been cancelled without the payment described in Article 11.2 paragraph b. having been made in full on those preferred shares, any such deficit shall be paid to those who held those preferred shares at the moment of such cancellation becoming effective;

b. to the extent that any Preferred Distribution (or part thereof) in relation to previous financial years has not yet been paid as described in this Article 35.1, any such deficit shall be paid on the preferred shares;

c. the Preferred Distribution shall be paid on the preferred shares in respect of the financial year to which the annual accounts pertain;

d. the Board shall determine which part of the remaining profits shall be added to the Company's reserves; and

e. any remaining profits shall be at the disposal of the General Meeting for distribution to the holders of ordinary shares in proportion to the aggregate nominal value of their ordinary shares.

To the extent that the distributions described in paragraphs a. through c. (or part thereof) cannot be paid out of the profits shown in the annual accounts, the deficit shall be paid out of the Company's reserves, subject to Article 34.1.

Distributions on the preferred shares (or to the former holders of preferred shares) as described in this Article 35.1 shall be paid in proportion to the amounts paid up (or formerly paid up) on those preferred shares.

For the avoidance of doubt, the preferred shares shall not carry any entitlement to profits other than as described in this Article 35.1.

35.2 Without prejudice to Article 34.1, a distribution of profits shall be made after the adoption of the annual accounts that show that such distribution is allowed.

35.3 For the purpose of calculating any distribution of profits, shares held by the Company in its own capital shall not be taken into account. No distribution of profits shall be made to the Company in respect of shares held by it.

DISSOLUTION AND LIQUIDATION
Article 36

36.1 In the event of the Company being dissolved, the liquidation shall be effected by the Board, unless the General Meeting in its resolution to dissolve the Company decides otherwise.

36.2 To the extent possible, these articles of association shall remain in effect during the

liquidation.

36.3 To the extent that any assets remain after payment of all of the Company's debts, those assets shall be distributed as follows, and in the following order of priority:

a. the amounts paid up on the preferred shares shall be repaid on those preferred shares;

b. to the extent that any preferred shares have been cancelled without the payment described in Article 11.2 paragraph b. having been made in full on those preferred shares, any such deficit shall be paid to those who held those preferred shares at the moment of such cancellation becoming effective; and

c. to the extent that any Preferred Distribution (or part thereof) in relation to financial years prior to the financial year in which the distribution referred to in paragraph a. occurs has not yet been paid as described in Article 35.1, any such deficit shall be paid on the preferred shares;

d. the Preferred Distribution shall be paid on the preferred shares calculated in respect of the part of the financial year in which the distribution referred to in paragraph a. occurs, for the number of days that have already elapsed during such part of the financial year; and

e. any remaining assets shall be distributed to the holders of ordinary shares in proportion to the aggregate nominal value of their ordinary shares.

Distributions on the preferred shares (or to the former holders of preferred shares) as described in this Article 36.3 shall be paid in proportion to the amounts paid up (or formerly paid up) on those preferred shares.

36.4 For the purpose of calculating any distribution as referred to in Article 36.3, shares held by the Company in its own capital shall not be taken into account. No distribution as referred to in Article 36.3 shall be made to the Company in respect of shares held by it.

36.5 After the liquidation has been completed, the Company's books, records and other information carriers shall be kept for the period prescribed by law by the person designated for that purpose in the resolution of the General Meeting to dissolve the Company. Where the General Meeting has not designated such a person, the liquidators shall do so.

Exhibit 4.1

The Terms and Conditions of the ProQR Therapeutics N.V. Equity Incentive Plan

Revised version (V.3) dated 22 May 2024

Rule 1 Definitions

In the Rules of this Plan, unless the context otherwise requires, the following words and expressions shall have the meanings as set out below:

Articles of Association	the articles of association of the Company as amended from time to time;
Business Day	a day which is not a Saturday or a Sunday and which is not a public holiday or a bank holiday in the Netherlands;
Board	the (one-tier) board of directors (*bestuur*) of the Company;
Cause by the relevant Group Company	in the context of termination of a Participant's status as an employee or officer of the relevant Group Company or as a service provider to the relevant Group Company, a reason which constitutes a serious cause on the side of the relevant Group Company within the meaning of Article 7:679 of the Dutch Civil Code, or other serious cause on the side of the relevant Group Company representing a material breach under the employment, service or other relevant agreement or engagement entered into with that Participant;
Cause by the Individual	in the context of termination of a Participant's status as an employee or officer of the relevant Group Company or as a service provider to the relevant Group Company, a reason which constitutes an urgent cause on the side of that Participant within the meaning of Article 7:678 or qualifies as a reasonable ground within the meaning of Article 7:669(3)(c up to and including (h) of the Dutch Civil Code, serious cause on the side of that Participant representing a material breach under the employment, service or other relevant agreement or engagement entered into with that Participant or a material breach by that Participant or his fiduciary tasks and duties towards the Company or the relevant Group Company;
Committee	such person or committee of persons and successor person or successor committee of persons appointed by the Board to whom the Board has delegated any of its powers under this Plan;
Company	the public company with limited liability ProQR Therapeutics N.V., having its office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands, registered with the Dutch Chamber of Commerce under registration number 54600790;
Compensation Policy	the compensation policy for the Board, as adopted by the General Meeting and as amended from time to time;

Control	in respect of the Company or a Group Company, the ability of a person or corporate body to, alone or together with one or more subsidiaries, whether or not in concert with others, (i) exercise or cause to exercise more than one-half of the voting rights in the shareholders' or members' meeting of the Company or such Group Company, or (ii) appoint more than one-half of the directors of the Company or such Group Company, or (iii) exercise decisive influence with regard to the general course of affairs of the Company or such Group Company;
Date of Grant	the date on which one or more Options and/or RSUs is/are offered to an Eligible Individual by the Company, which shall be the date specified in the Notice of Grant;
Effective Date	the date as from which this Plan is effective, as specified on the first page of this document;
Eligible Individual	(i) an Individual, not being a member of the Board, who has been selected by the Board to receive a Grant under the Plan; or (ii) an Individual being a member of the Board who has been selected by the Board to receive a Grant under the Plan in accordance with the Compensation Policy;
Exercise Period	the period during which a Vested Option can be exercised, as specified in the Notice of Grant;
Exit	a Sale, Liquidation or any combination thereof;
Market Value	the market value of one Share as appropriate, as specified in Rule 7 of this Plan;
General Meeting	the Company's general meeting of shareholders as mentioned in the Articles of Association;
Grant	one or more Options and/or RSUs granted to Participants in accordance with or as a result of an Eligible Individual's participation in the Plan;
Group	the Company and its Group Companies;
Group Company	any subsidiary or group company of the Company as defined in Articles 2:24a and 2:24b of the Dutch Civil Code, as may change from time to time;
Individual	any individual who has entered into employment or position with the Company or any Group Company; or an individual (whether or not through the use of a company of which that individual is the sole shareholder) that provides management and/or consulting services for the Company or a Group Company; or an individual who is appointed as an officer of the

	Company or of any Group Company or any other person as determined by the Board;
Insider Trading Rules	the internal code of conduct to be adopted by the Company on insider trading, as may be amended from time to time and/or the securities laws and regulations (including applicable stock exchange or listing rules) in the jurisdiction(s) where Shares or other securities issued by the Company or rights derived thereof) are and/or may be listed to the extent these relate to insider trading;
Liquidation	the liquidation, dissolution or other reorganization of the Company resulting in the Company's shareholders receiving cash or liquid securities as consideration or proceeds in excess of the aggregate subscription price and dividends payable in respect of the Shares held by them;
Notice of Exercise	a notice to the Company in a form to be determined by the Board whereby a Participant exercises an Option granted to him under the Rules of this Plan;
Notice of Grant	a notice to an Eligible Individual in a form to be determined by the Board whereby one or more Options and/or RSUs under this Plan are granted and for an Eligible Individual being a member of the Board, taking into consideration the compensation granted to him and, in general, Compensation Policy;
Option	the right to acquire one (1) Share against payment of the Option Price during the Exercise Period, which right is granted to a Participant under and in accordance with the Rules of this Plan;
Option Price	the price per Share, as determined by the Board at the Date of Grant, in respect of which an Option may be exercised, which shall be the Market Value at the Date of Grant, or such other price per Share as specified in the relevant Notice of Grant, provided that the Option Price per Share shall not be lower than the nominal value of the Share;
Participant	an Eligible Individual who has been offered and has accepted a Grant under the Rules of this Plan;
Performance Condition	one or more performance targets, if any, as set at the Date of Grant specified in the relevant Notice of Grant that should be attained during the relevant Performance Period in order to determine the level of Vesting of a Grant on the relevant Vesting Date;
Performance Period	the period, as determined in the relevant Notice of Grant, over which the attainment of Performance Conditions is measured;

Plan	this ProQR Therapeutics N.V. Equity Incentive Plan in its present form or as from time to time amended, in accordance with the provisions hereof;
Release	the issuance (‘*uitgifte’*) or transfer (‘*levering’*) of Shares to a Participant, and “Released” and “Release Date” shall be construed and interpreted accordingly;
Retirement	retirement at the normal statutory retirement age in a given country at which the relevant Individual becomes entitled to a state old age pension. This statutory retirement age can only be lowered if and to the extent that the Individual is entitled to a form of early retirement on the basis of an individual agreement or collective agreement on Company or Group Company level or in case the Board grants an individual exemption and approves such early retirement;
RSU	a restricted stock unit where each restricted stock unit covers (the value of) one Share that, if the conditions for Vesting have been met, will be settled by the Release of Shares or in cash which right is granted to a Participant under and in accordance with the Rules of this Plan;
Rules	the rules governing the operation of the Plan as may be amended from time to time;
Sale	the sale of more than 50% of the Shares or the sale, lease or licensing out of all or a substantial part of the Company’s assets resulting in the Company no longer exclusively controlling such assets or any other event resulting in a change of Control over the Company, all as determined by the Board;
Section 409A	Section 409A of the Internal Revenue Code of 1986, as amended;
Share	an ordinary share in the capital of the Company, having a nominal value of EUR 0.04 or any other nominal value such Share may have in the future;
Stock Exchange	NASDAQ Global Market or any other market the Shares are listed;
Total and Permanent Disability	the mental or physical disability, whether occupational or non-occupational in cause, which satisfies such definition in any insurance policy or plan provided to a Participant by the Company or a Group Company, or, alternatively, the relevant Participant’s applicable national legislation pertaining to persons with disability;
Vesting	the satisfaction of the requirements of Rule 4 of this Plan, and ‘Vested’ and ‘Vest’ shall be construed accordingly; and

Vesting Date the date on which Options and/or RSUs shall Vest, in whole or in part, as determined by the Board and as specified in the Notice of Grant and pursuant to Rule 4 of this Plan.

Rule 2 Interpretation

Words or expressions used in the Plan shall where appropriate:

(i) when denoting the masculine gender include the feminine and vice versa;

(ii) when denoting the singular include the plural and vice versa;

(iii) when referring to any enactment be construed as a reference to that enactment as for the time being consolidated, amended, re-enacted or replaced and shall include any regulations made there under;

(iv) when a period of time is specified and starts from a given day or the day of an act or event, be calculated inclusive of that day;

(v) be construed such that the headings and sub-headings are for ease of reference only, and do not affect the interpretation of any Rule;

(vi) when referring to any enactment or regulations under Dutch law be construed, at the discretion of the Board, as a reference to other (analogous) applicable laws or regulations of any other country (or region of a country);

(vii) references to tax and/or social security contributions and/or withholding taxes shall for the avoidance of doubt include those applicable under the laws of the Netherlands and any other jurisdiction to which a Participant may be subject;

(viii) when a period of time is specified and ends on a day which is not a Business Day, the end day of such period will be extended to the next Business Day; and

(ix) when referring to an 'officer' this will be construed as including a reference to directors of a Group Company and members of a board and references to someone holding "office" shall be interpreted accordingly.

Rule 3 Powers of the Board

3.1 The Plan shall be administered by the Board.

3.2 The Board shall have such powers and authority delegated to it as set out in the Plan and is responsible to take the Compensation Policy into account. The Board may determine as soon as practicable after the Effective Date if, how and to what extent any of their powers shall be delegated to (or revoked from) any Committee. After such delegation, the Committee shall have such powers and authority delegated to the Board as set out in the Plan in order to administer the Plan, until such time as the Board has revoked such powers and authority.

3.3 The Company shall have the authority and complete discretion to decide whether or not to make Grants under the Plan to Individuals, subject to Rule 3.4, and decide what percentage of the outstanding Shares will be used to give effect to such Grants.

3.4 The Board may select Individuals, not being members of the Board and effect such Grants, as Eligible Individuals and the Board may select Individuals being members of the Board, as Eligible

Individuals and make such Grants to them taking into account their respective compensation and the Compensation Policy in general.

3.5 Notwithstanding Rules 3.1, 3.2 and 3.3, the Board shall have the authority and complete discretion to construe and interpret the provisions of the Plan, any Notice of Grant or any Notice of Exercise and any other agreement or document executed pursuant to the Plan.

Rule 4 Grant and Vesting of Options and RSUs

4.1 Subject to Rules 3.3, 3.4 and 3.5, the Board can offer Options and/or RSUs to Eligible Individuals at any time on or after the Effective Date.

4.2 No Grant will be made if this is not permitted by any order, law, securities regulation, stock exchange rules and/or Insider Trading Rules as applicable to the Company from time to time. The Grant is subject to obtaining any necessary approval or consent required under any applicable regulation or enactment.

4.3 Notwithstanding Rule 4.1, Notices of Grants are concluded on a discretionary basis. A Grant shall therefore not be construed to give any Participant the right to receive future Grants.

4.4 Each Grant shall be evidenced by a signed Notice of Grant concluded between the Participant and the Company, setting forth the terms and conditions pertaining to such Grant. The Notice of Grant shall be available in each of the countries in which the Plan is operational and shall, together and concurrently with the Rules, govern the Grant in accordance with local legal and regulatory requirements and the stock exchange or listing rules to the extent applicable.

4.5 Each Notice of Grant shall include a schedule describing the date(s), event(s) or act(s) upon which an Option and/or RSU shall Vest in whole or part or, in case of Options, become exercisable and shall further specify at least:

(a) in case of Options, the Option Price;
(b) the number of Shares subject to the Grant;
(c) any Performance Conditions and Performance Period that may be imposed and attached to the Vesting of the Options and/or RSUs;
(d) in case of Options, the Exercise Period;
(e) the Date of Grant;
(f) the Vesting Period; and
(g) the date on which the Option(s) to which the Grant pertains will lapse.

4.6 If an Eligible Individual wishes to participate in the Plan, he is required to return a signed copy of the Notice of Grant to the Company or a party designated by the Company within fourteen (14) days following the date on which the offer is made. Options and/or RSUs that are not accepted in

full and in accordance with this Rule 4.6, will lapse automatically with immediate effect and without any consideration becoming due. By accepting a Grant the Participant accepts the Rules and all other regulations and documents relating to the Grant.

4.7 Vesting of the Options and/or RSUs is subject to the attainment of any Performance Conditions imposed and to the Participant remaining an Eligible Individual with continued employment or office with or providing services to the Company or any Group Company until the end of each of the respective Vesting Dates. Such Vesting conditions are specified in the relevant Notice of Grant. Once all Vesting conditions have been satisfied, the Options and/or RSUs Vest. The relevant Notice of Grant specifies on which date the fulfilment of the relevant conditions of Grants will be measured and/or determined. The attainment of the Performance Conditions and the satisfaction of the other Vesting conditions shall be determined by the corporate body or Committee which granted the Options and/or RSUs at its discretion.

4.8 If a Participant ceases to be an Eligible Individual:

(i) due to his death;
(ii) as a consequence of his Total and Permanent Disability or Retirement;
(iii) Cause by the Company; or
(iv) any other individual situation determined by the Board at its discretion,

the Board may, in its sole discretion and acting reasonably, determine that a portion of the outstanding Options and/or RSUs that are not Vested held by that Participant will Vest at the date such Participant ceases to be an Eligible Individual and, in relation to Options, to determine during what period that Participant's Vested Options will remain outstanding (if relevant, for the benefit of the Participant's legal successor(s) in case of death in accordance with Rule 8 of this Plan) whereby this period will not exceed the remaining Exercise Period as specified in the relevant Notice of Grant. In determining such portion the Board may take into consideration the period to the date of the Participant ceasing to be an Eligible Individual. After the expiry of the period during which the Vested Options can be exercised as determined in accordance with this Rule 4.8, the Options will lapse automatically without any consideration becoming payable. In case of death of the Participant, the Board may at its sole discretion also determine to cancel all outstanding Options and/or RSUs (whether Vested or not) and pay (for the benefit of that Participant's legal successor(s)), in case of Options, with respect to each of these Vested Options the (positive) difference between the Market Value of a Share at the date of cancellation and the Option Price, and in case of RSUs, with respect to each of these Vested RSUs an amount equal to the Market Value of a Share at the date of cancellation.

4.9 **Ultimate remedium and claw back** – The Board has for grants of Options and/or RSUs made to members of the Board the authority to adjust the number of unvested Options or unvested RSUs and/or to fully or partially recover Vested Options and Vested RSUs subject to the terms and conditions as contained in or applicable to the Notice of Grant and in general with due observance of Article 2:135 (6) and (8) of the Dutch Civil Code.

Rule 5 Rights of Exercise of Options and Lapse of Options and/or RSUs

5.1 Subject to Rules 4.6 to 4.8, Vested Options will become exercisable during the Exercise Period as specified in the Notice of Grant, except in case of an Exit in which case all Options and RSUs (whether Vested or not) will become exercisable/vested immediately following the occurrence of such Exit, unless otherwise provided for by Rule 13, or will Vest accelerated in accordance with Rule 4.8.

5.2 If a Participant ceases to be an Eligible Individual for any reason other than those set out in Rules 4.8 and 5.3, all the outstanding Options and/or RSUs held by that Participant that are not Vested at the date such Participant ceases to be an Eligible Individual shall lapse immediately at that time without any consideration becoming due. Notwithstanding Rule 5.1, the Participant's Vested Options are exercisable ninety (90) days following the date such Participant ceases to be an Eligible Individual within the Exercise Period, or, in case of Employees who started their Employment with the Company before 23 September 2014, two (2) years following the date such Participant ceases to be an Eligible Individual within the Exercise Period. After this ninety day or two year period, as applicable, (or, if earlier, upon the expiry of the Exercise Period), these Vested Options will lapse automatically without any consideration becoming due.

5.3 In case of termination of employment or office for Cause by the Individual, all the Options (irrespective of whether or not these Options have Vested) and/or unvested RSUs granted, shall immediately lapse at the date of such termination of employment or office, without any consideration becoming due.

5.4 In relation to Options, subject to Rules 4.8, 5.2 and 5.5 of this Plan, the Board may extend the periods during which Options held by a Participant are exercisable following the date such Participant ceases to be an Eligible Individual as described in Rules 4.8 and 5.2, if such an exercise would temporarily be prohibited by law, securities regulations, stock exchange or listing rules, or any applicable Insider Trading Rules. Such period during which the relevant Options are exercisable shall be extended by the length of such period of prohibition. This may apply differently if the Board, acting reasonably and given the specific circumstances of the Participant, determines otherwise, in which event the Board in its sole discretion and acting reasonably, shall determine the extent, and the terms, of the Participant's continued participation in the Plan, including, without limitation, the number of Shares to which his Options pertain and the remaining period during which those Options are exercisable).

5.5 All outstanding Options and/or RSUs of a Participant, whether Vested or not, shall lapse immediately and automatically, without any consideration becoming due, upon the occurrence of the earliest of the following events with respect to those Options and/or RSUs, as the case may be, or that Participant:

(i) in relation to Options, the tenth anniversary of the Date of Grant;
(ii) in relation to Options and/or RSUs, the expiry of any of the applicable periods specified in Rules 4.8, 5.2 and 5.4;
(iii) in relation to Options and/or RSUs, the date of termination of employment or office in case of termination of employment or office for Cause by the Individual pursuant to Rule 5.3;
(iv) in relation to Options and/or RSUs, the expiry of any of the periods which are determined on the basis of any adjustments made in respect of the events as specified in Rules 13 and 14;

(v) in relation to Options and/or RSUs, the Participant's attempted assignment, transfer or encumbrance of any of his Options and/or RSUs other than as permitted under Rules 8 and 13 or in case of another material breach by the Participant of the Rules, unless otherwise determined at the discretion of the Board.

Rule 6 Manner of Exercise of Options

6.1 Subject to Rules 4.8, 5.2, 5.4 and 9 of this Plan, in case of Options, a Grant may be exercised during the Exercise Period after the Options have Vested in accordance with Rule 4.7 and before the Option(s) to which the Grant pertains lapse(s) in accordance with Rules 4.8 and 5.

6.2 Subject to the Rules, an Option may be exercised by the signing of a Notice of Exercise by the Participant which will be effective upon receipt of the signed Notice of Exercise by the Company or a party designated by the Company.

Rule 7 Market Value

The Market Value on a certain date shall be the closing price of one (1) Share (or similar security) as quoted on the Stock Exchange on the last preceding Business Day on which trade in the Shares took place.

Rule 8 Non–transferability and nature of the Options and RSUs

A Grant made to a Participant is strictly personal and shall, in case of Options, if the Options to which such Grant pertains are Vested and during the lifetime of the Participant, be exercisable by the Participant alone, and, in case of Options and/or RSUs not be assignable or transferable and cannot be charged, pledged, encumbered or otherwise used for the purpose of creating security title or interest of whatever nature. The Company is under no obligation required to repurchase any Options, RSUs and/or any Shares pursuant to these Rules. In the event of the Participant's death, such Participant's Options and/or RSUs are transferable to the Participant's beneficiaries only by last will and testament or by the applicable hereditary laws. In all other events any attempted assignment, transfer or encumbrance by a Participant shall be null and void shall cause such Participant's Option(s) and/or RSUs to lapse with immediate effect.

Rule 9 Release of Shares

9.1 In case of Options, subject to Rules 5.4, 6 and this Rule 9 of this Plan, the Company shall Release the Shares to the Participant pursuant to the exercise of a Vested Option as soon as practicable following (i) the date the Participant has returned the Notice of Exercise signed by the Participant, and (ii) the payment of the relevant Option Price. If the Participant has indicated that he wishes to apply the exercise immediate sell method or the sell to cover method for funding the tax liability in accordance with Rule 11.3, the Company shall calculate the number of Shares to be sold under the exercise immediate sell method or sell to cover method, facilitate the sale of such Shares in accordance with Rule 11.3 and transfer the remainder of the cash proceeds following the exercise immediate sell method or the remainder of the Shares under the sell to cover method to the Participant. The remainder of the Shares shall be Released to the Participant concerned.

9.2 In case of RSUs, the Company shall, subject to Rule 5.4 and this Rule 9, Release the Shares subject to a Vested RSU as soon as practicable following the Vesting Date of such Vested RSU, and

ultimately within sixty (60) days from the Vesting Date. The Board may, at its sole discretion, in lieu of the Participant's right to receive Shares pursuant to this Rule, following the Vesting of a RSU, make a cash payment equal to the Market Value.

9.3 The Release is subject to (i) receipt of all required statutory approvals under the relevant laws and regulations and any listing rules of the stock exchanges where Shares (or rights derived therefrom) are traded and (ii) any applicable Insider Trading Rules.

9.4 Subject to Rule 5.4, where the exercise of any Option would temporarily be prohibited by law, securities regulations, stock exchange or listing rules, or any applicable Insider Trading Rules, the Exercise Period, in case of Options, shall be extended with the length of such period of prohibition provided that such Option may not be exercised after the expiry of that Option in accordance with any other Rule of this Plan.

9.5 A Participant shall not be entitled to any compensation of damage or losses insofar as such damage or losses arise(s) or may arise from a delayed exercise or Release under this Rule 9, unless it has been delayed unreasonably by the Company.

9.6 Participants are only permitted to sell, transfer or encumber the Shares acquired by them in accordance with the provisions of the applicable Insider Trading Rules.

Rule 10 Loss of office or employment

10.1 The Plan does not form part of the Participant's employment agreement or service agreement or other engagement with the Company or with any Group Company, and shall not be construed to give any Participant the right to remain in the employ of or continue to provide services to or continue to be an officer of the Company or any Group Company.

10.2 A Grant made to a Participant cannot be considered to be a guarantee to that Participant that the employment or office of that Participant with the Company or any other Group Company, or the providing of services by the Participant to the Company or to any Group Company will continue.

10.3 Any benefits derived by a Participant under this Plan shall not be taken into account for the purposes of determining that Participant's contribution or entitlement to benefits under any retirement arrangement or for the purposes of determining any other claim for compensation that Participant may have against the Company or against any Group Company.

10.4 Where the employment, office or service agreement with the Company or a Group Company of a Participant terminates for whatever reason, that Participant shall not be entitled to any compensation or damages (including damages following unfair dismissal), any other form of breach of contract or any claim for compensation for the loss of employment, office or services insofar as such compensation or damages arise or may arise from the Participant ceasing to have rights under this Plan as a result of such termination. The Plan shall not at any time affect the rights of the Company or a Group Company (or their relevant corporate bodies) to terminate such Participant's status as an officer, an employee or a service provider, whether with or without Cause by the Individual.

10.5 A Grant shall not entitle nor preclude the Participant to whom that Grant was awarded from participating in another Grant under the Plan or participation in any other plan operated by the Company or any Group Company.

Rule 11 Tax and social security

11.1 All applicable personal tax (e.g. any wage tax or income taxes) and employee social security levies as a consequence of or resulting from the Grant of one or more Options and/or RSUs, including, for the avoidance of doubt, as a consequence of or resulting from the Vesting of any Option or RSU, or exercise of any Option, or in respect of the implementation of the Plan shall be borne by the relevant Participant.

11.2 Each Participant shall permit the Company or any Group Company to withhold and account for an amount equal to any wage tax or income tax, employee's social security contributions liability and any other liabilities for which the Company or a Group Company as the case may be, has an obligation to withhold and account. In case an Option and/or RSU is cancelled for whatever reason, the relevant Participant will not be compensated for any taxes or employee social security levies (to be) paid in connection with that Option and/or RSU or the cancellation thereof.

11.3 In order to facilitate the funding of the wage tax, income tax and employee social security levies to be withheld upon exercise of the Options or Release of Shares subject to Vested RSUs, the Company shall allow the Participant to sell, without further action by the Company, all or sufficient Shares Released to such Participant to cover the relevant tax and social security liability ("exercise immediate sell" or "sell to cover" method) at such exercise. The sale proceeds from the application of such exercise immediate sell transaction or sell to cover transaction, after deduction of costs, shall be used to satisfy the withholding liability. The remainder of the cash proceeds or any rounding differences shall be paid in cash by the Participant.

11.4 The Plan is governed by the tax and social security legislation and regulations prevailing as at the date a certain taxable event occurs. If any tax and/or employee social security legislation or regulations are amended and any tax or employee social security levies become payable as a result of such legislative amendment, the costs and the risks related thereto shall be borne solely by the relevant Participant.

11.5 Where, in relation to an Option and/or RSU granted under this Plan, the Company or any Group Company (as the case may be) is liable, or is in accordance with current practice believed by the Board to be liable, to account for any tax or social security authority for any sum in respect of any tax or social security liability of the Participant, the Option may not be exercised or the Shares subject to Vested RSUs shall not be Released unless the relevant Participant has paid to the Company or the Group Company (as the case may be) an amount sufficient to discharge the liability.

11.6 For the avoidance of doubt, the provisions of Rules 11.1 to 11.5 shall apply to a Participant's liabilities that may arise on a taxable event in any jurisdiction.

Rule 12 Variation of Capital

12.1 Subject to the Articles of Association, in the event of a share split, reverse share split, any capitalisation issue, distribution of, extraordinary dividend, rights issue, issue of benefit, or bonus Shares, or rights offer or any reduction, sub-division, consolidation or other variation of the capital of the Company the number of Options and/or RSUs subject to any Grant and/or the Option Price in case of Options, as the case may be, may be adjusted by the Company without prejudice (including retrospective adjustments where appropriate) in such manner as the Company considers to be in its opinion fair and reasonable, or take whatever other reasonable actions the Board considers appropriate, it being understood that such actions may include an additional grant of the rights and/or securities to the relevant Participants, under the same conditions as apply to the variation of capital concerned.

12.2 Notice of any adjustment referred to in Rule 12.1 shall be given by the Company to those Participants affected by such adjustment. The Participant shall receive such a notice within one month following the date the adjustment has been made.

Rule 13 Change of Control of the Company

13.1 Subject to the Articles of Association, required approval of the relevant corporate body, bodies or Committee(s) of the Company and any applicable laws or regulations, in the event of an Exit, a merger, split, or consolidation or similar transaction in relation to the Company, a change in Control of the Company or a share-for-share exchange involving the Company, all outstanding Options and/or RSUs shall Vest in an accelerated manner effective immediately prior to the occurrence of such event, and in addition the Board shall have the power to decide to:

(i) provide for the exchange of each Option and/or RSU outstanding immediately prior to such event for options or RSUs with respect to some or all of the property for which securities are exchanged in such transaction and, as a result, in case of Options, make any necessary equitable adjustment in the Option Price of the new options, or the number of securities or amount of property subject to the Options and/or RSUs or, as appropriate, provide for a cash payment to the Participants to whom such Options and/or RSUs were granted in partial consideration for the exchange of the Options and/or RSUs; and/or

(ii) effective immediately prior to the occurrence of such event, cancel each outstanding Option and/or RSU and pay the Participants, in case of Options, for each of their respective Options thus cancelled, the (positive) difference between the underlying Market Value of a Share at the date of cancellation and the Option Price or, in case of RSUs, for each of their respective RSUs, the Market Value at the date of cancellation; and/or

(iii) take whatever other reasonable steps the Board considers appropriate.

13.2 Subject to Rule 13.1 all adjustments and/or payments described in Rule 13.1 shall be made by the Board and shall be reviewed and approved by an independent advisor appointed by the Board. Such approval shall be conclusive and binding on all persons.

13.3 Except as expressly provided in Rules 12 and 13, no Participant shall be afforded any rights by reason of any capital or corporate reorganisation of the Company or any other transaction as set out in Rule 13.1.

13.4 Except as expressly provided in Rules 12 and 13, a Grant effected pursuant to the Plan shall not affect in any way the right or power of the Company or any Group Company to effect any capital or corporate reorganisation.

13.5 If an event occurs constituting a change of Control of a Group Company due to which the Participant is no longer employed with or an officer of or no longer provide(s) service to the Group, the Board can at its absolute discretion provide for any adjustments or payments as deemed appropriate such as, *inter alia*, continuation of the Plan or settlement of the outstanding Options or RSUs of the Participant immediately prior to such event.

Rule 14 Plan amendments and special provisions

14.1 Subject to the Articles of Association and Rule 14.2, the Board acting reasonably may from time to time at its discretion amend or waive any requirement or conditions under any of the Rules, the Notice of Grant and/or the Notice of Exercise.

14.2 The Plan is adopted by the General Meeting. Any material amendment of the Rules of this Plan requires prior approval of the General Meeting.

14.3 Any action by the Board shall not be taken in relation to any Option or RSU held by a Participant subject to US taxation if it would cause the Option or RSU that is otherwise exempt from taxation under Section 409A to become subject to taxation under Section 409A, or that would cause an Option or RSU that is subject to taxation under Section 409A to fail to satisfy the requirements of Section 409A.

Rule 15 Notification

15.1 The administration of the Plan will be executed by the Company or a third party administrator as appointed by the Company.

15.2 Any notice or other document required to be given to any Participant with respect to the operation of this Plan shall be delivered to him at his home address or such other address as may appear to the Company to be appropriate, or by e-mail message or in any other format agreed in advance between the Participant and the person giving the notice on behalf of the Board. Any notice or other document required to be given to the Company or the Board shall be delivered in a format agreed in advance between the Participant and the person receiving the notice.

15.3 In the execution of the Plan, the Company will respect and comply with applicable data protection laws. Each Participant acknowledges by the acceptance of the Grant that processing, collection, recording, organising, storing and adapting of personal data by the Company or third party administrators involved in the operation and administration of the Plan may occur for that purpose only. This may also include transferring such information to countries or territories that fall outside of the European Economic Area and which may not provide the same level of data protection as the European Economic Area or the Participant's home country. The Company may also keep the personal data of each Participant to comply with statutory retention periods. Each Participant

acknowledges that this may restrict the Participant's rights. Each Participant has the right to access and/or correct personal data, if and when necessary, by contacting the Company. Information about how the Company processes personal data of Participants is set out in the Company's privacy policy, as amended from time to time.

15.4 The Board may, at its absolute discretion, issue written guidance setting out the procedures whereby the Plan shall be operated.

Rule 16 Insider Trading Rules

16.1 Participants and the Company shall be subject to and bound by the terms and conditions of any Insider Trading Rules. Such Insider Trading Rules may restrict the rights of the Participants and/or the Company under this Plan.

16.2 Participants are deemed to be familiar and are responsible for complying with any applicable Insider Trading Rules and any other information, guidance and/or regulations issued by the Company or relevant government or regulatory bodies. The Company shall incur no liability should a Participant act in breach of any Insider Trading Rules or any other information, guidance and/or regulations issued by the Company or relevant government or regulatory bodies.

Rule 17 Disputes

The decision of the Board, in any dispute or question relating to any Grant shall be final and conclusive subject to the terms of this Plan. The provisions of a Notice of Grant shall govern and prevail in the event of any conflict with the Rules.

Rule 18 Costs of the Plan

Without prejudice to Rule 11, the costs of introducing, operating and administering this Plan shall be borne by the Company. Any cost incurred with respect to the application of the exercise immediate sell method or sell to cover method as described in Rule 11.3, shall be borne by the Participant.

Rule 19 Governing law

This Plan shall be governed by and shall be construed in accordance with the law of The Netherlands. The Company and each Participant hereby irrevocably submit, in respect of any suit, action or proceeding related to the implementation or enforcement of this Plan, shall be settled by the Court of Amsterdam the Netherlands.

* * *

Exhibit 4.4

ADDENDUM TO THE CALL OPTION AGREEMENT

THIS ADDENDUM IS MADE ON 6 NOVEMBER 2018 BETWEEN

(1) ProQR Therapeutics N.V., a public company under Dutch law (*naamloze vennootschap*), having its official seat in Leiden, its office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands and registered in the Dutch Commercial Register under number 54600790 (the **Company**);

(2) Stichting Continuity ProQR Therapeutics, a foundation under Dutch law (*stichting*), having its official seat in Leiden, its office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands and registered in the Dutch Commercial Register under number 61435775 (the **Foundation**).

RECITALS

(A) The Company and the Foundation are a party to a call option agreement dated 23 September 2014 and the addendum thereto entered into in 2015 (the **Call Option Agreement**) with a view to the realisation of a situation in which the Foundation can delay, mitigate or prevent the acquisition or expansion of influence and/or control over the Company which the Foundation considers to be, or reasonably expects to lead to, a Threat.

(B) The Company and the Foundation wish to amend the Call Option Agreement in order to provide for an obligation for the Company to charge the Exercise Price (or part thereof) to the Company's reserves if so requested by the Foundation.

NOW HEREBY AGREE AS FOLLOWS:

1. DEFINITIONS

Unless specifically provided otherwise herein the definitions used in this Addendum will have the meaning set out in the Call Option Agreement.

2. AMENDMENT OF CLAUSE 2.4.5 OF THE CALL OPTION AGREEMENT

Clause 2.4.5 of the Call Option Agreement is hereby amended and will read as follows:

"2.4.5 Upon receipt of a request from the Foundation to charge the Exercise Price (or part thereof) against the Company's reserves as referred to in Article 2.4.4 (a), the Company will be obliged to facilitate such request but only up to the amount equal to the available freely distributable reserves. In deviation of Article 2.3.1 the Exercise Price shall be 100% of the total nominal value of the Preferred Shares if so requested by the Foundation. In the event the Exercise Price cannot be satisfied in full by charging it to the Company's reserves, the Management Board shall inform the Foundation as soon as possible but ultimately within two Business Days following receipt of the request. Upon receipt of a request from the Foundation to facilitate payment of the Exercise Price (or part thereof) in the manner as referred to in Article 2.4.4 (b) the Management Board shall inform the Foundation within two Business Days following the receipt of such request whether it wishes to facilitate such request and whether the Supervisory Board has approved this. If so, the Management Board shall inform the Foundation which part of the Exercise Price the Management Board

has determined to be satisfied as described in Article 2.4.4 (b), as well as the method(s) to be used for this purpose."

3. INTEGRAL PART

This Addendum forms an integral part of the Call Option Agreement and any reference to the Call Option Agreement will also be a reference to this Addendum and vice versa.

4. GOVERNING LAW AND JURISDICTION

4.1 Governing Law

This Addendum shall be governed by and construed in accordance with the laws of the Netherlands.

4.2 Jurisdiction

The Foundation and the Company agree that any dispute in connection with this Addendum or any agreement resulting therefrom shall be submitted to the exclusive jurisdiction of the competent court in Amsterdam.

(signature page follows)

Signature page to the Addendum to the Call Option Agreement

ProQR Therapeutics N.V.
Name:
Title:

Stichting Continuuity ProQR Therapeutics
Name:
Title:

Stichting Continuity ProQR Therapeutics
Name:
Title:

Exhibit 4.5

ADDENDUM TO THE CALL OPTION AGREEMENT

THIS ADDENDUM IS MADE ON 27 FEBRUARY 2025 BETWEEN

(1) ProQR Therapeutics N.V., a public company under Dutch law (*naamloze vennootschap*), having its official seat in Leiden, its office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands and registered in the Dutch Commercial Register under number 54600790 (the **Company**);

(2) Stichting Continuity ProQR Therapeutics, a foundation under Dutch law (*stichting*), having its official seat in Leiden, its office address at Zernikedreef 9, 2333 CK Leiden, the Netherlands and registered in the Dutch Commercial Register under number 61435775 (the **Foundation**).

RECITALS

(A) The Company and the Foundation are a party to a call option agreement originally dated 23 September 2014 (the **Call Option Agreement**) with a view to the realisation of a situation in which the Foundation can delay, mitigate or prevent the acquisition or expansion of influence and/or control over the Company which the Foundation considers to be, or reasonably expects to lead to, a Threat.

(B) On 23 May 2024 the Company changed its two-tier board system into a one-tier board system. In view of the foregoing the Company and the Foundation wish to update the Call Option Agreement in this respect.

NOW HEREBY AGREE AS FOLLOWS:

1. DEFINITIONS

Unless specifically provided otherwise herein the definitions used in this Addendum will have the meaning set out in the Call Option Agreement.

2. ONE-TIER BOARD

2.1 As of 23 May 2024, any and all powers, rights, and obligations that were previously allocated to the Management Board and the Supervisory Board are assumed by the Company's one-tier board, referred to as the Board of Directors.

2.2 A new definition will be included in clause 1.1.1 of the Call Option Agreement, reading as follows:

"Board of Directors The Company's board of directors."

2.3 The definitions "Management Board" and "Supervisory Board" will be abolished.

2.4 All references to the "Management Board" and the "Supervisory Board" throughout the Call Option Agreement will be replaced by the "Board of Directors."

3. INTEGRAL PART

This Addendum forms an integral part of the Call Option Agreement and any reference to the Call Option Agreement will also be a reference to this Addendum and vice versa.

4. GOVERNING LAW AND JURISDICTION

4.1 Governing Law

This Addendum shall be governed by and construed in accordance with the laws of the Netherlands.

4.2 Jurisdiction

The Foundation and the Company agree that any dispute in connection with this Addendum or any agreement resulting therefrom shall be submitted to the exclusive jurisdiction of the competent court in Amsterdam.

(signature page follows)

ProQR Therapeutics N.V.
Name: **R. Beukema**
Title: **Chief Corporate Development and General Counsel**

Stichting Continuuity ProQR Therapeutics
Name: **J. Hommen**
Title: **Chairman of the Board**

Stichting Continuity ProQR Therapeutics
Name: **S. Hepkema**
Title: **Board Member**

Exhibit 4.6

INDEMNIFICATION AGREEMENT

[●]

BETWEEN

PROQR THERAPEUTICS N.V.
the Company

[●]
the Indemnitee

A&O SHEARMAN

Allen Overy Shearman Sterling LLP

CONTENTS

THIS AGREEMENT IS MADE AND ENTERED INTO AS OF [DATE]

BETWEEN:

(1) **PROQR THERAPEUTICS N.V.**, a public limited liability company (*naamloze vennootschap met beperkte aansprakelijkheid*) organized under the laws of the Netherlands, having its corporate seat at Leiden and its address at Zernikedreef 9, 2333 CK, Leiden, registered with the trade register of the Dutch Chamber of Commerce under number 54600790 (the **Company**), and

(2) [name], an individual, born on [date] in [city], currently residing at [address] (the **Indemnitee**),

The Company and the Indemnitee hereinafter jointly also referred to as the **Parties** and each individually as a **Party**,

WHEREAS

(A) The articles of association of the Company contain an indemnification for current and former Directors and provide that the Board may stipulate additional terms, conditions and restrictions in relation to the indemnification. Further, the indemnification for current and former Directors also applies *mutatis mutandis* to such other current and former Officers of the Company as the Board of the Company may determine in its sole discretion.

(B) Both the Company and the Indemnitee recognize the increased risk of expensive and time-consuming litigation and other claims being asserted against directors and officers of companies and that highly competent and experienced persons have become more reluctant to serve or continue to serve companies as directors or officers unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of companies.

(C) The Board has determined that:

(a) an increased difficulty in attracting and retaining highly competent persons, such as the Indemnitee, is detrimental to the best interests of the Company and its business;

(b) the Company may not be able – now or in the future – to obtain and keep liability insurance with full and adequate coverage for directors and officers;

(c) it is reasonable, prudent and in the best interests of the Company and its business to, in furtherance of the Company's articles of association, enter into this Agreement (i) to provide for the indemnification of and advancement of expenses to the Indemnitee as set forth in this Agreement in order to provide increased certainty of protection to the Indemnitee and induce the Indemnitee to provide and continue to provide services to the Company, and (ii) pursuant to article 24.3 of the Company's articles of association, stipulate additional terms, conditions and restrictions as set forth in this Agreement in relation to such indemnification.

(D) The Indemnitee [serves/has agreed to serve/has been requested by the Company to serve] as a [Director/ /Officer [insert title/position]].

THE PARTIES NOW HEREBY AGREE as follows

1. DEFINITIONS AND INTERPRETATION

1.1 The following capitalized terms and expressions in this Agreement shall have the following meanings:

Advance means an advance as referred to in Clause 3.1;

Agreement has this indemnification agreement;

Board means the Company's board of directors;

Director means a member of the Board;

Business Day means a day (other than a Saturday or Sunday) on which banks are generally open in the Netherlands for the conduct of normal business;

Clause means a clause of this Agreement;

Disinterested means a Director;

Director means the case may be, who is not and was not a party to the Proceeding in respect of which indemnification is sought by the Indemnitee;

Expenses means all attorney's fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, printing and binding costs, telephone charges, postage and all other actual out-of-pocket expenses, not including any compensation for time spent by the Indemnitee, any settlement payments or any amount of judgments, arbitral awards or fines;

Independent Counsel means an attorney or firm of attorneys that is experienced in matters of corporation law in the appropriate jurisdictions and neither currently is, nor in the past three (3) years has been, retained to represent: (a) the Company or the Indemnitee in any matter material to either such party (other than with respect to matters concerning the Indemnitee under this Agreement and/or the indemnification provisions of the Company's articles of association, or of other indemnitees under similar indemnification agreements), or (b) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" does not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interests in representing either the Company or the Indemnitee in an action to determine the Indemnitee's rights under this Agreement;

Liabilities means any financial losses or damages;

Officer means an officer of the Company who is not a Director;

Proceeding means any threatened, pending or completed suit, claim, action or legal proceedings, whether civil, criminal, administrative or investigative and whether formal or informal.

1.2 For the purpose of this Agreement:

(a) *Gender and number* Words denoting the singular shall include the plural and vice versa, unless specifically defined otherwise. Words denoting one gender shall include another gender.

(b) *Reference to include* The words "include", "included" or "including" are used to indicate that the matters listed are not a complete enumeration of all matters covered and will be construed

as meaning including without limitation except to the extent specifically provided otherwise in this Agreement.

(c) *Headings* The headings are for convenience or reference only and are not to affect the construction of this Agreement or to be taken into consideration in the interpretation of this Agreement.

(d) *Days* Unless the context clearly indicates a contrary intention, when any number of days is prescribed in this Agreement, it must be calculated exclusively of the first and inclusively of the last day unless the last day falls on a day other than a Business Day, in which case the last day will be the next succeeding day which is a Business Day.

(e) *Drafting party* No provision of this Agreement shall be interpreted adversely against a Party solely because that Party was responsible for drafting that particular provision. It is acknowledged that representatives of each Party have participated in the drafting and negotiation of this Agreement.

(f) *Language* If there is a discrepancy between an English language word and a Dutch language word used to clarify it and then to the extent of the conflict only, the meaning of the Dutch language word shall prevail.

(g) *Dutch concepts* References to any Dutch legal concept in any jurisdiction other than the Netherlands shall be deemed to include the concept which in that jurisdiction most closely approximates the Dutch legal concept.

(h) *No right to be retained* Nothing in this Agreement shall be construed as giving the Indemnitee any right to be retained in the employ or otherwise in the service of the Company.

(i) *Final and binding decisions* Any reference in this Agreement to a final and binding decision of a court or arbitral tribunal, shall mean: (i) with respect to a court, a final and binding, full or partial, decision of a court (*geheel of gedeeltelijk gerechtelijk eindvonnis met gezag van gewijsde*), without possibility for appeal, and (ii) with respect to an arbitral tribunal, a final and binding, full or partial, decision of an arbitral tribunal (*geheel of gedeeltelijk arbitraal eindvonnis met gezag van gewijsde*), without possibility for arbitral appeal to the same or another arbitral tribunal.

2. INDEMNIFICATION

2.1 The Company shall indemnify the Indemnitee against:

(a) any Liabilities incurred by the Indemnitee; and

(b) any Expenses reasonably paid or incurred by the Indemnitee in connection with any Proceeding,

to the extent this directly relates to his position as a Director, Officer or former Officer with the Company, in each case to the fullest extent permitted by applicable law.

2.2 Notwithstanding any other provision of this Agreement, no indemnification shall be given to the Indemnitee:

(a) if a Dutch court has established, without possibility for appeal, that the acts or omissions of the Indemnitee that led to the Liabilities or Proceeding as described in Clause 2.1 result from an improper performance of his duties as a Director, former Director, Officer or former Officer, as applicable, or from an unlawful or illegal act;

(b) to the extent that his Liabilities and Expenses are covered by an insurance and the insurer has settled these Liabilities and Expenses (or has indicated that it would do so);

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by the Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by the Indemnitee against the Company or its Directors, Officers or person indemnified by the Company, unless (i) the Board authorized the Proceeding (or any part of any Proceeding) prior to its initiation, (ii) such Proceeding or part of a Proceeding is brought by the Indemnitee to interpret or enforce this Agreement or any related indemnification obligations in a Company policy of insurance or the Company's governing documents (unless and to the extent a competent court or arbitral tribunal with jurisdiction over such action determines, in a final and binding decision, that the material assertions or defences asserted by the Indemnitee in such action were made in bad faith or were frivolous, however the indemnification shall in any event not extend to payments to be made by the Indemnitee under any order for costs given in such Proceeding) or (iii) the Company voluntarily elects to provide the indemnification, in its sole discretion, and without any obligation to do so, if and to the extent permitted by applicable law; and

(d) to the extent that his Liabilities and Expenses are paid or incurred by virtue of any other capacity of the Indemnity than referred to in Clause 2.1, including being a shareholder or stock option holder of the Company.

2.3 The exclusion of Clause 2.2(a) shall apply *mutatis mutandis* if (and to the extent) a similar decision has been rendered by another competent court or arbitral tribunal.

2.4 For the avoidance of doubt, unlawful acts and improper performance of duties as referred to in Clause 2.2(a) shall include wilful (*opzettelijk*), intentionally reckless (*bewust roekeloos*) or seriously culpable (*ernstig verwijtbaar*) conduct of the Indemnitee.

3. ADVANCEMENT OF EXPENSES

3.1 Notwithstanding Clause 4.7 and any other provision of this Agreement (but subject to the entirety of this Clause 3, including Clause 3.2), the Company shall advance or reimburse all Expenses reasonably paid or incurred by the Indemnitee in connection with any Proceeding to the extent this relates to his position as a Director, former Director, Officer or former Officer ultimately within ten (10) Business Days after receipt by the Company of a statement or statements from the Indemnitee requesting such advance (an **Advance**) from time to time, or within such shorter period as indicated by the Indemnitee if necessary to secure the Indemnitee's rights in such Proceedings, whether prior to or after final resolution of such Proceeding. Such statement or statements shall reasonably evidence the Expenses reasonably paid or incurred by the Indemnitee and shall include or be preceded or accompanied by a binding and irrevocable written undertaking by or on behalf of the Indemnitee to immediately repay such Advance if it is ultimately determined by a competent court or arbitral tribunal, as applicable, in a final and binding decision, that the Indemnitee is not entitled to be indemnified for such Expenses. It is understood between the Company and the Indemnitee, and the Indemnitee hereby explicitly accepts (to the extent necessary, in advance), that any future Advance pursuant to this Agreement is made to the Indemnitee under the condition that the Indemnitee shall repay any such Advance if and to the extent that it is ultimately determined by a competent court or arbitral tribunal, as applicable, in a final and binding decision, that the Indemnitee is not entitled to be indemnified by the Company for the Expense to which the Advance relates. Any Advances and undertakings to repay pursuant to this Clause 3.1 shall be unsecured and interest free.

3.2 The Indemnitee will not be entitled to any Advance in connection with any of the matters for which indemnity is excluded pursuant to Clause 2.2.

4. DETERMINATION OF ENTITLEMENT TO AND PAYMENT OF INDEMNIFICATION

4.1 The Indemnitee may deliver to the Company a written request to have the Company indemnify and hold harmless the Indemnitee in accordance with this Agreement. Subject to Clause 4.9, such request may be delivered from time to time and at such time(s) as the Indemnitee deems appropriate in his or her sole discretion. Such request shall include such relevant documentation and information as is reasonably available to the Indemnitee. Following such a written request for indemnification, the Indemnitee's entitlement to indemnification shall be determined in accordance with Clause 4.2.

4.2 Upon written request by the Indemnitee for indemnification pursuant to Clause 4.1, an initial determination with respect to the Indemnitee's entitlement thereto will be made by one of the following, at the election of the Company:

(a) so long as there are Disinterested Directors with respect to such Proceeding, a majority vote of the Disinterested Directors,

(b) so long as there are Disinterested Directors with respect to such Proceeding, a committee of such Disinterested Directors designated by a majority vote of such Disinterested Directors, or

(c) Independent Counsel in a written opinion delivered to the Board, a copy of which will also be delivered to the Indemnitee.

The specific election by the Company in any given case to use the person, persons or entity enumerated above to make such determination is to be included in a written notification to the Indemnitee. The person, persons or entity chosen to make such initial determination under this Agreement of the Indemnitee's entitlement to indemnification shall act reasonably and in good faith in making such determination.

4.3 Any determination pursuant to Clause 4.2 shall not in any way (a) preclude the Company from (i) arguing before a competent court or arbitral tribunal, as applicable, that the Indemnitee is not entitled to be indemnified by the Company hereunder, and (ii) recovering any amounts paid to the Indemnitee under this Agreement (including Advances) following a determination by a competent court or arbitral tribunal, as applicable, in a final and binding decision, that the Indemnitee is not entitled to be indemnified by the Company hereunder, or (b) limit or otherwise adversely affect any right or the position of the Company in any proceedings before a competent court or arbitral tribunal, as applicable. A competent court or arbitral tribunal, as applicable, shall not in any way be bound by the determination made pursuant to Clause 4.2.

4.4 If the determination pursuant to Clause 4.2 will be made by an Independent Counsel, the Independent Counsel will be selected by the Company and the Company will give written notice to the Indemnitee advising Indemnitee of the identity of the Independent Counsel so selected. The Indemnitee may, within five (5) Business Days after such written notice of selection is given, deliver to the Company a written objection to such selection; *provided, however,* that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "Independent Counsel" as defined in this Agreement, and the objection will set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected will act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a competent court or arbitral tribunal, as applicable, has determined that such objection is without merit. If the determination pursuant to Clause 4.2 will be made by an Independent Counsel, and within fifteen (15) Business Days after submission by Indemnitee of a written request for indemnification pursuant to Clause 4.1, no Independent Counsel is selected, or an Independent Counsel for which an objection thereto has been properly made remains unresolved, either the Company or the Indemnitee may, at the Company's expense, petition a competent court or arbitrator, as applicable, for resolution of any

objection which has been made by the Indemnitee to the Company's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court may designate. The Company will pay any and all reasonable and necessary fees and expenses incurred by such selected Independent Counsel in connection with the determination pursuant to Clause 4.2.

4.5 In making a determination, pursuant to Clause 4.2, the person, persons or entity making such determination will presume that the Indemnitee is entitled to indemnification under this Agreement and anyone seeking to overcome this presumption will have the burden of proof.

4.6 The Company will use all reasonable efforts to cause any determination required to be made pursuant to Clause 4.2 to be made as promptly as practicable after the Indemnitee has submitted a written request for indemnification pursuant to Clause 4.1.

4.7 All payments of Expenses and other amounts by the Company to the Indemnitee pursuant to this Agreement will be made as soon as practicable after a written request or demand therefor by the Indemnitee is received by the Company, but in no event later than ten (10) Business Days after such request or demand is received or such later date as it has been found in the initial determination pursuant to Clause 4.2 that the Indemnitee shall be indemnified under this Agreement; *provided, however,* that an Advance will be made within the time provided in Clause 3.1. The written request of the Indemnitee for indemnification and payments shall constitute a binding and irrevocable undertaking of the Indemnitee towards the Company providing that the Indemnitee undertakes (*verplicht zich ertoe*) to the fullest extent allowed by applicable law to repay any such indemnification payment if and to the extent that it is ultimately determined by a competent court or arbitral tribunal, as applicable, in a final and binding decision that the Indemnitee is not entitled to be indemnified by the Company under this Agreement. It is understood between the Company and the Indemnitee, and the Indemnitee hereby explicitly accepts (to the extent necessary, in advance), that any future indemnification payment pursuant to this Agreement is made to the Indemnitee under the condition that the Indemnitee shall repay any such indemnification payment if and to the extent that it is ultimately determined by a competent court or arbitral tribunal, as applicable, in a final and binding decision, that the Indemnitee is not entitled to be indemnified by the Company under this Agreement.

4.8 The Indemnitee will fully co-operate with the person, persons or entity making a determination pursuant to Clause 4.2, including providing to such person, persons or entity, upon reasonable advance request, any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to the Indemnitee and reasonably relevant to such determination. Any actual and reasonable out-of-pocket expenses incurred by the Indemnitee in so co-operating with the person, persons or entity making such determination will be borne by the Company, unless it is ultimately determined that by a competent court or arbitral tribunal, as applicable, in a final and binding decision, that the Indemnitee is not entitled to indemnification under this Agreement.

4.9 The Indemnitee will in any event be required to submit any request for indemnification pursuant to this Clause 4 within a reasonable time, not to exceed one (1) year, after any judgment, order, settlement, dismissal, arbitration award, conviction, or other full or partial final determination or disposition of the Proceeding. The failure to timely submit the request to the Company shall not relieve the Company of any obligation which it may have to the Indemnitee under this Agreement or otherwise, unless and only to the extent that such failure or delay adversely prejudices the Company.

5. NOTIFICATION AND DEFENSE OF PROCEEDINGS

5.1 The Indemnitee agrees to promptly notify the Company in writing upon receipt of a complaint, demand letter, writ of summons, or other document in relation to (or upon otherwise becoming aware of) any Proceeding against the Indemnitee for which indemnification will or could be sought under this

Agreement. The failure to notify the Company shall not relieve the Company of any obligation which it may have to the Indemnitee under this Agreement or otherwise, unless and only to the extent that such failure or delay adversely prejudices the Company.

5.2 The Company will be entitled to participate in any Proceeding notified to the Company in accordance with Clause 5.1 and any other Proceeding against the Indemnitee for which indemnification will or, in the reasonable determination of the Company, could be sought under this Agreement. Any participation of the Company in any Proceeding in accordance with the previous sentence, shall not in any way limit or otherwise adversely affect the right of the Company to dispute the Indemnitee's right to indemnification hereunder.

5.3 With respect to any Proceeding notified to the Company in accordance with Clause 5.1, the Company shall be entitled to assume the defense thereof, with counsel selected by the Company and reasonably satisfactory to Indemnitee. The Company shall consult the Indemnitee on the conduct of the defense. The Company shall, however, have the right to conduct the defense as it sees fit in its sole discretion, provided that the Company shall conduct the defense in good faith and in a diligent manner. The Indemnitee shall have the right to employ its own counsel in such Proceeding, but any fees and expenses of such counsel incurred after notice from the Company of its assumption of the defense thereof shall be at the Indemnitee's expense, unless: (a) the employment of counsel by the Indemnitee has been authorized in writing by the Company; (b) an actual conflict of interest arises between the Company and the Indemnitee in the conduct of such defense or representation by such counsel retained by the Company and the Company has not appointed new counsel who does not have a conflict of interest; or (c) the Company does not continue to retain counsel and the Company has not appointed new counsel reasonably satisfactory to the Indemnitee to assume the defense of such Proceeding, in which cases the reasonable fees and expenses of counsel shall be at the expense of the Company.

5.4 The Company shall have no obligation to indemnify the Indemnitee under this Agreement for any amounts paid or expenses incurred in connection with a settlement of any Proceeding effected without the Company's prior written consent, which consent shall not be unreasonably withheld.

5.5 The Company shall not, without the prior written consent of the Indemnitee, consent to the entry of any judgment or award against the Indemnitee or enter into any settlement or compromise which (a) contains any non-monetary remedy imposed on the Indemnitee or a Liability for which the Indemnitee is not wholly indemnified under this Agreement or (b) with respect to any Proceeding with respect to which the Indemnitee is made a party or a participant or is otherwise entitled to seek indemnification hereunder, does not include a full and unconditional release of the Indemnitee from all liability in respect of such Proceeding. Neither the Company nor the Indemnitee will unreasonably withhold its consent to any proposed settlement.

5.6 The Indemnitee shall fully co-operate with the Company and its counsel and shall give the Company and its counsel, at the Company's expense, all information and access to documents and files, and to the Indemnitee's advisors and representatives, to the extent within the Indemnitee's power, in each case as may be reasonably requested by the Company or its counsel with respect to any Proceeding that was (or should have been) notified to the Company in accordance with Clause 5.1.

6. LIABILITY INSURANCE

6.1 The Company will use its reasonable endeavours to obtain and maintain. a policy or policies providing liability insurance to the Indemnitee with coverage up to such amount as will be determined by the Board for any Liabilities incurred by the Indemnitee and any expense reasonably paid or incurred by the Indemnitee in connection with any Proceeding, to the extent such Liabilities and Expenses relate to his position as a Director, former Director, Officer or former Officer.

6.2 The Company undertakes to give prompt written notice of the commencement of any claim hereunder to its insurers in accordance with the procedures set forth in each of the policies providing liability insurance to the indemnitee to the extent that, in the reasonable determination of the Company, insurance coverage is available in respect of such claim. Upon written request by the Indemnitee, the Company shall provide the Indemnitee with a copy of such notice. The Company shall thereafter diligently take all actions reasonably necessary under the circumstances to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such Proceeding in accordance with the terms of such policies. This Clause 6.2 shall not affect the Company's authority to freely negotiate or reach any compromise with the insurer that is reasonable in the Company's sole discretion, provided that the Company shall act in good faith and in a diligent manner.

6.3 The Indemnitee will co-operate in all ways with the Company and its counsel and, if required by the Company, with the insurers issuing the Company's Directors', and Officers' or other relevant liability insurance, to the extent the Company deems such co-operation reasonably necessary.

7. NON-EXCLUSIVITY

The rights and remedies of the Indemnitee hereunder shall not be deemed exclusive of any other rights or remedies the Indemnitee may at any time have under applicable law, any agreement other than this Agreement, any insurance policy or otherwise and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The exercise of any right or remedy hereunder, or otherwise, shall not prevent the concurrent exercise of any other right or remedy.

8. SUBROGATION

8.1 In the event of any payment by the Company under this Agreement, the Company will be subrogated to the extent of such payment to all of the rights of recovery of the Indemnitee with respect thereto, including rights under any policy of insurance or other indemnity agreement or obligation, and the Indemnitee will execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to enforce such rights inside or outside of court.

8.2 To the extent the subrogation referred to in Clause 8.1 is not possible for whatever reason, the Indemnitee shall, at the request and expense of the Company, take all reasonable steps to enforce such right of recovery in his own name (credit being given to the Company for any sum recovered by Indemnitee by reason of such right of recovery) or assign the right of recovery to the Company.

9. PARTIAL INDEMNIFICATION

If the Indemnitee is entitled under any provision of this Agreement to indemnification by the Company for some or a portion of the Liabilities or Expenses incurred by him in the investigation, defense, appeal or settlement of any Proceeding but not, however, for the total amount thereof, the Company shall nevertheless indemnify the Indemnitee for the portion of such Liabilities or expenses to which the Indemnitee is entitled. Moreover, notwithstanding any other provision of this Agreement, to the extent that the Indemnitee has been successful on the merits or otherwise in defense of any or all claims, issues or matters relating in whole or in part to an indemnifiable event, occurrence or matter hereunder, including dismissal without prejudice, the Indemnitee shall be indemnified against all Expenses actually and reasonably incurred in connection with such specific defences on which Indemnitee prevailed.

10. NO DUPLICATIVE PAYMENTS

10.1 The Company shall not be required under this Agreement to make any payment of amounts otherwise indemnifiable hereunder, if and to the extent that the Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

10.2 If and to the extent the Indemnitee receives a payment under any insurance policy, contract, agreement (other than this Agreement) or otherwise after the Company has indemnified the Indemnitee for a Liability or expense, the Indemnitee shall reimburse to the Company the amounts received from the Company under this Agreement in connection with such Liability or expense promptly upon receipt of such payment by the Indemnitee.

11. DURATION OF AGREEMENT

This Agreement shall remain in effect until and terminate upon the latest of (a) the statute of limitations applicable to any claim that could be asserted against the Indemnitee with respect to which the Indemnitee is entitled to indemnification under this Agreement, (b) ten years after the date that the Indemnitee has ceased to serve as a Director or Officer or (c) if, at the later of the dates referred to in (a) and (b)above, there is a pending Proceeding in respect of which the Indemnitee is granted rights of indemnification hereunder or there is a pending Proceeding in connection with this Agreement, one year after the final termination of such Proceeding (including any and all appeals).

12. MISCELLANEOUS PROVISIONS

12.1 Entire Agreement

This Agreement contains the entire agreement between the Parties relating to the subject matter covered hereby and supersedes any previous oral or written agreements, arrangements and understandings between the Parties, *provided however* that it is agreed that the provisions contained in this Agreement are a supplement to, and not a substitute for, any provisions regarding the same subject matter contained in the Company's articles of association as they may read from time to time and any employment or similar agreement between the Parties.

12.2 Invalid provisions

In the event that a provision of this Agreement is null and void or unenforceable (either in whole or in part), the remainder of this Agreement shall continue to be effective to the extent that, given this Agreement's substance and purpose, such remainder is not inextricably related to the null and void or unenforceable provision. The Parties shall make every effort to reach agreement on a new provision which differs as little as possible from the null and void or unenforceable provision, taking into account the substance and purpose of this Agreement.

12.3 Amendment

No amendment to this Agreement shall have any force or effect unless and until it is in writing and signed by the Parties.

12.4 No implied waiver; no forfeit of rights

(a) Any waiver under this Agreement must be given by written notice to that effect.

(b) Where a Party does not exercise any right under this Agreement (which shall include the granting by a Party to any other Party of an extension of time in which to perform its obligations under any provision hereof), this shall not be deemed to constitute a forfeit of any such rights (*rechtsverwerking*).

The rights of each Party under this Agreement may be exercised as often as necessary and are cumulative and not exclusive of rights and remedies provided by law.

12.5 Third party stipulations

This Agreement does not grant any rights to any third party (*derdenbedingen*), including for the avoidance of doubt any insurer.

12.6 Notice

(a) Any notice or other communication under or in connection with this Agreement shall be in writing and delivered by hand or sent by registered mail or sent as an email to the relevant email address set out in Clause 12.6(b). Delivery by courier shall be regarded as delivery by hand.

(b) Notices under this Agreement shall be sent to the addresses of the Parties as specified below:

if to the Company:
ProQR Therapeutics N.V.
Attn: Board
Email address: ddeboer@proqr.com
Address Zernikedreef 9
2333 CK LEIDEN
The Netherlands
With copy to:
ProQR Therapeutics N.V.
Attn: Mr. P.E. de Ridders
Email address: pederidders@proqr.com; legal@proqr.com
Address Zernikedreef 9
2333 CK LEIDEN
The Netherlands
if to Indemnitee:
to the address set forth below Indemnitee's signature to this Agreement.
Attn: [●]
Email address: [●]
Address [●]

or such other address as the Party to be given notice may have notified to the other Party from time to time in accordance with this Clause for that purpose.

(c) A notice shall be effective, in the absence of earlier receipt:

(i) if delivered by hand to the relevant address referred to in Clause 12.6(b), at the time of delivery;

(ii) if sent by registered mail to the relevant address referred to in Clause 12.6(b) and that address is in the same country as the sender, at the expiration of two (2) Business Days after the time of posting;

(iii) if sent by registered mail to the relevant address referred to in Clause 12.6(b) and that address is not in the same country as the sender, at the expiration of seven (7) Business Days after the time of posting;

(iv) if sent by email to the relevant email address referred to in Clause 12.6(b), one Business Day after the time of transmission;

(d) If a notice or communication would otherwise be deemed to have been delivered outside normal business hours (being 9am to 5pm on a Business Day) in the time zone of the territory of the recipient under the preceding provisions of this Clause 12.6, it shall be deemed to have been delivered at the next opening of such normal business hours in the territory of the recipient.

(e) In proving service of the notice or communication, it shall be sufficient to show that delivery by hand was made or that the envelope containing the notice or communication was properly addressed and posted as registered mail or that the email was recorded in the IT system of the sender as having been sent and that the sender did not receive within 12 hours of sending the email an error message indicating failure to deliver. For the avoidance of doubt, a notification that the recipient of an email is out of the office, or no longer working at an organisation, shall not constitute an error message indicating failure to deliver.

(f) The provisions of this Clause 12.6 shall not apply in relation to the service of documents for the purpose of litigation.

12.7 Counterparts

This Agreement may be executed in two or more counterparts (including by facsimile signature), each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement.

12.8 Assignment; successors

(a) No Party may assign this Agreement (*contractsoverneming*) or assign any of its rights hereunder without the prior written consent of the other Party.

(b) This Agreement shall be binding upon the Company and its successors and shall inure to the benefit of the Indemnitee and the Indemnitee's heirs, executors and administrators. The Company shall require and cause any of its successors (whether direct or indirect by merger, demerger or otherwise) in respect of this Agreement, to confirm that it has assumed the Company's rights and obligations under this Agreement and that it agrees to perform this Agreement in the same manner and to the same extent that the Company would be required to perform if no such succession had taken place.

12.9 Choice of law

This Agreement shall be exclusively governed by and construed in accordance with the laws of the Netherlands, without giving effect to any conflict of laws principles.

12.10 Disputes

(a) The Parties agree that any dispute in connection with this Agreement or any agreement resulting therefrom shall be exclusively and finally settled in accordance with the Arbitration Rules of the Netherlands Arbitration Institute (*Nederlands Arbitrage Instituut*, "NAI") as at present in force.

(i) The arbitral proceedings and all documents delivered to or by the arbitrators shall be conducted in English.

(ii) The place of arbitration shall be Amsterdam, the Netherlands.

(iii) The arbitral tribunal shall comprise three arbitrators. Each Party shall appoint 1 (one) arbitrator and the NAI shall appoint a third arbitrator who shall be the chairman of the

arbitration tribunal. If a Party has not appointed an arbitrator within 30 (thirty) days of having requested or received notice of the arbitration, such arbitrator shall be appointed by the NAI.

(iv) The arbitral tribunal shall decide in accordance with the rules of law.

(b) The Parties shall not be precluded from applying for injunctive relief in summary proceedings (*kort geding*) before any competent court instead of arbitrators.

SIGNATORIES

THIS AGREEMENT has been entered into on the date first written above.

For and on behalf of
PROQR THERAPEUTICS N.V.

_____

By:
Title:

For and on behalf of
INDEMNITEE

_____

Name:
Address:
Email:

Exhibit 4.16

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 and restated articles of association (the "Articles of Association") filed with the Securities and Exchange Commission (the "SEC") on the Annual Report on Form 20-F of which this Exhibit 4.16 is a part, and the applicable provisions of Dutch law.

Authorized Share Capital

Our authorized share capital is € 13,600,000, divided into 170,000,000 Ordinary Shares and 170,000,000 preferred shares (the "Preferred Shares"), each with a nominal value of € 0.04. 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 board. Our general meeting of shareholders may authorize our 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.

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 board. Our general meeting of shareholders may authorize our board to restrict or exclude the preemptive rights in respect of newly issued Ordinary Shares. Such authorization for the 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 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 Securities—Anti-Takeover Measure*," is an irrevocable and repeatedly exercisable right to subscribe for Preferred Shares.

On May 22, 2024, our general meeting of shareholders adopted a resolution pursuant to which the board was delegated the authority for a period of five years from the date of the resolution of the general meeting of shareholders to, in accordance with applicable laws and Nasdaq listing rules: (a) issue Ordinary Shares up to 100% of the Company's authorized share capital for general purposes and issuances under Company's equity incentive or stock option plans with the proviso that the issuances under equity incentive or stock option plans are limited to 15% of the Company's issued share capital from time-to-time (minus any treasury shares); (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 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 board determines. After reservation by the board of any profit, the remaining profit will be at the disposal of the general meeting of shareholders. The board is permitted, subject to certain requirements, to declare interim dividends without the approval of the general meeting of shareholders.

Distributions shall be payable in such currency as determined by our board. We intend that distributions, if any, shall be payable on such date as determined by our board. Our 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 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 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 in the amount of the nominal value of the Preferred Shares (to the extent paid-up) plus unpaid accrued dividends and deficits (if any) in preferred dividends, and (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 are currently 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

In connection with a convertible debt financing in July 2020, we entered into a registration rights agreement with certain investors party thereto, pursuant to which we agreed to file and keep effective one or more registration statements with the SEC for the purpose of registering for resale the shares issuable upon conversion of certain term loans and/or exercise of certain warrants. In August 2020, we entered into a joinder and first amendment to the loan agreement and joinder to registration rights agreement to expand our loan facility and accommodate the participation of an additional lender, pursuant to which such additional lender became party to the registration rights agreement. In January 2021, we entered into the second amendment to the loan agreement, which extended the availability periods for the late withdrawal loans. In December 2021, we entered into the third amendment to the loan agreement to expand our loan facility and accommodate the participation of an additional lender, and we entered into a registration rights agreement with the parties thereto, pursuant to which we agreed to file and keep effective one or more registration statements with the SEC for the purpose of registering for resale the shares issuable upon conversion of the loans and warrants issued under the third amended loan agreement. In September 2022, we extinguished our debt by repaying all outstanding principal amounts. The warrants remain in place until their five-year economic life expires in 2025 and 2026.

In addition, in connection with a private placement in September 2021, we entered into a share purchase agreement (the "2021 Share Purchase Agreement") with Eli Lilly and Company ("Lilly"), pursuant to which we agreed to issue and sell to Lilly 3,989,976 shares of our Ordinary Shares (the "2021 Lilly Shares"). The issuance of the 2021 Lilly Shares occurred concurrently with the entry into a collaboration agreement. Pursuant to the terms of the 2021 Share Purchase Agreement, Lilly may not, subject to certain limited exceptions, dispose of any of the 2021 Lilly Shares for a period commencing on September 3, 2021 until the earlier of (i) March 3, 2022 and (ii) the date that the collaboration agreement is terminated.

In December 2022, we entered into a share purchase agreement (the "2022 Share Purchase Agreement," and together with the 2021 Share Purchase Agreement, the "Share Purchase Agreements") with Lilly, pursuant to which we agreed to issue and sell to Lilly 9,381,586 shares of our Ordinary Shares (the "2022 Lilly Shares," and together with the 2021 Lilly Shares, the "Lilly Shares"). The issuance of the 2022 Lilly Shares occurred concurrently with the entry into an amended collaboration agreement.

Under the terms of the Share Purchase Agreements, Lilly may participate in some public offerings and private placements of the Company, subject to share ownership requirements and other limitations set forth in the Share Purchase Agreements. Additionally, we also granted Lilly certain customary registration rights with respect to the Lilly Shares, including registering such shares for resale on or prior to the expiration of the lockup periods described above.

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 at least 25% will be due upon issuance, and may also be issued against the Company's reserves if so requested by the protection 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 board. The sub-register shall be kept by our agent on behalf of the board. Our shareholders' register includes the names and addresses and other relevant details of all holders of registered shares, and shows 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 of usufruct ('*vruchtgebruik'*) or a right of pledge ('*pandrecht'*) in respect of any shares. Our registered Ordinary Shares are held through DTC and therefore DTC is 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 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.

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 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.

On May 22, 2024, our general meeting of shareholders adopted a resolution pursuant to which the board was delegated the authority to perform acquisitions by the Company of (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 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 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 can be held in Leiden, Amsterdam, Rotterdam, Schiphol Airport (municipality Haarlemmermeer), The Hague, 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 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 board has 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 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 board convene a shareholders' meeting and the 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 board. In addition, the agenda for a general meeting of shareholders may include such items as have been included therein by our 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 60th day before the day that the relevant general meeting of shareholders is to be 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 and 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 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 chairperson of the general meeting of shareholders may, in his or her 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 board. If the chairman of our board is absent and has not charged another person to chair the meeting in his place, the non-executive directors present at the meeting shall appoint one of themselves to be chairperson. If no 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 executive director present at the meeting and, if none of them is present, the general meeting of shareholders shall appoint its own chairperson. The person who should chair the meeting may appoint another person in his or her stead.

The chairperson of the general meeting of shareholders may decide at his or her discretion to admit other persons to the meeting. The chairperson 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 chairperson 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 chairperson of the general meeting of shareholders is authorized to eject any person from the general meeting of shareholders if the chairperson considers that person to disrupt the orderly proceedings. The general meeting of shareholders shall be conducted in the English language.

Quorum Requirements

Voting rights may be exercised by shareholders or by a duly appointed proxy holder (the written proxy being acceptable to the chairperson 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 chairperson 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 chairperson of the general meeting of shareholders shall decide on the method of voting and may determine the voting procedure. The determination made by the chairperson of the general meeting of shareholders with regard to the results of a vote shall be decisive. However, where the accuracy of the chairperson'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 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 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 Liability

Pursuant to Dutch law, we are required to publish our annual accounts within eight days after adoption and ultimately within 12 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 five months by the general meeting of shareholders on account of special circumstances, our board will prepare the annual accounts. The annual accounts must be accompanied by an auditor's certificate, a report of the 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 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 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 Authority for the Financial Markets (the "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."

Dutch 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) holds 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*') (the "Enterprise Chamber") 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 notice in a newspaper with a national circulation.

A shareholder that holds 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, and 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 (e.g. 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 board.

Dutch Corporate Governance Code

The Dutch Corporate Governance Code ("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 provisions of the DCGC that are addressed to the 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 board, shareholders and general meetings of shareholders, financial reporting, auditors, disclosure, compliance and enforcement standards. The principles and best practice provisions apply to our board, for example in relation to its role and composition, conflicts of interest, independence requirements for board members, 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 Nasdaq and U.S. securities laws that apply to us, or because such provisions do not reflect best practices of global companies listed on Nasdaq.

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

- Best practice provision 1.1.5 stipulates that a policy for dialogue with the relevant stakeholders on the sustainability aspects of the strategy should be drawn up. The Company has not formulated such policy as it believes this is already covered by our regular process for public disclosure of information.

- Pursuant to the best practice provisions 3.1.2.vi and 3.1.2.vii of the DCGC, options granted to our executive board members should not be exercisable during the first three years after the date of grant; shares granted to our executive board members for no financial consideration should be retained by them for a period of at least five years or until they cease to hold office, whichever is the shorter period; and the number of options and/or shares granted to our executive board members should be

dependent on the achievement of pre-determined performance criteria. We do not intend to comply with all of the above requirements as we believe it is in the best interest of the Company to attract and retain highly skilled executive board members on conditions based on market competitiveness.

- Pursuant to best practice provision 3.2.3 the remuneration of the executive board members in the event of dismissal may not exceed one year's salary. The management services agreements with our executive board members provide for a lump-sum equal to 24 months of the individual's monthly gross fixed salary in case of dismissal following a change of control. Based on the risk profile of the Company and to be able to attract highly skilled management, we believe this period to be appropriate.

- Best practice provision 3.3.2 prohibits the granting of shares or rights to shares to non-executive members of the board as remuneration. It is common practice for companies listed on The Nasdaq Stock Market LLC to grant shares to the non-executive members of the board as compensation, in order to align the interests of the non-executive members of the board with our interests and those of our shareholders, and we have granted and expect to grant options to acquire Ordinary Shares to all or some of our non-executive board members.

- Pursuant to best practice provision 3.3.3, any shares held by non-executive board members are long-term investments. We do not request our non-executive board members to comply with this provision. We believe it is in the best interest of the Company not to apply this provision in order to be able to attract and retain highly skilled non-executive board members on internationally competitive terms.

- Best practice provision 4.2.2 stipulates that an outline policy on bilateral contacts with the shareholders shall be formulated and published on the company's website. The Company has not formulated such policy as it believes this is already covered by our regular process for public disclosure of information.

- 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 board or a resolution to dismiss such member by an absolute majority of the votes cast. It may be provided that such majority should represent a given proportion of the issued capital, but this proportion may not exceed one third. In addition, best practice 4.3.3 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 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 board for the appointment or dismissal of a member of our 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 and therefore, we do not intend to comply with all of the above requirements.

Market Abuse

Regulation (EU) No 596/2014 of the European Parliament and of the Council of 16 April 2014 on market abuse ("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. As a result, the provisions of the EU Market Abuse Regulation do not currently apply to us.

Dutch Financial Reporting Supervision Act

Under the Dutch Financial Reporting Supervision Act (*Wet toezicht financiële verslaggeving*) (the "FRSA"), the AFM supervises the application of financial reporting standards by, among others, companies whose corporate seats are in the Netherlands and whose securities are listed on a regulated market within the EU or in a non-EU country on a system similar to a regulated market. Since our Company has its corporate seat in the Netherlands and our Ordinary Shares are listed on The Nasdaq Stock Market LLC, 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 if, based on publicly known facts or circumstances, it has reason to doubt our financial reporting meets such standards and (ii) recommend to us that we make available further explanations and file these with the AFM. 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	We have a single-tier board system. consisting of executive directors and non-executive directors. Under Dutch law, the executive directors are responsible for the day-to-day management and execution of the strategy, policy and operations of a company. The non-executive directors are responsible for supervising the conduct of, and providing advice to, the executive directors and for supervising the company's general affairs and business. Each member of the board 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

Delaware	The Netherlands
duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. 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.	specific circumstances generally dictate how such duty is to be applied. Any board resolution concerning a material change in the identity or character of the company or its business requires shareholders' approval. The 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 non-executive director 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 non-executive director may serve, although the DCGC recommends that a non- executive director is appointed for a period of four years and may then be reappointed once for another four-year period. The non-executive director 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 board. A non-executive director 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 board member by at least 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 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 board members of a company such as ours are appointed by the general meeting of shareholders, rather than appointed by the board as is typical for a Delaware corporation. Under our Articles of Association, board members are appointed by our general meeting of shareholders upon the binding nomination by our 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 board may draw up a new binding nomination.

Delaware	The Netherlands
Conflict-of-Interest Transactions	
Under the Delaware General Corporation Law, transactions with directors must be approved by disinterested directors or by the shareholders, or otherwise proven to be fair to the company as of the time it is approved. Such transaction will be void or voidable, unless (1) the material facts of any interested directors' interests are disclosed or are known to the board of directors and the transaction is approved by the affirmative votes of a majority of the disinterested directors, even though the disinterested directors constitute less than a quorum; (2) the material facts of any interested directors' interests are disclosed or are known to the shareholders entitled to vote thereon, and the transaction is specifically approved in good faith by vote of the shareholders; or (3) the transaction is fair to the company as of the time it is approved.	Under Dutch law, a board member with a direct or indirect personal interest that conflicts with the interests of the company or of the business connected with it must abstain from participating in the decision-making process (i.e., the deliberations and the decision-making) with respect to the relevant matter. A board member with such a conflict of interest must promptly notify the other directors of his or her conflict. If it becomes apparent that such member was indeed involved in the decision-making process, then such decision may be nullified. Our Articles of Association provide that if as a result of a conflict of interest of board members no resolution of the board can be adopted, the resolution can nonetheless be adopted by our board as if there was no conflict of interest. In that case, each board member is entitled to participate in the discussion and decision-making process and to cast a vote. Board members with a conflict of interest remain authorized to represent the Company. 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.
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 board member may issue a proxy for a specific meeting of the board but only in writing to another 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.	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 board members.

Delaware	The Netherlands
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.	Pursuant to our Articles of Association, our 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 in case the board fails to so in a timely manner upon request. The agenda for a general meeting of shareholders must contain such items as the 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 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 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.

Delaware	The Netherlands
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.
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 title of succession ('*algemene titel*'), our board may acquire shares only if our general meeting of shareholders has authorized the board to do so. An authorization by the general meeting of shareholders

Delaware	The Netherlands
	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 on Nasdaq with the intention of transferring such Ordinary Shares to our employees under an applicable employee stock purchase plan. On May 22, 2024, our general meeting of shareholders adopted a resolution pursuant to which the board was delegated the authority to perform acquisitions by the Company of (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	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 to which we have granted a perpetual and repeatedly exercisable call option; ● a provision that our board members may only be appointed upon a binding nomination by our board, which can be set aside by a two-thirds majority of

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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.	our shareholders representing more than half of our issued share capital; ● a provision that our 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 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 board that has been approved by our 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.

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	As of May 1, 2021, the Statutory Reflection Period for Listed Companies came into force. The purpose is to give the board of a listed company more time for careful policymaking to weigh the interests of the company and its stakeholders in the event of an unsolicited takeover bid or other pressure being put on the board to change the course of the company, for example from activist shareholders. The board of a listed company may invoke a reflection period of up to 250 days in the event of: (i) a request by one or more shareholders for consideration of a proposal to appoint, suspend or dismiss one or more members of the board, or (ii) when a public bid has been announced or made for the shares without agreement having been reached on the bid with the target company. The decision by the board to invoke the reflection period is subject to board approval. In addition, to invoke the reflection period, the request under (i) and the public bid under (ii) must in the view of the board be substantially contrary to the interest of the company and its affiliated enterprise and the reflection period should be used for careful policy making.
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 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 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	Under our Articles of Association, the general meeting of shareholders is at all times entitled to suspend or remove a 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 board in which case a simple majority of the votes cast is sufficient.

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directors, at an election of the class of directors of which he is a part.	
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 board. Our general meeting of shareholders may authorize our board to restrict or exclude the preemptive rights in respect of newly issued Ordinary Shares. Such authorization for the 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 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 22, 2024, our general meeting of shareholders adopted a resolution pursuant to which the board was delegated the authority for a period of five years from the date of the resolution of the general meeting of shareholders to, in accordance with applicable laws and Nasdaq listing rules: (a) issue Ordinary Shares up to 100% of the Company's authorized share capital for general purposes and issuances under Company's equity incentive or stock option plans with the proviso that the issuances under equity incentive or stock option plans is limited to 15% of the Company's issued share capital from time-to-time (minus any treasury shares); (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	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

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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.	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 are outstanding. Any amount remaining out of the profit is carried to reserve as the board determines. After reservation by the 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 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 in cash of the judicially determined fair value of the stockholder's shares, in connection with certain mergers and consolidations.	Under Dutch law, resolutions of the board concerning a material change in the identity or character of the company or its business are subject to the approval of the general meeting of shareholders. Such changes include in any event: ● a transfer of all or materially all of our business to a third party; ● the entry into or termination of a long-lasting alliance of the company or of a subsidiary either with another entity or company, or as a fully liable partner of a limited partnership or partnership, if this alliance or termination is of significant importance for the company; and ● the acquisition or disposition of an interest in the capital of a company by the company or by a subsidiary with a value of at least one third of the value of the assets, according to the balance sheet with explanatory notes or, if the company prepares a consolidated balance sheet, according

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	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) holds 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, 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 board adopt the compensation policy for the board, which includes the outlines of the compensation of any members who serve on our board. The board determines the compensation of the board members in accordance with the compensation policy. A proposal by the board with respect to compensation schemes in the form of shares or rights to shares is submitted for approval by the 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 board and the criteria for granting such shares. Best practice under Dutch law is that executive board members are not authorized to participate in the discussion and the decision-making process regarding the determination of the remuneration of the executive board members.

Stock Exchange Listing

Our Ordinary Shares are listed on the Nasdaq Stock Market LLC 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 Stock Market LLC in book-entry form.

Transfer Agent and Registrar

We have appointed Equiniti Trust Company, LLC (formerly known as 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.

Exhibit 8.1

SUBSIDIARIES OF PROQR THERAPEUTICS N.V.

The following is a list of subsidiaries of the Company (and jurisdiction of incorporation) as of December 31, 2024.

Name of Subsidiary	Jurisdiction of Incorporation or Organization
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 V 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

Exhibit 11.1

PROQR THERAPEUTICS N.V. GROUP

SECURITIES TRADING POLICY

1. Summary

The Securities Trading Policy contains the rules for trading in shares of ProQR Therapeutics N.V. and any type of Financial Instruments (for definitions see the policy) related thereto, which includes options. In short, you are not allowed to trade with ProQR shares or related Financial Instruments when you are in the possession of Inside Information related to the company. Inside Information may include a broad range of information, including without limitation clinical trial results, (potential) business development deals and important financial information, as further described in this policy. The company may also impose black-out periods for the entire company or certain groups of colleagues, during which no trading is allowed. In case of doubt as to whether you can trade, please contact the Securities Trading Compliance Officer.

Please read this policy carefully. If you have any questions concerning this policy or its application to you in any situation, please speak with your supervisor or the Securities Trading Compliance Officer. You may also be asked periodically in succeeding years to confirm in writing your awareness of, and compliance, with this policy.

I entrust these principles and policies to you. Please give them your thoughtful and frequent attention.

Sincerely,

Daniel de Boer, CEO

1. Introduction

This Securities Trading Policy provides an overview of certain prohibitions and restrictions under Dutch and United States securities laws and regulations.

This Securities Trading Policy does not purport to be, and should not be relied upon as being, an exhaustive overview of all prohibitions and restrictions under Dutch and United States securities laws and regulations. If any person subject to this Securities Trading Policy has any questions concerning the application or interpretation thereof, or concerning the applicable rules under securities laws and regulations in general, he or she should first seek the advice of his or her immediate supervisor or department head, who will make a determination whether to consult the Securities Trading Compliance Officer. Persons subject to this Securities Trading Policy without an immediate supervisor or department head, may turn directly to the Securities Trading Compliance Officer.

This Securities Trading Policy has initially been adopted by the Management Board on 28 August, 2014, and it was amended on October 9, 2017, July 11, 2019, April 15, 2021, July 1, 2022, August 2, 2023 and most recently by the Board onMay 22, 2024.

2. Definitions

For the purpose of this Securities Trading Policy, capitalized terms shall have the meanings set forth below:

"Affiliated Persons" shall mean, in respect of an Insider for Notification Purposes:

(a) his or her spouse, registered partner, or life partner or other persons co-habitating with him or her in a similar fashion;

(b) his or her children who fall under his or her parental authority or who are placed under guardianship and for whom he or she was appointed as a guardian;

(c) his or her other relatives by blood or marriage with whom he or she, on the date of the relevant transaction, has shared a common household for a period of at least one year; and

(d) an entity, trust or partnership, (i) the executive responsibility of which is vested in the relevant Insider for Notification Purposes or any of his or her Affiliated Persons as referred to under (a) through (c) above, or (ii) which is controlled by, which has been incorporated for the benefit of, or whose economic interests are essentially equivalent to those of, the individuals referred to in item (i);

"CEO" shall mean the chief executive officer of ProQR Therapeutics N.V.

"Company" shall mean ProQR Therapeutics N.V.;

"Derivative Instrument" shall mean a financial instrument of which the value is determined, or partly determined, by the value of Ordinary Shares (including options, futures and swaps);

"Exchange Act" shall mean the U.S. Securities Exchange Act of 1934, as amended;

"Financial Instrument"; shall mean an Ordinary Share or a Derivate Instrument;

"Inside Information" shall mean awareness of information that qualifies as material, non-public information about the Company, which could reasonably be expected to affect the price of Financial Instruments;

"Insiders" shall initially mean the members of the Board, as well as:

(a) any person who determines or co-determines the Company's daily affairs, or supervises the Company's policies and general affairs;

(b) any person having access to Inside Information as a result of his or her employment, profession or position; and

(c) any person having Inside Information as a result of his or her involvement in criminal acts; and

(d) the Company's and its subsidiaries' employees (including consultants and freelancers providing services who are well embedded within the organization (such at the discretion of the Securities Trading Compliance Officer);

"Board" shall mean the Company's Board;

"Ordinary Shares" shall mean the ordinary shares in the Company's share capital which are listed on NASDAQ;

"Rule 10b5-1 Plan" shall mean a trading plan, arrangement or instruction that meets the requirements of Rule 10b5-1 of the Exchange Act;

"SEC" shall mean the United States Securities and Exchange Commission;

"Securities Trading Compliance Officer" shall mean the VP Legal;

3. Examples of Inside Information

While it is not possible to identify in advance all information that will be considered Inside Information, examples could include non-public information concerning the following matters:

(a) important information regarding the Company's financial position and/or results:

(i) the Company's financial condition, results of operations or cash flows;

(ii) the Company's projections, forecasts or expectations, information that indicates that the Company's financial results may exceed or fall short of such projections, forecasts or expectations, or significant differences from previous projections, forecasts or expectations;

(iii) the announcement of periodic financial results;

(iv) the introduction or development of significant new products or services;

(v) substantial changes in loans and collateral provided for such loans, including the breaking of covenants;

(vi) the cancellation of important credit facilities by one or more banks;

(vii) substantial changes to the financial reporting procedure;

(viii) negative equity;

(ix) changes in auditors, auditor notification that the Company may no longer rely on the auditor's report, or any other information related to the auditors' activities;

(x) actual or threatened litigation, governmental investigations or other regulatory processes or requirements;

(xi) important legal claims, product liability or environmental damages;

(xii) changes in the Company's credit ratings;

(xiii) insolvency of relevant debtors;

(xiv) changes in the value of the Company's assets;

(xv) physical destruction of uninsured goods;

(xvi) the acquisition, or the increase or decrease in value of, licenses, patents or registered trademarks;

(b) important information regarding the Company's strategy:

(i) pending or contemplated mergers, demergers, acquisitions, asset purchases or sales, purchase or sale of important shareholdings or business units, or similar transactions;

(ii) the initiation, change or termination of important joint ventures or partnerships;

(iii) changes in the Company's investment policy;

(iv) receiving acquisition bids for relevant assets, shareholdings or business units;

(v) withdrawal from or entry into new core business areas;

(vi) the potential gain or loss of a major supplier, customer, order or contract;

(vii) changes in the value of the Company's Ordinary Shares;

(viii) restructurings or reorganizations that have an effect on the Company'sassets and liabilities, financial position or profits and losses;

(ix) changes to the Company's strategy and radical changes to its business;

(x) filing for suspension of payments or bankruptcy;

(xi) dissolution of the Company;

(c) important information on capital and governance:

(i) changes in senior management;

(ii) securities offerings (including debt securities or warrants to buy or subscribe for securities), capital reductions, or other events regarding the Company's shares, including stock splits or reverse stock splits;

(iii) changes to the rights attached to the Ordinary Shares;

(iv) dividend announcements, including the ex-dividend date or changes thereto and changes to dividend policy;

(v) significant changes to the distribution of share ownership and/or free float;

(vi) the initiation or implementation of protective measures;

(vii) decisions concerning buy-back programs or transactions in Ordinary Shares;

It should be noted that the fact that an event does not appear on the above list does not mean it cannot be Inside Information, nor does the fact that an event is included on the above list mean that it automatically will be Inside Information. This assessment should be made on a case- by-case basis.

It should also be noted that Inside Information also encompasses information which relates indirectly to the Company or to the trading in Ordinary Shares.

4. Prohibition on the Use or Disclosure of Inside Information and Tipping

Insiders are prohibited from:

(a) using Inside Information to conduct or effect (or attempting to conduct or effect) a transaction in Financial Instruments (whether directly or through others on an Insider's behalf), which includes purchasing or selling Financial Instruments while the Insider is aware of any Inside Information;

(b) disclosing Inside Information relating to the Company or Financial Instruments to a third party;

(c) recommending or inducing a third party to conduct or effect transactions in Financial Instruments;

(d) pledging Financial Instruments as collateral for a loan (or modifying an existing pledge) unless the pledge (or modification of the pledge) would not violate applicable laws or regulations and has been approved by the Company's Audit Committee;

(e) selling any Financial Instruments that are not owned by such Insider at the time of the sale (a "short sale");

(f) buying or selling puts, calls, other Derivative Instruments or an opportunity, direct or indirect, to profit from any change in the value of Financial Instruments or engaging in any other hedging transaction with respect to Financial Instruments, at any time, unless such transaction would not violate applicable laws or regulations and has been approved by the Company's Audit Committee;

(g) using Financial Instruments as collateral in a margin account; or

(h) giving or making any other transfer of Financial Instruments without consideration (e.g., a gift) during a period when the Insider is not permitted to trade under applicable laws and regulations and/or this Securities Trading Policy.

5. Prohibition on Market Manipulation

Insiders and others are also prohibited from doing the following:

(a) to conduct or effect a transaction in, or a trading order for, Ordinary Shares which gives, or is likely to give, false or misleading signals as to the offer of, demand for or price of those Ordinary Shares;

(b) to conduct or effect a transaction in, or a trading order for, Ordinary Shares in order to maintain the price of those Ordinary Shares at an artificial level;

(c) to conduct or effect a transaction in, or a trading order for, Ordinary Shares using deception or contrivance; or

(d) to disseminate information which gives, or is likely to give, false or misleading signals as to the offer of, demand for or price of Ordinary Shares, while the disseminator of such information knows or should reasonably suspect such information to be false or misleading.

6. Reporting and Pre-Clearing of Transactions

All Insiders and their respective Affiliated Persons, as well as any other person specified from time to time by the Securities Trading Compliance Officer, must pre-clear their respective contemplated transactions as referred to in this paragraph 6 with the Securities Trading Compliance Officer. A pre-clearing request should be made by means of submitting a request to the Securities Trading Compliance Officer by email, stating the details of the transaction (including in any event the number and type of Financial Instruments concerned and any further details as may be requested by the Securities Trading Compliance Officer). Insiders may make a pre-clearing request on behalf of their respective Affiliated Persons. A pre-clearing request must be made in a timely manner and at least two (2) trading days prior to the proposed transaction date, so that the Securities Trading Compliance Officer can coordinate, prepare and make any such filings with the SEC and/or filings with or notifications to any other competent authority, as may be required under applicable securities laws and regulations.

7. Prohibition on Transactions During a Blackout Period

Without prejudice to the prohibitions described in paragraphs 4 and 5 of this Securities Trading Policy, Insiders are not permitted to trade in Financial Instruments, whether directly or indirectly, during any of the following blackout periods:

(a) the period commencing at the close of market 21 days before the Company's issuance of a press release (or other method of broad public dissemination) announcing its quarterly or annual earnings, and ending at the market open on the second full trading day following such announcement;

(b) the period of 30 days immediately preceding the announcement of a dividend or an interim dividend;

(c) the period of one month immediately preceding the first publication of a prospectus relating to a share issuance by the Company, unless the Company can demonstrate that the decision-making process takes less than one month, in which case such shorter period shall apply; or

(d) any additional blackout period imposed by the Company, for example:

(i) a period during which the Company is in the process of assembling potentially material information for public dissemination (other than as described under (a) through (c) above) by means of a press release, filing with the SEC or by other means; or

(ii) because of material developments, or potentially material developments, known to the Company and not yet disclosed to the public.

From time to time, the Securities Trading Compliance Officer shall inform the Insiders of all blackout periods as referred to under (a) through (d) above (e.g., by means of an announcement on the Company's intranet or by email), as promptly as practicable if and when the occasion arises.

8. Other Restrictions and Requirements for Insiders

Without prejudice to the prohibitions described in paragraphs 4, 5 and 7 of this Securities Trading Policy, Insiders:

(a) should refrain from any use of Inside Information, and should avoid the mixing of corporate interests with personal interests, or the reasonably foreseeable appearance thereof;

(b) should treat available information derived from a corporate environment in a prudent manner, and should separate such information from their private domain;

(c) are not permitted to do any of the following:

(i) to conduct a transaction in Financial Instruments, if this could reasonably create the appearance of using, or being able to use, Inside Information;

(ii) to sell Financial Instruments within six months after having purchased any such Financial Instrument, or to purchase Financial Instruments within six months after having sold any such Financial Instrument;

Insiders are required to provide to the Securities Trading Compliance Officer any information concerning transactions in Financial Instruments conducted by them, at their instruction, or for their benefit, that is necessary for the Securities Trading Compliance Officer to ensure and monitor compliance with this Securities

Trading Policy. Insiders are also required to instruct and authorize their bank, investment manager or other institution where their respective securities accounts are administered to provide any information to the Securities Trading Compliance Officer concerning transactions as referred to in the previous sentence.

9. Exceptions

Transactions conducted or effected pursuant to a pre-approved Rule 10b5-1 Plan will not be subject to the preclearing procedures described in paragraph 6 or the trading restrictions during blackout periods described in paragraph 7. Rule 10b5-1 of the Exchange Act provides an affirmative defense from insider trading liability under U.S. federal securities laws for trading plans that meet certain requirements. A Rule 10b5-1 Plan enables Insiders to establish arrangements to trade in Financial Instruments during blackout periods described in paragraph7, even when in possession of Inside Information. If an Insider intends to trade pursuant to a Rule 10b5-1 Plan, such plan must:

(a) satisfy the requirements of Rule 10b5-1 of the Exchange Act;

(b) be documented in writing;

(c) be established outside a blackout period described in paragraph 7 and at a time when such Insider does not possess Inside Information; and

(d) be pre-approved by the Securities Trading Compliance Officer.

Any deviation from, or alteration to, the specifications of a pre-approved Rule 10b5-1 Plan (including, without limitation, the amount, price or timing of a purchase or sale as described therein) must be reported immediately to the Securities Trading Compliance Officer.

The pre-clearing procedures described in paragraph 6 and the trading restrictions during blackout periods described in paragraph 7 do not apply to the following transactions:

(e) The exercise of an option to acquire Financial Instruments when payment of the exercise price is made in cash. However, the Financial Instruments acquired upon the exercise of such an option will be subject to all of the requirements of this Securities Trading Policy, including those described in paragraphs 6 and 7.

(f) The use of outstanding Financial Instruments to constitute all or part of the exercise price of an option to acquire Financial Instruments, any net option exercise, any exercise of a share appreciation right, share withholding, any sale of Ordinary Shares as part of a broker-assisted cashless exercise of an option, or any other market sale for the purpose of generating the cash needed to pay the exercise price of an option to acquire Financial Instruments.

For the avoidance of doubt, the exceptions stipulated in this paragraph 9 shall not exempt persons subject to this Securities Trading Policy from restrictions or prohibitions that follow from mandatory applicable laws and regulations.

10. Penalties for Violation

Violation of any of the foregoing rules is grounds for disciplinary action by the Company, including termination of office or employment. In addition to any disciplinary action the Company may take, violation of any of the foregoing rules can result in administrative, civil and/or criminal proceedings which can result in significant

fines and/or civil penalties, being barred from service as an officer or director of a public company, or being sent to jail.

11. Dispensation by the Securities Trading Compliance Officer

At the request of an Insider, the Securities Trading Compliance Officer may grant dispensation from the preclearing requirements described in paragraph 6 and/or the prohibitions and restrictions described in paragraphs 7 and 8 of this Securities Trading Policy, but only in exceptional circumstances and only in consultation with the CEO. A dispensation request shall be made in writing and shall be supported by reasons. Any dispensation granted by the Securities Trading Compliance Officer shall be granted in writing.

12. Contact Details, Powers and Duties of the Securities Trading Compliance Officer

Pieter Erik de Ridders is the Company's Securities Trading Compliance Officer. The Securities Trading Compliance Officer can be reached as follows:

Telephone: +31 (0)88 1667000 or +31647011435

Email: pederidders@proqr.com

In case (and for the duration) of absence or inability to act of the Securities Trading Compliance Officer, René Beukema shall replace, and shall have all duties and powers of, the Securities Trading Compliance Officer. Mr.Beukema can be reached as follows:

Telephone: +31 (0)88 1667000

Email: rbeukema@proqr.com

The Securities Trading Compliance Officer has the duties and powers conferred by this Securities Trading Policy. The Board may confer additional duties and powers on the Securities Trading Compliance Officer as it deems appropriate.

The Securities Trading Compliance Officer is authorized to hold an inquiry, or to procure the holding of an inquiry, into transactions in Financial Instruments conducted by, at the instruction of, or for the benefit of an Insider. The Securities Trading Compliance Officer may report in writing on the outcome of any such inquiry to the CEO, but only after the subject of the inquiry has been given the opportunity to respond to the outcome thereof.

Within three months after the end of every year, the Securities Trading Compliance Officer shall report to the CEO on how he or she has exercised his or her duties and powers under this Securities Trading Policy.

13. Document History

Revision number	Reason
01	NA, new document
02	Change of ProQR entity and Compliance Officer names; Sections updated to comply with changes in applicable law. Section 6 “Insiders list” has been deleted due to this reason.
03	Formatting changes; section 1 ‘summary’ included; change of Compliance Officer names; addition of summary.
04	Section 8 ‘by email’ included; change of Compliance Officer replacement name.
05	Section 8 ‘by email’ included; change of Compliance Officer replacement name.
06	Various minor textual changes.
07	Changes made in relation to one-tier governance structure.

Exhibit 12.1

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 13, 2025

By: /s/ Daniel de Boer
Name: Daniel de Boer
Title: *Chief Executive Officer*
(Principal Executive Officer)

Exhibit 12.2

Certification by the Principal Financial Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Jurriaan Dekkers, 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 13, 2025

By: /s/ Jurriaan Dekkers
Name: Jurriaan Dekkers
Title: *Chief Financial Officer*
(Principal Financial Officer)

Exhibit 13.1

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 Jurriaan Dekkers, the Chief 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, 2024 (the "Report") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; 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 13, 2025

By:	/s/ Daniel de Boer
Name:	Daniel de Boer
Title:	*Chief Executive Officer*
	(Principal Executive Officer)

By:	/s/ Jurriaan Dekkers
Name:	Jurriaan Dekkers
Title:	*Chief Financial Officer*
	(Principal Financial Officer)

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the registration statements No. 333-260801 and No. 333-199451 on Form S-8 and the registration statements No. 333-270943, No. 333-263166, No. 333-248740, and No. 333-282419 on Form F-3 of our reports dated March 13, 2025, with respect to the consolidated financial statements of ProQR Therapeutics N.V. and the effectiveness of internal control over financial reporting.

/s/ KPMG Accountants N.V.

Amstelveen, the Netherlands
March 13, 2025