

As filed with the Securities and Exchange Commission on March 1, 2022

Registration No. 333-

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

FORM F-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

PROQR THERAPEUTICS N.V.

(Exact Name of Registrant as Specified in its Charter)

Not Applicable

(Translation of Registrant's Name into English)

The Netherlands
(State or other Jurisdiction of
Incorporation or Organization)

Not applicable
(I.R.S. Employer
Identification No.)

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The Netherlands
+31 88 166 7000**

(Address and telephone number of Registrant's principal executive offices)

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**Approximate Date of Commencement of Proposed Sale of the Securities to the Public:
From time to time after the effective date of this Registration Statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

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

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

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

If this Form is a registration statement pursuant to General Instruction I.C. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.C. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933.

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 7(a)(2)(B) of the Securities Act.

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

[†] 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.

PROSPECTUS



Up to 3,665,224 Ordinary Shares

This prospectus relates to the resale or other disposition, from time to time, by the selling shareholders identified in this prospectus, and any of their respective donees, pledgees, transferees, or other successors-in-interest, of up to 3,665,224 of our ordinary shares, nominal value €0.04 per share, that are issuable pursuant to the terms of certain convertible notes due June 29, 2026 (the “Convertible Notes”) and warrants issued to the holders of the Convertible Notes (the “Warrants”), as further described in this prospectus.

The number of ordinary shares being registered hereunder is comprised of: (i) 3,288,272 ordinary shares issuable upon conversion of the Convertible Notes, which Convertible Notes are convertible into shares of our ordinary shares at a conversion price of \$11.9379 per share; and (ii) 376,952 ordinary shares issuable upon the exercise of the Warrants, which Warrants are exercisable for shares of our ordinary shares at an exercise price of \$11.9379 per share. The number of ordinary shares registered by the Registrant represents a good faith estimate of the number of ordinary shares which will be issued upon conversion of the Convertible Notes, assuming for purposes hereof, that the Convertible Notes will accrue interest through June 29, 2026, at a rate of 8.2% per annum. If the Convertible Notes convert after the Registrant has paid some of the principal balance or accrued interest on the Convertible Notes, the actual number of shares issuable to the selling shareholders upon conversion of the Convertible Notes, if any, could be materially less than 3,288,272 shares of ordinary shares depending on the amount of principal and accrued but unpaid interest that is converted into shares of ordinary shares at the time. This presentation is not intended to constitute an indication or prediction of the date on which the selling shareholders will convert the Convertible Notes into ordinary shares, if at all.

We are registering the resale of our ordinary shares covered by this prospectus as required by a registration rights agreement we entered into as part of a private transaction involving the selling shareholders, as further described in this prospectus. We will not receive any of the proceeds from the sale of the ordinary shares by the selling shareholders.

The selling shareholders and their respective donees, pledgees, transferees or other successors-in-interest may offer the ordinary shares in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices, or in trading markets for our ordinary shares. Additional information on the selling shareholders, and the times and manner in which they may offer and sell our ordinary shares under this prospectus, is provided under “*Selling Shareholders*” and “*Plan of Distribution*” in this prospectus.

The selling shareholders may sell any, all or none of the securities offered by this prospectus from time to time and we do not know when or in what amount the selling shareholders may sell the shares hereunder following the effective date of the registration statement of which this prospectus forms a part.

Our ordinary shares are listed on the Nasdaq Global Market under the symbol “PRQR.” On February 23, 2022, the last reported sale price of our ordinary shares on the Nasdaq Global Market was \$1.07 per share.

ProQR Therapeutics N.V. is a public company with limited liability (*naamloze vennootschap*) incorporated under the laws of the Netherlands. Our principal executive offices are located at Zernikedreef 9, 2333 CK Leiden, The Netherlands. Our telephone number at such address is +31 88 166 7000.

Investing in our securities involves a high degree of risk. See the section entitled “*Risk Factors*” beginning on page 8 of this prospectus as well as those contained in the applicable prospectus supplement and any related free writing prospectus, and in the other documents that are incorporated by reference into this prospectus or the applicable prospectus supplement.

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

The date of this prospectus is _____, 2022.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any applicable prospectus supplement or free writing prospectus, including the documents that we incorporate by reference herein, includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the “Securities Act,” and Section 21E of the Securities Exchange Act of 1934, as amended, or the “Exchange Act.” For this purpose, any statements contained herein, other than statements of historical fact, including statements regarding: our clinical development plans or our future financial performance, our development programs, including timing, plans, results and therapeutic potential with respect to our product candidates, our business operations, including timing of commencing clinical trials and enrollment of patients therein, our other programs and business operations (including Axiomer[®] and Trident[®]), collaborations with partners, the expected impact of the ongoing COVID-19 pandemic on our business operations, including our research and development plans and timelines and the supply chain for our clinical and development programs; and any other statements about management’s future expectations, beliefs, goals, plans or prospects constitute forward-looking statements. We may, in some cases, use words such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “project,” “should,” “target,” “will,” “would” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the risks described under the heading “Risk Factors” in this prospectus and our most recent Annual Report on Form 20-F, as well as any amendments thereto reflected in subsequent filings with the Securities and Exchange Commission, or the “SEC.” If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any acquisitions, mergers, dispositions, business development transactions, joint ventures or investments we may enter into or make in the future.

You should rely only on information contained, or incorporated by reference, in this prospectus, the registration statement of which this prospectus is a part, the documents incorporated by reference in this prospectus, and any applicable prospectus supplement or free writing prospectus and understand that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law. Before deciding to purchase our securities, you should carefully consider the risk factors included or incorporated herein by reference, in addition to the other information set forth in this prospectus, any accompanying prospectus supplement, any free writing prospectus and in the documents incorporated by reference.

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

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form F-3 that we filed with the Securities and Exchange Commission (the “SEC”) utilizing a “shelf” registration process. Under this shelf registration process, certain selling shareholders may from time to time sell the securities, as described in this prospectus, in one or more offerings. This prospectus does not contain all of the information set forth in the registration statement, certain parts of which are omitted in accordance with the rules and regulations of the SEC. Accordingly, you should refer to the registration statement and its exhibits for further information about us and our securities. Copies of the registration and its exhibits are on file with the SEC. Statements contained in this prospectus concerning the documents we have filed with the SEC are not intended to be comprehensive, and in each instance we refer you to a copy of the actual document filed as an exhibit to the registration statement or otherwise filed with the SEC.

When the selling shareholders sell securities using this prospectus, to the extent necessary, we will provide you with a prospectus supplement that will contain specific information about the terms of that offering, including the number of shares being offered, the manner of distribution, the identity of any underwriters or other counterparties and other specific terms related to the offering. The prospectus supplement may also add, update or change information contained in this prospectus. To the extent that any statement made in an accompanying prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the accompanying prospectus supplement. You should read both this prospectus and any prospectus supplement together with any additional information described under the headings “*Where You Can Find Additional Information*” and “*Incorporation of Certain Information By Reference*” before deciding to invest in any of the securities being offered. The information contained in this prospectus and any supplement to this prospectus, or incorporated by reference herein, is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus or of any sale of our ordinary shares. Our business, financial condition, results of operations and prospects may have changed since those dates.

You should rely only on this prospectus, the information incorporated or deemed to be incorporated by reference in this prospectus and any free writing prospectus prepared by us or on our behalf. Neither we nor the selling shareholders have authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus. Neither we nor the selling shareholders take any responsibility for, nor can provide assurance as to the reliability of, any other information that others may give you. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Unless the context otherwise indicates, references in this prospectus to the “Registrant,” the “Company,” “we,” “ours,” “our,” “us” and similar designations refer to ProQR Therapeutics N.V., a company organized under the laws of the Netherlands, and where appropriate, our consolidated subsidiaries. We use various trademarks and trade names, including without limitation our corporate name and logo, that we use in connection with the operation of our business. This prospectus, any applicable prospectus supplement and the information incorporated herein or therein by reference may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. Solely for convenience, the trademarks, service marks and trade names referred to or incorporated by reference in this prospectus, any applicable prospectus supplement or any free writing prospectus may appear without the ®, ™ or SM symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner of these trademarks, service marks and trade names will not assert, to the fullest extent under applicable law, its rights.

Our consolidated financial statements are presented in euros and have been prepared in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board (“IFRS”). In presenting and discussing our financial position, operating results and cash flows, management uses certain non-GAAP financial measures. These non-GAAP financial measures should not be viewed in isolation as alternatives to the equivalent IFRS measure and should be used in conjunction with the most directly comparable IFRS measure(s).

All references in this prospectus to “U.S. dollars” or “\$” are to the legal currency of the United States, and all references to “€” or “euro” are to the currency of the European Economic and Monetary Union. Our business to date has been conducted primarily in the European Union, and we maintain our books and records in euro. We present our financial statements in euro, which is the Company’s functional currency. Unless otherwise specified in this prospectus, translations from euros to U.S. dollars were made at a rate of \$1.1344 to €1.00, the official exchange rate quoted by the European Central Bank at the close of business on February 23, 2022.

No action is being taken in any in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus in that jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

PROSPECTUS SUMMARY

The following summary provides a brief overview of the key aspects of ProQR Therapeutics N.V. and certain material terms of the securities that may be offered that are known as of the date of this prospectus. Before you decide to invest in our securities, you should carefully consider the risks and discussion of risks set forth under the heading “Item 3. Key Information — D. Risk Factors” in our Annual Report on Form 20-F for the year ended December 31, 2020, filed with the SEC on March 24, 2021, and the subsequent Annual Reports on Form 20-F and Reports of Foreign Private Issuer on Form 6-K that we file with the SEC. For a more complete understanding of the terms of a particular issuance of offered securities, and before making your investment decision, you should read the entire prospectus carefully, including the matters discussed under the heading “Risk Factors” in this prospectus and the documents referred to in “Where You Can Find Additional Information” for information about us, as well as our financial statements.

Overview

We are developing a pipeline of potentially life-changing RNA therapies for genetic eye diseases, with a focus on inherited retinal diseases, a group of rare debilitating eye diseases, or IRDs. IRDs are affecting over five million people in the world and except for a few thousand patients, there are no treatment options. We believe our RNA platform based on intravitreal delivery may be suitable to repair defective RNA and stop progression or even reverse vision loss associated with the diseases. Our current clinical-stage pipeline consists of programs in ophthalmology.

Beyond our clinical portfolio, we discovered and developed two novel proprietary RNA editing platform technologies, Axiomer[®] and Trident[®]. Axiomer’s editing oligonucleotides, or EONs, are designed to recruit endogenous Adenosine Deaminases Acting on RNA, or ADAR, enzymes to make single nucleotide changes in the RNA in a highly specific and targeted manner at a desired location. We believe our Axiomer[®] platform may be broadly applicable to more than 20,000 disease-causing mutations. Trident[®] is our RNA pseudouridylation platform that enables the selective suppression of nonsense mutations that cause human genetic disease.

We continuously evaluate opportunities for beneficial collaborations or partnerships to efficiently develop our investigational therapies for patients. In addition, using our discovery engine that is designed to generate a broad pipeline of product candidates, we seek to enter into strategic partnerships for programs that we believe will benefit from such a partnership. An example of this is our partnership with Lilly around our Axiomer[®] RNA editing platform technology.

Impact of the Ongoing COVID-19 Pandemic

The ongoing COVID-19 pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. We are closely monitoring the impact of the COVID-19 pandemic on all aspects of our business, including how it has impacted and may continue to impact our operations and the operations of our suppliers, vendors and business partners. We have taken steps to identify and mitigate the adverse impacts on, and risks to, our business posed by its spread and actions taken by governmental and health authorities to address this pandemic; however, the spread of COVID-19 has caused us to modify our business practices, including implementing a hybrid work arrangement for all employees who are able to perform their duties remotely and enacting COVID-19 safety measures for all employees and visitors to our facility. We expect to continue to take actions as may be required or recommended by government authorities or as we determine are in the best interests of our employees and other business partners in light of COVID-19. The extent to which COVID-19 impacts our business, results of operations and financial condition will depend on future developments, which, despite progress in vaccination efforts, are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, new information that may emerge concerning the severity of COVID-19, such as new strains of the virus, including the Delta and Omicron variants and any future variants that may emerge, which may impact rates of infection and vaccination efforts, developments or perceptions regarding the safety of vaccines and the extent and effectiveness of actions to contain COVID-19 or treat its impact, including vaccination campaigns and lockdown measures, among others. In addition, recurrences or additional waves of COVID-19 cases could cause other widespread or more severe impacts depending on where infection rates are highest. We cannot presently predict the scope and severity

of any potential business shutdowns or disruptions, but if we or any of the third parties with whom we engage were to experience prolonged business shutdowns or other disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, results of operations and financial condition. Our estimates of the impact on our business may change based on new information that may emerge concerning COVID-19 and the actions to contain it or treat its impact and the economic impact on local, regional, national and international markets. See “Risk Factors” contained in the Annual Report on Form 20-F for the fiscal year ended December 31, 2020, filed with the SEC on March 24, 2021, incorporated by reference in this prospectus.

Implications of Being a Foreign Private Issuer

We report under the Exchange Act as a non-U.S. company with foreign private issuer status. 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 management and supervisory boards will be required to notify the Dutch Authority for the Financial Markets of certain transactions they may undertake, including with respect to our ordinary shares, our officers, directors and principal shareholders will be exempt from the requirements to report transactions in our equity securities and from the short-swing profit liability provisions contained in Section 16 of the Exchange Act. These exemptions and leniencies will reduce the frequency and scope of information and protections available to you in comparison to those applicable to a U.S. domestic reporting companies.

Furthermore, as a foreign private issuer, we are permitted to follow the corporate governance practices of our home country in lieu of certain provisions of the Nasdaq. We therefore follow Dutch corporate governance practices in lieu of certain Nasdaq corporate governance requirements to seek shareholder approval for a specified issuance of securities.

Company Information

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, and our registered office is at Zernikedreef 9, 2333 CK Leiden, the Netherlands, and our telephone number is +31 88 166 7000. Our website address is *www.ProQR.com*. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus. Our website address is included in this document as an inactive textual reference only.

ProQR was formed in February 2012 by Daniel de Boer, Gerard Platenburg, the late Henri Termeer and Dinko Valerio. Mr. de Boer is a passionate and driven entrepreneur and has assembled an experienced team of successful biotech executives as co-founders and early investors. ProQR’s team has extensive experience in discovery, development and commercialization of RNA therapeutics. We have received grants, loans and other funding from patient organizations and government institutions supporting our programs, including from Foundation Fighting Blindness and the Dutch government under the innovation credit program. Our headquarters are located in Leiden, the Netherlands.

Listing

Our ordinary shares are listed on the Nasdaq Global Market under the symbol “PRQR.” If any other securities are to be listed or quoted on a securities exchange or quotation system, the applicable prospectus supplement will so state.

THE OFFERING

Ordinary shares offered by the selling shareholders	Up to 3,665,224 ordinary shares (representing the maximum shares issuable pursuant to the terms of the Convertible Notes and the Warrants).
Ordinary shares outstanding before this offering	71,154,571 ordinary shares as of September 30, 2021.
Ordinary shares outstanding after this offering	Up to 74,819,205 ordinary shares (as more fully described in the notes following this table), assuming that the full amount of the registered securities are issued pursuant to the terms of the Convertible Notes and the Warrants.
Plan of distribution	The selling shareholders, including their respective donees, pledgees, transferees or other successors-in-interest, may from time to time offer some or all of the ordinary shares in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices, or in trading markets for our ordinary shares. See “ <i>Plan of Distribution.</i> ”
Use of proceeds	We will not receive any proceeds from the sale of our ordinary shares by the selling shareholders pursuant to this prospectus. However, if all of the Warrants were exercised for cash, we would receive gross proceeds of \$4,500,819. We currently intend to use such proceeds, if any, for general corporate purposes, which may include, but are not limited to, working capital, strategic acquisitions and other potential business development activities, ongoing research and development activities and capital expenditures. See “ <i>Use of Proceeds.</i> ”
Risk factors	Investing in our securities involves a high degree of risk. Please read the information contained in and incorporated by reference under the heading “ <i>Risk Factors</i> ” in this prospectus, and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus, together with the other information included in or incorporated by reference into this prospectus, before deciding whether to invest in our securities.
Nasdaq Global Market symbol	PRQR

The number of ordinary shares expected to be outstanding after this offering and, unless otherwise indicated, the information in this prospectus are based on 71,154,571 ordinary shares outstanding as of September 30, 2021, plus an additional 3,665,224 ordinary shares offered by the selling shareholders upon the issuance of the ordinary shares in connection with the conversion of the Convertible Notes and the exercise of the Warrants, as applicable, and excludes:

- up to 302,676 ordinary shares issuable upon exercise of warrants to purchase ordinary shares at an exercise price of \$7.88 per share;

- the conversion of the initial tranche under our original debt facility with Pontifax Medison Financing and Kreos Capital into our ordinary shares at a conversion price of \$7.88 per ordinary share. As of September 30, 2021, we had drawn down amounts under these facilities totaling approximately €14 million;
- 2,556,566 ordinary shares that we issued to a Dutch foundation named Stichting Bewaarneming Aandelen ProQR for the administration of option exercises or vesting and settlement of restricted stock units under our equity incentive plans. Such shares are held by the aforementioned foundation until they are transferred to a grantee upon the exercise of options or vesting and settlement of restricted stock units. As of September 30, 2021, (i) 7,588,054 options have been granted by us with a weighted average exercise price of €5.94 per share and (ii) 458,237 restricted stock units have been granted by us with a weighted average grant date fair value of €4.34 per share; and
- 1,152,244 treasury shares held by us, which had been reserved to transfer ordinary shares to grantees upon exercise of awards under our equity incentive plans as of September 30, 2021.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before investing in our securities, you should carefully consider the risks described below and in the “Risk Factors” section of our Annual Report on Form 20-F for the year ended December 31, 2020, filed with the SEC on March 24, 2021, as updated or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus, together with all of the other information contained in this prospectus and incorporated by reference herein, and any free writing prospectus that we may authorize for use in connection with this offering. Some of these factors relate principally to our business and the industry in which we operate. Other factors relate principally to your investment in our securities. The risks and uncertainties described therein and below are not the only risks facing us. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also materially and adversely affect our business and operations. If any of the matters included in the following risks were to occur, our business, financial condition, results of operations, cash flows or prospects could be materially and adversely affected. In such case, you may lose all or part of your investment. See the sections titled “Where You Can Find Additional Information” and “Incorporation of Certain Information By Reference” in this prospectus for additional information.

The terms of our loan and security agreement require us to meet certain operating covenants and place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

In July 2020, we entered into a Loan and Security Agreement with certain lenders party thereto (as amended to date, the “Loan Agreement”), that is secured by a lien covering all of our assets, other than our intellectual property. 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. In December 2021, we further amended the Loan Agreement to, among other things, to replace the two remaining undrawn tranches with three new tranches and effect the drawdown of the first of those three new tranches. The Loan Agreement contains customary affirmative covenants, negative covenants and events of default. Affirmative covenants include, among others, covenants requiring us to protect and maintain our intellectual property and comply with all applicable laws, deliver certain financial reports, maintain certain minimum cash and other financial covenants, and maintain insurance coverage. Negative covenants include, among others, covenants restricting us from transferring any part of our business or intellectual property, incurring additional indebtedness, engaging in mergers or acquisitions, repurchasing shares, paying dividends or making other distributions, making investments, and creating other liens on our assets, in each case subject to customary exceptions. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility. These restrictions may include, among other things, limitations on borrowing and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem capital stock or make investments, without the prior written consent of the lenders. If we default under the terms of the Loan and Agreement or any future debt facility, the lenders may accelerate all of our repayment obligations and take control of our pledged assets, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, the lenders’ right to repayment would be senior to the rights of the holders of our ordinary shares. The lenders could declare a default upon the occurrence of any event that they interpret as a material adverse effect as defined under the Loan Agreement. Any declaration by the lenders of an event of default could significantly harm our business and prospects and could cause the price of our ordinary shares to decline.

Repayment of the Convertible Notes, if they are not otherwise converted, will require a significant amount of cash, and we may not have sufficient cash resources to make payments on our indebtedness.

Our ability to pay the principal of and/or interest on the Convertible Notes depends on our cash position, which is subject to economic, financial, competitive and other factors beyond our control. We may not have sufficient cash resources at the time of repayment to service the Convertible Notes or other future indebtedness. If we are unable to secure such cash resources, we may be required to adopt and implement one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional debt financing or equity financing on terms that may be onerous or highly dilutive. Our ability to refinance

the Convertible Notes or other future indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations, including the Convertible Notes.

The issuance of ordinary shares upon conversion of the Convertible Notes and exercise of the Warrants could substantially dilute your investment and could impede our ability to obtain additional financing.

The Convertible Notes are convertible into and the Warrants are exercisable for shares of our ordinary shares and give the holders an opportunity to profit from a rise in the market price of our ordinary shares such that conversion or exercise thereof could result in dilution of the equity interests of our shareholders. We have no control over whether the holders will exercise their right to convert their Convertible Notes or exercise their Warrants. While the Convertible Notes are convertible at a fixed price of \$11.9379 per share and the Warrants are exercisable at a fixed price of \$11.9379 per share, both of which are higher than our current market price, we cannot predict the market price of our ordinary shares at any future date, and therefore, cannot predict whether the Convertible Notes will be converted or whether the Warrants will be exercised. The existence and potentially dilutive impact of the Convertible Notes and the Warrants may prevent us from obtaining additional financing in the future on acceptable terms, or at all. In addition to the ordinary shares underlying the Convertible Notes and the Warrants registered by the registration statement of which this prospectus forms a part, we also have outstanding additional convertible loans and warrants issued to our senior lenders in July 2020 and August 2020.

DESCRIPTION OF THE TRANSACTION

Private Placement of Convertible Notes and Warrants

On December 29, 2021 (the “Amendment Date”), we and certain of our subsidiaries entered into a Third Amendment (the “Third Amendment”) to Loan and Security Agreement (as conformed through the Third Amendment, the “Amended Loan Agreement”) with Pontifax Medison Finance (Israel) L.P., Pontifax Medison Finance (Cayman) L.P. (together, the “Pontifax Lenders”), Kreos Capital VI (UK) Limited, Kreos Capital 2020 Opportunity (UK) Limited (together, the “Kreos Lenders”) and the other financial institutions or entities from time to time parties thereto (collectively, referred to as “Lenders”) and Pontifax Medison Finance GP, L.P., in its capacity as administrative agent and collateral agent for itself and Lenders (in such capacity, “Agent”). Such Third Amendment further modified certain terms and conditions of our then-existing Loan and Security Agreement, dated as of July 14, 2020 (the “Closing Date”), with the Pontifax Lenders and the Agent (the “Original Loan Agreement”). The Original Loan Agreement provided for loans to be made available by Pontifax Lenders to us in three tranches, of which the first tranche had been drawn down as of the Closing Date (the “Original Term Loan”). The Original Loan Agreement was later amended by the Joinder and First Amendment to Loan Agreement, dated as of August 4, 2020, among the Pontifax Lenders, the Kreos Lenders, the Agent and us, which provided for an incremental loan made by Kreos Lenders to us (the “Incremental Term Loan”). The Amended Loan Agreement, among other things, replaced the two undrawn tranches under the Original Loan Agreement. The Original Term Loan and the Incremental Term Loan remain outstanding and unmodified (except as specified in the Amended Loan Agreement), including with respect to amounts outstanding, interest rate, maturity date and repayment schedule. The Lenders under the Loan Agreement are referred to herein as the “selling shareholders.”

Under the Amended Loan Agreement, Lenders agreed to make available to us certain additional term loans in an aggregate principal amount of up to \$90.0 million (in addition to the Original Term Loan and the Incremental Term Loan), subject to funding in three tranches as follows: (a) on December 30, 2021, a loan in the aggregate principal amount of \$30.0 million (the “First Installment”), (b) during a period of nine months from the Amendment Date subject to the Company’s achievement of a specified milestone, a loan in the aggregate principal amount of \$30.0 million (the “Second Installment”), and (c) upon the Company’s achievement of a specified milestone by no later than 18 months following the Amendment Date, a loan in the aggregate principal amount of \$30.0 million (the “Third Installment” and collectively with the First Installment and Second Installment, the “Installment Loans”).

The obligations of Lenders to fund the Installment Loans are subject to certain conditions precedents as set forth in the Amended Loan Agreement. As security for our obligations under the Amended Loan Agreement, we granted Lenders a first priority security interest on all of our assets, excluding intellectual property, and a negative pledge on intellectual property.

The maturity date of the Original Term Loan and the Incremental Term Loan is 54 months after the Closing Date, with amortized payments commencing 24 months following the Closing Date in ten equal quarterly payments. The maturity date of the Installment Loans is 54 months after the Amendment Date, with amortized payments commencing 33 months after the Amendment Date in eight equal quarterly payments. The Original Term Loan, the Incremental Term Loan and the First Installment bear an interest rate of 8.2% per annum, and the Second Installment and Third Installment bear an interest rate of 8.0% per annum, in each case based on a year consisting of 365 days. In addition, we are required to pay an unused line fee of 0.5% per annum on the amount of the Second Installment or Third Installment, as applicable, plus an additional fee of 1.0% per annum on the amount of the Second Installment or Third Installment, as applicable, to be paid retroactively in one payment and calculated from the Amendment Date until the date on which the applicable milestones for the Second Installment or Third Installment, as applicable, are achieved.

After 12 months following the Amendment Date, we may prepay, from time to time, an amount of not less than \$1.0 million or all of the then outstanding principal balance and all accrued and unpaid interest thereon with respect to the Installment Loans, subject to at least five (5) business days prior written notice to Agent and the payment of a prepayment fee equal to 1.0% of the principal amount being prepaid. The Original Term Loan and the Incremental Term Loan may be prepaid from time to time after six months

following the Amendment Date, subject to at least five (5) business days prior written notice to Agent and the payment of a prepayment fee equal to 1.0% of the principal amount being prepaid. During the notice period, Lenders may elect to convert such outstanding amounts into our ordinary shares on the conversion terms described in greater detail below.

The Amended Loan Agreement contains customary affirmative covenants, negative covenants and events of default, as defined in the Amended Loan Agreement, including covenants and restrictions that, among other things, require us to satisfy certain minimum cash and other financial covenants, and in certain circumstances restrict our ability to incur liens, incur additional indebtedness, engage in mergers and acquisitions, or make asset sales without the prior written consent of Lenders. A failure to comply with these covenants could permit Lenders to declare our obligations under the Amended Loan Agreement, together with accrued interest and fees, to be immediately due and payable, plus any applicable additional amounts relating to a prepayment or termination, as described above.

Under the Amended Loan Agreement, Lenders may elect to convert the outstanding Installment Loans into our ordinary shares at any time prior to repayment at a conversion price equal to \$11.9379 per share, which was 1.5 times the average closing price of the Company's Ordinary Shares during the seven trading days prior to the Amendment Date, subject to certain adjustments as provided in the Amended Loan Agreement (the "Conversion Price"). We also have the right to convert at any time all or any portion of the then outstanding Installment Loans and all accrued and unpaid interest thereon into our ordinary shares at the Conversion Price, subject to fulfilment of certain conditions as set forth in the Amended Loan Agreement.

In addition, in connection with the entry into the Third Amendment and the Amended Loan Agreement, and the drawdown of the First Installment, we issued to the Pontifax Lenders, Kreos Capital VI (Expert Fund) L.P. and Kreos Capital 2020 Opportunity L.P. (collectively, the "Kreos Warrant Holders") warrants to purchase up to an aggregate of 376,952 Ordinary Shares (the "Installment Warrants") at an exercise price equal to \$11.9379 per share, which was 1.5 times the average closing price of our ordinary shares during the seven trading days prior to the Amendment Date. Additional Installment Warrants may be issued under certain circumstances described in the Amended Loan Agreement, including in connection with the drawdown of the Second Installment and the Third Installment, at an exercise price equal to 1.5 times the average closing price of our ordinary shares during the seven trading days prior to the drawdown of the Second Installment or Third Installment, as applicable. The Installment Warrants may be exercised, in whole or in part, at any time until the 5th anniversary of their issuance date.

Concurrently with the execution of the Loan Agreement, we entered into a Registration Rights Agreement (the "Registration Rights Agreement"), dated as of December 29, 2021, by and among us, the Pontifax Lenders and the Kreos Warrant Holders, pursuant to which we agreed to file and keep effective one or more registration statements with the Securities and Exchange Commission for the purpose of registering for resale the shares issuable upon conversion of the loans and warrants issued under the Amended Loan Agreement. The registration statement of which this prospectus forms a part registers the ordinary shares underlying the First Installment loan and the Installment Warrants.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization on an actual basis as of September 30, 2021. The information in this table should be read in conjunction with and is qualified by reference to the financial information thereto and other financial information incorporated by reference into this prospectus.

	<u>As of September 30, 2021</u>
	<u>(€ in thousands, except share and per share data)</u>
Cash and cash equivalents	<u>€156,141</u>
Total debt:	
Lease liability	15,109
Borrowings	<u>17,513</u>
Total debt	<u>32,622</u>
Equity:	
Equity attributable to owners of the Company	128,606
Non-controlling interests	<u>(585)</u>
Total equity	<u>128,021</u>
Total capitalization	<u>€160,643</u>

The table above excludes:

- up to 302,676 ordinary shares issuable upon exercise of warrants to purchase ordinary shares at an exercise price of \$7.88 per share;
- the conversion of the initial tranche under our original debt facility with Pontifax Medison Financing and Kreos Capital into our ordinary shares at a conversion price of \$7.88 per ordinary share. As of September 30, 2021, we had drawn down amounts under these facilities totaling approximately €14 million;
- 2,556,566 ordinary shares that we issued to a Dutch foundation named Stichting Bewaarneming Aandelen ProQR for the administration of option exercises or vesting and settlement of restricted stock units under our equity incentive plans. Such shares are held by the aforementioned foundation until they are transferred to a grantee upon the exercise of options or vesting and settlement of restricted stock units. As of September 30, 2021, (i) 7,588,054 options have been granted by us with a weighted average exercise price of €5.94 per share and (ii) 458,237 restricted stock units have been granted by us with a weighted average grant date fair value of €4.34 per share; and
- 1,152,244 treasury shares held by us, which had been reserved to transfer ordinary shares to grantees upon exercise of awards under our equity incentive plans as of September 30, 2021.

USE OF PROCEEDS

All shares of our ordinary shares offered by this prospectus are being registered for the account of the selling shareholders. We will not receive any proceeds from the sale of our ordinary shares offered hereby. However, if all of the Warrants were exercised for cash, we will receive proceeds of \$4,500,819. We currently intend to use such proceeds, if any, for general corporate purposes, which may include, but are not limited to, working capital, strategic acquisitions and other potential business development activities, ongoing research and development activities and capital expenditures. If the selling shareholders elect to exercise the Warrants by means of a “cashless exercise,” as is allowed pursuant to the terms of the Warrants, we will not receive any proceeds upon exercise of the Warrants.

The selling shareholders will pay all underwriting discounts, selling commissions and expenses incurred by them for brokerage, accounting, tax or legal services or any other expenses incurred by the selling shareholders in connection with the sale of the shares, if any. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, Nasdaq listing fees and fees and expenses of our counsel and our accountants.

SELLING SHAREHOLDERS

The ordinary shares being offered for resale by the selling shareholders pursuant to the Form F-3 of which this prospectus forms a part are the ordinary shares issuable to the selling shareholders pursuant to the terms of the Convertible Notes and upon exercise of the Warrants. For additional information regarding the issuance of those Convertible Notes and Warrants, see “*Description of the Transaction.*” We are registering the ordinary shares in order to permit the selling shareholders to offer the shares for resale from time to time. Except for the ownership of the Convertible Notes and the Warrants issued pursuant to the Loan Agreement and as described below, the selling shareholders have not had any material relationship with us within the past three years.

The table below lists the selling shareholders and other information regarding the beneficial ownership of ordinary shares by each of the selling shareholders. The second column lists the number of ordinary shares beneficially owned by each selling shareholder, based on its ownership of the Convertible Notes and Warrants, as of March 1, 2022, assuming conversion of all Convertible Notes at the conversion price of \$11.9379 per share that the Convertible Notes will accrue interest through June 29, 2026 at a rate of 8.2% per annum, and the exercise of Warrants that are held by the selling shareholders. The third column lists the ordinary shares being offered by this prospectus by the selling shareholders. The fourth column lists the ordinary shares held by each selling shareholder after completion of this offering, and assumes the full exercise of the Warrants held by each of the selling shareholders and that each selling shareholder subsequently sells all of the shares covered by this prospectus and assumes full conversion of the Convertible Notes. The fifth column lists the percentage ownership held by each selling shareholder after completion of this offering to the extent such percentage exceeds 1% of the total number of ordinary shares outstanding at that time. The information presented regarding the selling shareholders is based, in part, on information the selling shareholders provided to us in writing specifically for use in this prospectus. The selling shareholders may sell all, some or none of their shares in this offering. See “*Plan of Distribution.*”

In addition to the assumptions described above, beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power over securities. To our knowledge, unless otherwise indicated, all persons named in the table below have sole voting and investment power with respect to their ordinary shares. Percentage of beneficial ownership is based on 71,154,571 shares of our ordinary shares outstanding as of September 30, 2021.

Name of Selling Shareholder	Number of Ordinary Shares Owned Prior to Offering	Maximum Number of Ordinary Shares to be Sold Pursuant to this Prospectus	Number of Ordinary Shares Owned After Offering	Percentage of Ordinary Shares Owned After Offering (to the extent greater than 1%)
Pontifax Medison Finance (Israel) L.P. ⁽¹⁾	569,603 ⁽²⁾	569,603	—	—
Pontifax Medison Finance (Cayman) L.P. ⁽³⁾	244,891 ⁽⁴⁾	244,891	—	—
Kreos Capital VI (UK) Limited ⁽⁵⁾	1,705,030 ⁽⁶⁾	1,705,030	—	—
Kreos Capital VI (Expert Fund) L.P. ⁽⁷⁾	195,457 ⁽⁸⁾	195,457	—	—
Kreos Capital 2020 Opportunity (UK) Limited ⁽⁹⁾	852,515 ⁽¹⁰⁾	852,515	—	—
Kreos Capital 2020 Opportunity L.P. ⁽¹¹⁾	97,728 ⁽¹²⁾	97,728	—	—

* Denotes less than 1%.

- (1) Pontifax Medison Finance (Israel), Limited Partnership (“Pontifax Israel”), is a limited partnership registered under the laws of the State of Israel. Decisions with respect to the disposition of securities are taken by the fund’s investment committee. The members of the investment committee are Mr. Tomer Kariv, Mr. Ran Nussbaum, Mr. Shlomo (Momi) Karako and Mr. Gil Gurfinkel. In addition, Pontifax Medison Finance GP Limited Partnership (“Pontifax Management”) is the general partner of Pontifax Israel. Pontifax Management 4 G.P. (2015) Ltd. is the general partner of Pontifax Management. Mr. Tomer Kariv and Mr. Ran Nussbaum are directors of Pontifax Management 4 G.P. (2015) Ltd.,

- and as such, hold voting and/or dispositive power over the shares held by Pontifax Israel. The address of the entities affiliated with Pontifax Israel is 14 Shenkar St., Herzeliya, Israel.
- (2) Consists of (i) 511,022 ordinary shares issuable under the Convertible Notes and (ii) 58,581 ordinary shares issuable upon exercise of the Warrants.
 - (3) Pontifax Medison Finance (Cayman), L.P. (“Pontifax Cayman”), is a limited partnership registered under the laws of the Cayman Islands. Decisions with respect to the disposition of securities are taken by the fund’s investment committee. The members of the investment committee are Mr. Tomer Kariv, Mr. Ran Nussbaum, Mr. Shlomo (Momi) Karako and Mr. Gil Gurfinkel. In addition, Pontifax Medison Finance GP Limited Partnership (“Pontifax Management”) is the general partner of Pontifax Cayman. Pontifax Management 4 G.P. (2015) Ltd. is the general partner of Pontifax Management. Mr. Tomer Kariv and Mr. Ran Nussbaum are directors of Pontifax Management 4 G.P. (2015) Ltd., and as such, hold voting and/or dispositive power over the shares held by Pontifax Cayman. The address of the entities affiliated with Pontifax Cayman is 14 Shenkar St., Herzeliya, Israel.
 - (4) Consists of (i) 219,705 ordinary shares issuable under the Convertible Notes and (ii) 25,186 ordinary shares issuable upon exercise of the Warrants.
 - (5) Kreos Capital VI (UK) Limited (“Kreos VI UK”), is a company incorporated in England and Wales and is a fully owned subsidiary of Kreos Capital VI (Expert Fund) L.P. (“Kreos VI LP”). Decisions with respect to the disposition of securities are taken by the Kreos VI LP’s General Partner, Kreos Capital Group VI Limited in its capacity as general partner to Kreos Capital Group VI LP. The registered office address of Kreos VI UK is Amf Building, 25 Old Burlington Street, London W1S 3AN.
 - (6) Represents 1,705,030 ordinary shares issuable under the Convertible Notes.
 - (7) Kreos VI LP is a limited partnership incorporated in Jersey. Decisions with respect to the disposition of securities are taken by the Kreos VI LP’s General Partner, Kreos Capital Group VI Limited in its capacity as general partner to Kreos Capital Group VI LP. The registered office address of Kreos VI LP is 47 Esplanade, St Helier, Jersey JE1 0BD.
 - (8) Represents 195,457 ordinary shares issuable upon exercise of the Warrants.
 - (9) Kreos Capital 2020 Opportunity (UK) Limited (“Kreos 2020 UK”), is a company incorporated in England and Wales and is a fully owned subsidiary of Kreos Capital 2020 Opportunity L.P. (“Kreos 2020 LP”). Decisions with respect to the disposition of securities are taken by the Kreos 2020 LP’s General Partner, Kreos Capital Group 2020 Opportunity Limited in its capacity as general partner to Kreos Capital Group 2020 Opportunity LP. The registered office address of Kreos Capital UK is Amf Building, 25 Old Burlington Street, London W1S 3AN.
 - (10) Represents 852,515 ordinary shares issuable under the Convertible Notes.
 - (11) Kreos 2020 LP is a limited partnership incorporated in Jersey. Decisions with respect to the disposition of securities are taken by the Kreos 2020 LP’s General Partner, Kreos Capital Group 2020 Opportunity Limited in its capacity as general partner to Kreos Capital Group 2020 Opportunity LP. The registered office address of Kreos 2020 LP is 47 Esplanade, St Helier, Jersey JE1 0BD.
 - (12) Represents 97,728 ordinary shares issuable upon exercise of the Warrants.

PLAN OF DISTRIBUTION

We are registering the ordinary shares issuable pursuant to the terms of the Convertible Notes and upon exercise of the Warrants to permit the resale of these shares by the holders of the Convertible Notes and Warrants from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling shareholders of the ordinary shares.

The selling shareholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling ordinary shares or interests in ordinary shares received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their ordinary shares or interests in ordinary shares on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling shareholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling shareholders to sell a specified number of such shares at a stipulated price per share;
- one or more underwritten offerings on a firm commitment or best effort basis;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

Pursuant to registration rights agreements, certain selling shareholders are generally entitled to be paid all registration expenses in connection with their registration obligations, regardless of whether a registration statement is filed or becomes effective.

The selling shareholders may, from time to time, pledge or grant a security interest in some or all of the ordinary shares owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the ordinary shares, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending the list of selling shareholders to include the pledgee, transferee or other successors in interest as selling shareholders under this prospectus. The selling shareholders also may transfer the ordinary shares in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of ordinary shares or interests therein, the selling shareholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the ordinary shares in the course of hedging the positions they assume. The selling shareholders may also sell ordinary shares short and deliver these securities to close out their short positions, or loan or pledge the ordinary shares to broker-dealers that in turn may sell these securities. The selling shareholders may also enter into option or other transactions with broker-dealers or other financial institutions or the

creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling shareholders from the sale of the ordinary shares offered by them will be the purchase price of the ordinary shares less discounts or commissions, if any. Each of the selling shareholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of ordinary shares to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling shareholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, if available, or pursuant to other available exemptions from the registration requirements under the Securities Act, rather than this prospectus, provided that they meet the criteria and conform to the requirements of that rule. Registration of the ordinary shares covered by this prospectus does not mean that any ordinary shares will be offered or sold.

The selling shareholders may engage in at-the-market offerings and offer the ordinary shares into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act on the terms described in the prospectus supplement relating thereto. Underwriters, dealers and agents who participate in any at-the-market-offerings will be described in the prospectus supplement relating thereto.

The selling shareholders and any underwriters, broker-dealers or agents that participate in the sale of the ordinary shares or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling shareholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the ordinary shares to be sold, the names of the selling shareholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the ordinary shares may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the ordinary shares may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

If at the time of any offering made under this prospectus, a member of FINRA participating in the offering has a “conflict of interest” as defined in FINRA Rule 5121 (“Rule 5121”), that offering will be conducted in accordance with the relevant provisions of Rule 5121.

We have advised the selling shareholders that the anti-manipulation rules of Regulation M promulgated under the Exchange Act may apply to sales of shares in the market and to the activities of the selling shareholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling shareholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling shareholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling shareholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling shareholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (1) such time as all of the shares covered by this prospectus and actually issued or issuable upon conversion of the Term Loans have been sold and (2) the date on which all of the shares may be sold without restriction pursuant to Rule 144 of the Securities Act.

LEGAL MATTERS

Legal matters with respect to U.S. federal and New York law in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters with respect to Dutch law in connection with the validity of the ordinary shares being offered by this prospectus and other legal matters will be passed upon for us by Allen & Overy LLP, Amsterdam, the Netherlands. Additional legal matters may be passed upon for us or any underwriters, dealers or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financials statements of ProQR Therapeutics N.V. as of December 31, 2020 and 2019 and for each of the three years in the period ended December 31, 2020, incorporated by reference in this prospectus by reference to the Company's Annual Report on Form 20-F for the year ended December 31, 2020, and the effectiveness of the Company's internal control over financial reporting' have been audited by Deloitte Accountants B.V., an independent public accounting firm, as stated in their reports. Such financial statements are incorporated by reference in reliance upon the reports of such firm given their authority as experts in accounting and auditing.

CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

On May 25, 2020, our audit committee recommended the termination of the engagement of Deloitte Accountants B.V. ("Deloitte") as the Company's independent public accountant, and the engagement of KPMG Accountants N.V. ("KPMG") as the Company's independent public accountant for the year ending December 31, 2021. The annual general meeting of shareholders approved this recommendation on June 23, 2020. Please refer to the relevant disclosure reported under the heading "Change in Registrant's Certifying Accountant" of our Annual Report on Form 20-F for the fiscal year ended December 31, 2020, filed with the SEC on March 24, 2021, and to the accompanying Exhibit 16.1 of such Annual Report on Form 20-F ([File No. 333-36622](#)).

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated under the laws of the Netherlands. Substantially all of our business is conducted, and substantially all of our assets are located, in the Netherlands. Most of our directors and the experts named in this prospectus are residents of, and most of their assets are located in, jurisdictions outside the United States. As a result, it may be difficult for you to serve process on us or these persons within the United States or to enforce against us or these persons in courts in the United States, judgments of these courts predicated upon the civil liability provisions of U.S. securities laws. In addition, it is not clear whether a Dutch court would impose civil liability on us, members of our management board, supervisory board or any of the experts named in this prospectus in an original action based solely upon the federal securities laws of the United States brought in a court of competent jurisdiction in the Netherlands. We have appointed Smital Shah as our agent for service of process in the United States with respect to any action brought against us in the United States District Court for the Southern District of New York under the securities laws of the United States or any State of the United States or any action brought against us in the Supreme Court of the State of New York in the County of New York under the securities laws of the State of New York.

As there is no treaty on the reciprocal recognition and enforcement of judgments in civil and commercial matters between the United States and the Netherlands, courts in the Netherlands will not automatically recognize and enforce a final judgment rendered by a U.S. court. In order to obtain a judgment enforceable in the Netherlands, claimants must obtain from a Dutch court leave to enforce the judgment rendered by a U.S. court. Under current practice, however, a Dutch court may be expected to render a judgment in accordance with the judgment rendered by the U.S. court, without a review on the merits of the underlying claim, if it finds that:

- the jurisdiction of the U.S. court has been based on grounds that are internationally acceptable;
- the final judgment has not been rendered in violation of the elementary principles of fair trial in the Netherlands;

- the final judgment does not contravene public policy of the Netherlands; and
- the final judgment is not incompatible with (a) a prior judgment of a Netherlands court rendered in a dispute between the same parties, or (b) a prior judgment of a foreign court rendered in a dispute between the same parties, concerning the same subject matter and based on the same cause of action, provided that such prior judgment is capable of being recognized in the Netherlands.

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

EXPENSES

The following table sets forth the expenses related to the filing of the registration statement of which this prospectus forms a part, all of which will be paid by us. In addition, we may incur additional expenses in the future in connection with the offering of our securities pursuant to this prospectus. If required, any such additional expenses will be disclosed in a prospectus supplement. All amounts other than the SEC registration fee and filing fee are estimates.

SEC registration fee	\$4,056.16
Legal fees and expenses	*
Printing expenses	*
Accountants' fees and expenses	*
Miscellaneous expenses	*
Total	\$ <u> </u> *

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

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

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

- [our Annual Report on Form 20-F for the year ended December 31, 2020, filed with the SEC on March 24, 2021;](#)
- our Reports of Foreign Private Issuer on Form 6-K, filed with the SEC on [January 7, 2021](#), [March 24, 2021 \(two filings\)](#), [April 1, 2021](#), [April 6, 2021](#), [April 20, 2021](#), [May 4, 2021](#), [May 6, 2021](#), [May 20, 2021](#), [August 5, 2021](#), [September 8, 2021](#), [September 9, 2021](#), [October 4, 2021](#), [November 4, 2021](#), [November 18, 2021 \(two filings\)](#), [December 16, 2021](#), [December 30, 2021](#), [January 4, 2022](#) and [February 11, 2022](#); and
- [the description of our ordinary shares contained in our registration statement on Form 8-A \(File No. 001-36622\), filed with the SEC on September 16, 2014, including any other amendments or reports filed for the purpose of updating such description \(other than any portion of such filings that are furnished under applicable SEC rules rather than filed\).](#)

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

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

Zernikedreef 9
2333 CK Leiden
The Netherlands
Attention: Company Secretary
Tel.: +31 88 166 7000
IR@proqr.com

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file reports and other information with the SEC, including annual reports on Form 20-F and reports of foreign private issuer on Form 6-K, which you may review at www.sec.gov.

This prospectus is part of a registration statement on Form F-3 that we have filed with the SEC. To see more detail, you should read the registration statement and the exhibits and schedules filed with, or incorporated by reference into, our registration statement.

This registration statement, including the exhibits contained or incorporated by reference therein, can be read at the SEC website referred to above. Any statement made or incorporated by reference in this prospectus concerning the contents of any contract, agreement or other document is only a summary of the actual contract, agreement or other document. If we have filed or incorporated by reference any contract, agreement or other document as an exhibit to the registration statement, you should read the exhibit for a more complete understanding of the document or matter involved. Each statement regarding a contract, agreement or other document is qualified in its entirety by reference to the actual document.

We maintain a corporate website at www.ProQR.com. Information contained on, or that can be accessed through, our website does not constitute a part of this prospectus and our website address is included in this prospectus as an inactive textual reference only.



**Up to 3,665,224
Ordinary Shares**

PROSPECTUS

, 2022

PART II**INFORMATION NOT REQUIRED IN PROSPECTUS****ITEM 8. INDEMNIFICATION OF DIRECTORS AND OFFICERS**

Although Dutch law does not expressly provide for the indemnification of directors, the concept of indemnification of directors of a company for liabilities arising from their actions as members of the management board and supervisory board is, in principle, accepted in the Netherlands. Our articles of association provide that we will indemnify our management board members, supervisory board members, former management board members and former supervisory board members against (i) any financial losses or damages incurred by such indemnified person and (ii) any expense reasonably paid or incurred by such indemnified person in connection with any threatened, pending or completed suit, claim, action or legal proceedings, whether civil, criminal, administrative or investigative and whether formal or informal, in which he becomes involved, to the extent this relates to his position with the company, in each case to the fullest extent permitted by applicable law. No indemnification shall be given to an indemnified person (a) if a Dutch court has established, without possibility for appeal, that the acts or omissions of such indemnified person that led to the financial losses, damages, suit, claim, action or legal proceedings result from either an improper performance of his duties as an officer of the company or an unlawful or illegal act and (b) to the extent that his financial losses, damages and expenses are covered by an insurance and the insurer has settled these financial losses, damages and expenses (or has indicated that it would do so). Our supervisory board may stipulate additional terms, conditions and restrictions in relation to such indemnification.

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

ITEM 9. EXHIBITS

The exhibit index set forth immediately prior to the signature page is incorporated herein by reference.

ITEM 10. UNDERTAKINGS

The undersigned Registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports

- filed with or furnished to the SEC by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
 - (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
 - (4) To file a post-effective amendment to the registration statement to include any financial statements required by Item 8.A of Form 20-F at the start of any delayed offering or throughout a continuous offering. Financial statements and information otherwise required by Section 10(a)(3) of the Securities Act need not be furnished, provided, that the Registrant includes in the prospectus, by means of a post-effective amendment, financial statements required pursuant to this paragraph (4) and other information necessary to ensure that all other information in the prospectus is at least as current as the date of those financial statements. Notwithstanding the foregoing, a post-effective amendment need not be filed to include financial statements and information required by Section 10(a)(3) of the Securities Act or Rule 3-19 of Regulation S-X if such financial statements and information are contained in periodic reports filed with or furnished to the SEC by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in this registration statement.
 - (5) That, for the purpose of determining liability under the Securities Act to any purchaser, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.
 - (6) That, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
 - (7) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.
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EXHIBIT INDEX

Exhibit No.	Description
3.1	<u>Amended Articles of Association of the Registrant (incorporated by reference to Exhibit 1.1 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) for the month of July 2021, filed with the SEC on July 8, 2021).</u>
5.1*	<u>Opinion of Allen & Overy LLP, Dutch counsel to the Registrant.</u>
10.1	<u>Amended Loan and Security Agreement, dated as of December 29, 2021, by and between ProQR Therapeutics N.V. and the parties named therein (incorporated by reference to Exhibit 10.2 to the Registrant's Report of Foreign Private Issuer on Form 6-K (File No. 001-36622) for the month of December 2021, filed with the SEC on December 30, 2021).</u>
10.2	<u>Registration Rights Agreement, dated 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) for the month of December 2021, filed with the SEC on December 30, 2021).</u>
10.3	<u>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) for the month of December 2021, filed with the SEC on December 30, 2021).</u>
23.1*	<u>Consent of Deloitte Accountants B.V., Independent Registered Public Accounting Firm.</u>
23.2*	<u>Consent of Allen & Overy LLP (included in Exhibit 5.1).</u>
24.1*	<u>Power of Attorney (included in signature page to this Registration Statement).</u>
107*	<u>Filing Fee Table</u>

* Filed herewith.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the undersigned Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Leiden, the Netherlands, on March 1, 2022.

PROQR THERAPEUTICS N.V.

By: /s/ Daniel de Boer

Name: Daniel de Boer

Title: *Chief Executive Officer***POWER OF ATTORNEY**

Each person whose signature appears below hereby constitutes and appoints each of Daniel de Boer and Smital Shah his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution for him and in his name, place and stead, in any and all capacities, to sign any or all amendments or supplements to this Registration Statement, whether pre-effective or post-effective and any and all additional registration statements pursuant to Rule 462(b) of the Securities Act of 1933, as amended, and to file the same with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing necessary or appropriate to be done with respect to this Registration Statement or any amendments or supplements hereto or any and all additional registration statements pursuant to Rule 462(b) of the Securities Act of 1933, as amended, in the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute or substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed below by the following persons in the capacities indicated on March 1, 2022.

SIGNATURES	TITLE	DATE
/s/ Daniel de Boer Daniel de Boer	Chief Executive Officer and Director, Management Board <i>(Principal Executive Officer)</i>	March 1, 2022
/s/ Smital Shah Smital Shah	Chief Business and Financial Officer <i>(Principal Financial and Accounting Officer)</i>	March 1, 2022
/s/ Dinko Valerio Dinko Valerio	Chairman, Supervisory Board	March 1, 2022
/s/ Antoine Benjamin Papiernik Antoine Benjamin Papiernik	Director, Supervisory Board	March 1, 2022
/s/ James Shannon James Shannon	Director, Supervisory Board	March 1, 2022
/s/ Alison Lawton Alison Lawton	Director, Supervisory Board	March 1, 2022
/s/ Bart Filius Bart Filius	Director, Supervisory Board	March 1, 2022

AUTHORIZED UNITED STATES REPRESENTATIVE

Pursuant to the requirement of the Securities Act of 1933, as amended, the undersigned, the duly authorized representative in the United States of the aforementioned Registrant, has signed this Registration Statement on March 1, 2022.

Smital Shah
Authorized Representative in the United States

By: /s/ Smital Shah

March 1, 2022

Name: Smital Shah

ProQR Therapeutics N.V.
 Zernikedreef 9
 2333 CK Leiden
 The Netherlands

Allen & Overy LLP
 Apollolaan 15
 1077 AB Amsterdam The Netherlands

 PO Box 75440
 1070 AK Amsterdam The Netherlands

 Tel +31 20 674 1000
 Fax +31 20 674 1111

Amsterdam, 1 March 2022
 Subject **Legal Opinion Dutch law**
 Our ref 0117407-0000001 EUO3: 2007488499.1

Dear Addressee,

1. We have acted as legal counsel to ProQR Therapeutics N.V, a public limited liability company (*naamloze vennootschap*) incorporated under the laws of the Netherlands, with its corporate seat in Leiden (the Netherlands) (the **Company**) on matters of Dutch law in connection with its filing of a registration statement on Form F-3 (the **Registration Statement**) with the U.S. Securities Exchange Commission (the **SEC**) on 1 March 2022 for the resale by the selling shareholders identified in the Registration Statement of up to 3,665,224 ordinary shares, nominal value of EUR 0.04 each, in the Company's share capital (the **Ordinary Shares**).

This legal opinion is rendered to you in order to be filed as an exhibit to the Registration Statement.

2. We have examined and relied upon the following documents in rendering this legal opinion:
 - (a) a pdf copy of the \$30,000,000.00 loan and security agreement dated 14 July 2020 by and between, among others, the Company as borrower, the other companies listed therein as borrowers and guarantors, Pontifax Medison Finance (Israel) L.P. and Pontifax Medison Finance (Cayman) L.P. as lenders, and Pontifax Medison Finance GP, L.P., as administrative agent and collateral agent for itself and Pontifax Medison Finance (Israel) L.P. and Pontifax Medison Finance (Cayman) L.P. (the **Loan and Security Agreement**);
 - (b) a pdf copy of the Third Amendment to the Loan And Security Agreement dated 29 December 2021 between the Company and each of its (in)direct subsidiaries as borrower, Pontifax Medison Finance (Israel) L.P., Pontifax Medison Finance (Cayman) L.P., Kreos Capital VI (UK) Limited and Kreos Capital 2020 Opportunity (UK) Limited as lenders and Pontifax Medison Finance GP, L.P., as administrative agent and collateral agent for itself and the Lenders (the **Third Amendment Agreement**, and together with the Loan and Security Agreement, the **Loan Agreement**).
 - (c) pdf copies of the executed ordinary share purchase warrants between the Company and Kreos Capital VI (Expert Fund) L.P. signed on behalf of the Company on 30 December 2021;
 - (d) pdf copies of the executed ordinary share purchase warrants between the Company and Kreos Capital 2020 Opportunity L.P. signed on behalf of the Company on 30 December 2021;
 - (e) pdf copies of the executed ordinary share purchase warrants between the Company and Pontifax Medison Finance (Cayman) L.P. signed on behalf of the Company on 30 December 2021;
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- (f) a pdf copy of the executed ordinary share purchase warrant between the Company and Pontifax Medison Finance (Israel) L.P. signed on behalf of the Company on 30 December 2021;
- (g) a pdf copy of the Registration Statement;
- (h) a pdf copy of the Form 20-F for the year ended December 31, 2020, filed with the SEC on 24 March 2021;
- (i) an electronic copy of the registration of the Company in the trade register of the Chamber of Commerce (**Trade Register, Handelsregister**) dated 25 February 2022, and confirmed to us by telephone by the Trade Register to be correct on 25 February 2022 (the **Excerpt**);
- (j) a pdf copy of the written resolutions of the Company's supervisory board (the **Supervisory Board**) dated 28 December 2021;
- (k) a pdf copy of the written resolutions of the Company's management board (the **Management Board**) dated 28 December 2021;
- (l) a pdf copy of the internal rules for the Management Board adopted by the Management Board on 23 September 2014 (the **Management Board Rules**);
- (m) a pdf copy of the internal rules for the Supervisory Board adopted by the Supervisory Board on 23 September 2014 (the **Supervisory Board Rules**);
- (n) a pdf copy of the deed of incorporation (*akte van oprichting*) of the Company, as executed by a civil-law notary on 21 February 2012;
- (o) a pdf copy of the deed of conversion and amendment to the articles of association of the Company dated 23 September 2014, pursuant to which deed the Company converted from a B.V. to a N.V. (the **Deed of Conversion**);
- (p) a pdf copy of the articles of association (*statuten*) of the Company dated 10 June 2021 (the **Articles of Association**); and
- (q) a copy of the Company's shareholders' register within the meaning of Article 2:85 of the Dutch Civil Code (the **Shareholders' Register**).

The documents (c) up to and including (f) are collectively referred to as the **Warrant Agreements**. The documents (j) and (k) are collectively referred to as the **Resolutions**.

Unless explicitly stated in this legal opinion, we have not examined any other agreement, deed or document entered into by or affecting the Company or any other corporate records of the Company and have not made any other inquiry concerning it.

This legal opinion is rendered to you at your request.

3. We assume:

- (a) the genuineness of all signatures on the documents referred to in paragraph 2 above;
 - (b) the authenticity and completeness of all documents submitted to us as originals and the completeness and conformity to originals of all documents submitted to us as copies or by electronic means;
 - (c) that any relevant supplement to the Registration Statement with respect to the Ordinary Shares has been filed with the SEC, and shall become effective;
 - (d) (i) that the Management Board Rules and the Supervisory Board Rules are the regulations as in force on the date hereof; and (ii) the Articles of Association of the Company are its articles of association (*statuten*) currently in force. Although not constituting conclusive evidence thereof, the Extract supports item (ii) of this assumption;
 - (e) that the Company has not been dissolved (*ontbonden*), granted a moratorium (*surseance verleend*) or declared bankrupt (*failliet verklaard*) (although not constituting conclusive evidence thereof, this assumption is supported by (a) the contents of the Excerpt and (b) an online search in the central insolvency register on 25 February 2022;
 - (f) that the Deed of Incorporation is a valid notarial deed (*authentieke akte*), the contents thereof complied with the statutory requirements at the date of incorporation and there were no defects in the incorporation of the Company (not appearing on the face of the Deed of Incorporation) on the basis of which a court might dissolve the Company or deem it never to have existed;
 - (g) that the Deed of Conversion is a valid notarial deed (*authentieke akte*), the contents thereof complied with the statutory requirements at the date of conversion and there were no defects in the conversion of the Company from a B.V. into a N.V. (not appearing on the face of the Deed of Conversion) on the basis of which a court might nullify the conversion of the Company;
 - (h) the Resolutions, including any power of attorney therein have not been and will not be annulled, modified, revoked or rescinded and are in full force and effect as at the date hereof and each power of attorney validly authorises the person or persons purported to be granted power of attorney thereunder to represent and bind the Company vis-à-vis the other parties to the relevant agreement in relation to the transactions contemplated by and for the purposes stated in agreements under any applicable law other than Dutch law, and that the Resolutions have been made with due observance of the statutory requirements and the provisions of the Articles of Association relating to the convening of meetings and the making of resolutions (although not constituting conclusive evidence thereof, failure to observe such provisions is not apparent on the face thereof) and that each factual confirmation and statement in the Resolutions (including any confirmation or statement on conflict of interest (*tegenstrijdig belang*)) is correct;
 - (i) the Company has sufficient ordinary shares in its authorized capital to issue the Ordinary Shares;
 - (j) none of the opinions stated in this opinion letter will be affected by any foreign law; and
 - (k) that the documents referred to in paragraph 2 above were at their date (where applicable), and have through the date hereof remained, valid, accurate and in full force and effect.
-

4. This legal opinion is limited to the laws of the Netherlands currently in force (unpublished case law not included), excluding tax law (except as specifically referred to herein), the laws of the EU (insofar as not implemented in Dutch law or directly applicable in the Netherlands), market abuse laws and competition or procurement laws.

No undertaking is assumed on our part to revise, update or amend this opinion letter in connection with or to notify or inform you of, any developments and/or changes of Dutch law subsequent to the date hereof.

We express no opinion as to matters of fact in this legal opinion. We assume that there are no facts not disclosed to us, which could affect the conclusions in this legal opinion.

Our willingness to render this opinion letter is based on the condition that you accept and agree that (i) the competent courts at Amsterdam, the Netherlands have exclusive jurisdiction to settle any issues of interpretation or liability arising out of or in connection with this opinion letter, (ii) all matters related to the legal relationship between yourself and Allen & Overy LLP and all individuals associated with Allen & Overy LLP, including the above submission to jurisdiction, are governed by Dutch law and the general terms and conditions of Allen & Overy LLP, (iii) any liability arising out of or in connection with this opinion letter shall be limited to the amount which is paid out under the insurance policy of Allen & Overy LLP in the matter concerned and (iv) no person other than Allen & Overy LLP may be held liable in connection with this legal opinion.

This legal opinion is strictly limited to the matters stated in it and does not relate to any other agreement or matter and may not be read as extending by implication to any matters not specifically referred to. Nothing in this opinion should be taken as expressing an opinion in respect of any representation, warranty or other statement or other information as to factual matters contained in any document referred to herein or examined in connection with this opinion except as expressly confirmed herein.

5. Based on the foregoing and subject to the qualifications set out below, we are of the opinion that:

- (a) **Corporate status.** The Company has been duly incorporated as a private limited liability company (*besloten vennootschap met beperkte aansprakelijkheid*) and is validly existing as a public limited liability company (*naamloze vennootschap*) under the laws of the Netherlands.
- (b) **New Shares.** Subject to receipt by the Company of payment in full for the Ordinary Shares, and when issued and accepted in accordance with the Loan Agreement, the Warrant Agreements, as the case may be, the Resolutions and the Articles of Association, the Ordinary Shares will be validly issued, fully paid and non-assessable.

6. This legal opinion is subject to the following qualifications:

- (a) The opinions expressed in this legal opinion may be affected or limited by (i) the general defences available to obligors under Netherlands law in respect of the validity and enforceability of agreements; and (ii) the provisions of any applicable bankruptcy (*faillissement*), insolvency, moratorium (*surseance van betaling*), fraudulent conveyance (*Actio Pauliana*), reorganisation and other or similar laws of general application now or hereafter in effect, relating to or affecting the enforcement or protection of creditors' rights.
 - (b) As used in the opinions in paragraph 5(b) above of this opinion letter, the term “non-assessable” – which term has no equivalent in Dutch – means that a holder of a share will not by reason of merely being such a holder, be subject to assessment or calls by the Company or its creditors for further payment on such share.
 - (c) Under Dutch law, each power of attorney (*volmacht*) or mandate (*lastgeving*), whether or not irrevocable, granted by the Company will terminate by force of law and without notice, upon bankruptcy of the Company. To the extent that the appointment by the Company of a process agent would be deemed to constitute a power of attorney or a mandate, this qualification would apply.
 - (d) This opinion letter does not purport to express any opinion or view on the operational rules and procedures of any clearing or settlement system or agency.
-

7. In this opinion, Dutch legal concepts are expressed in English terms and not in their original Dutch terms. The concepts concerned may not always be identical to the concepts described by the English terms as such terms may be understood under the laws of other jurisdictions. This legal opinion is given on the express basis, accepted by each person who is entitled to rely on it, that this legal opinion and all rights, obligations or liability in relation to it are governed by Dutch law.
8. This legal opinion is given exclusively in connection with our representation of the Company and for no other purpose.
9. Notwithstanding the previous sentence, this opinion may be disclosed, quoted, or referred to without our written express consent (i) if such disclosure, quotation or reference without our written consent is required by law, court order or any competent regulatory authority, *provided* that you shall notify us immediately or as soon as otherwise possible after such disclosure, quotation or reference or (ii) to the extent that such disclosure, quotation or reference is required (a) to any of your insurers in respect of any claim or potential claim against you or (b) for evidence in court or similar proceedings in which you are a defendant, *provided*, in each of the events referred to in (a) and (b), that you shall notify us prior to any such disclosure, reference or quotation being made.
10. We consent to the filing of this opinion letter as an exhibit to the Registration Statement and also consent to the reference to Allen & Overy LLP in the Final Prospectus Supplement under the caption "Legal Matters".

Yours faithfully,

/s/ Allen & Overy LLP

Allen & Overy LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in this Registration Statement on Form F-3 of our reports dated March 24, 2021 relating to the financial statements of ProQR Therapeutics N.V. and the effectiveness of ProQR Therapeutics N.V.'s internal control over financial reporting, appearing in the Annual Report on Form 20-F of ProQR Therapeutics N.V. for the year ended December 31, 2020. We also, consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ Deloitte Accountants B.V.

Amsterdam, The Netherlands

February 25, 2022

Calculation of Filing Fee Tables

Form F-3
(Form Type)**ProQR Therapeutics N.V.**
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity	Ordinary shares, nominal value €0.04 per share	457(a)	3,288,272 ⁽¹⁾⁽²⁾	\$ 11.9379 ⁽⁴⁾	\$ 39,261,967.68	\$ 0.0000927	\$ 3,639.58				
	Equity	Ordinary shares, nominal value €0.04 per share	457(a)	376,952 ⁽¹⁾⁽³⁾	\$ 11.9379 ⁽⁴⁾	\$ 4,500,806.88	\$ 0.0000927	\$ 417.22				
Fees Previously Paid	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				
Carry Forward Securities												
Carry Forward Securities	-	-	-	-	-	-	-	-	-	-	-	-
				Total Offering Amounts		\$ 43,762,774.56		\$ 4,056.80				
				Total Fees Previously Paid				-				
				Total Fee Offsets				-				
				Net Fee Due				\$ 4,056.80				

- (1) This Registration Statement also covers an indeterminate number of additional ordinary shares, nominal value €0.04 per share, of ProQR Therapeutics N.V. (the "Registrant") that may be offered or issued to prevent dilution resulting from share splits, share dividends or similar transactions in accordance with Rule 416 under the Securities Act of 1933, as amended (the "Securities Act").
- (2) Represents ordinary shares issuable upon conversion of certain of the Registrant's convertible notes due June 29, 2026 (inclusive of principal and/or interest thereon the "Convertible Notes"), which were acquired by the selling shareholders in a private placement. The number of ordinary shares registered by the Registrant represents a good faith estimate of the number of ordinary shares which will be issued upon conversion of the Convertible Notes, assuming for purposes hereof, that the Convertible Notes will accrue interest through June 29, 2026 at a rate of 8.2% per annum. If the Convertible Notes convert after the Registrant has paid some of the principal balance or accrued interest on the Convertible Notes, the actual number of shares issuable to the selling shareholders upon conversion of the Convertible Notes, if any, could be materially less than 3,288,272 ordinary shares depending on the amount of principal and accrued but unpaid interest that is converted into shares of ordinary shares at the time. This presentation is not intended to constitute an indication or prediction of the date on which the selling shareholders will convert the Convertible Notes into ordinary shares, if at all.
- (3) Represents the maximum number of ordinary shares issuable upon exercise of warrants to purchase ordinary shares, which were issued to the selling shareholders in a private placement.
- (4) Represents the fixed conversion price of the Convertible Notes and fixed exercise price of the warrants to purchase ordinary shares, which were issued to the selling shareholders in a private placement.