Registration No. 333-

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-8

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

PROQR THERAPEUTICS N.V.

(Exact name of registrant as specified in its charter)

The Netherlands

(State or other jurisdiction of incorporation or organization)

Not applicable (I.R.S. Employer Identification Number)

Zernikedreef 9 2333 CK Leiden The Netherlands +31 88 166 7000 (Address of Principal Executive Offices)

ProQR Therapeutics N.V. Equity Incentive Plan (Full title of the plan)

> Smital Shah 245 Main Street Cambridge, MA 02142 (415) 231-6431

(Name, address and telephone number of agent for service)

Copies to:

Mitchell S. Bloom, Esq. Danielle M. Lauzon, Esq. James Xu, Esq. Goodwin Procter LLP 100 Northern Avenue Boston, MA 02210 (617) 570-1000 Smital Shah, Chief Business and Financial Officer ProQR Therapeutics N.V. Zernikedreef 9 2333 CK Leiden The Netherlands +31 88 166 7000

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Non-accelerated filer Accelerated filer⊠Smaller reporting company□Emerging Growth Company□

If an emerging growth company, 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.

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Amount to be Registered ⁽¹⁾	Proposed Maximum Offering Price per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee

Ordinary Shares, nominal value €0.04 per share (ordinary shares issuable pursuant to outstanding options)	4,087,636	\$8.65 ⁽²⁾	\$35,358,051.40 ⁽²⁾	\$3,277.69
Ordinary Shares, nominal value €0.04 per share (ordinary shares issuable pursuant to outstanding restricted stock units)	458,237	\$7.91 ⁽³⁾	\$3,624,654.67 ⁽³⁾	\$336.01
Ordinary Shares, nominal value €0.04 per share (unallocated ordinary shares reserved for issuance)	2,449,191	\$7.91 ⁽³⁾	\$19,373,100.81 ⁽³⁾	\$1,795.89
Total	6,995,064		\$58,355,806.88	\$5,409.59

- (1) This Registration Statement on Form S-8 (this "Registration Statement") covers (i) ordinary shares, nominal value €0.04 per share, of ProQR Therapeutics N.V. (the "Registrant"), issuable pursuant to the ProQR Therapeutics N.V. Equity Incentive Plan (the "Equity Incentive Plan"), and (ii) pursuant to Rule 416(a) under the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement shall be deemed to cover any additional ordinary shares that may, from time to time, become issuable under the Equity Incentive Plan by reason of any share dividend, share split, recapitalization or any other similar transaction effected without the receipt of consideration which results in an increase in the number of the Registrant's outstanding ordinary shares.
- (2) Estimated solely for the purpose of calculating the amount of registration fee in accordance with Rule 457(h) promulgated under the Securities Act. The offering price per share and the aggregate offering price are calculated on the basis of \$8.65, which is the weighted average exercise price per share of the outstanding share options granted pursuant to the Equity Incentive Plan.
- (3) Estimated solely for the purpose of calculating the amount of registration fee pursuant to Rules 457(c) and 457(h) promulgated under the Securities Act, and based upon the average of the high and low prices of the Registrant's ordinary shares, as reported on the Nasdaq Global Market, on November 1, 2021.

EXPLANATORY NOTE

This Registration Statement registers additional ordinary shares under the Registrant's Equity Incentive Plan. The additional shares relating to the Registrant's Equity Incentive Plan are of the same class as other securities for which the Registrant's registration statement filed on Form S-8 (File No. 333-199451) on October 17, 2014 is effective. The information contained in the Registrant's registration statement on Form S-8 (File No. 333-199451) is hereby incorporated by reference pursuant to General Instruction E, except for "Item 8. Exhibits."

PART II.

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

The Registrant hereby incorporates by reference into this Registration Statement the following documents filed with the Securities and Exchange Commission (the "SEC"), except that the Registrant does 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:

- (a) the Registrant's Annual Report on Form 20-F for the year ended December 31, 2020, filed with the SEC on March 24, 2021 (File No. 001-36622), which contains audited financial statements for the Registrant's latest fiscal year for which such statements have been filed;
- (b) the Registrant's Reports of Foreign Private Issuer on Form 6-K filed with the SEC on January 7, 2021, February 25, 2021, March 24, 2021 (two filings), April 1, 2021, April 6, 2021, April 20, 2021, May 4, 2021, May 6, 2021, May 20, 2021, July 8, 2021, August 5, 2021, September 8, 2021, September 9, 2021, and October 4, 2021; and
- (c) the description of the Registrant's ordinary shares contained in its <u>Registration Statement on Form 8-A (File No. 001-36622)</u>, 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).

All other reports and documents subsequently filed by the Registrant pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") on or after the date of this Registration Statement and prior to the filing of a post-effective amendment to this Registration Statement which indicates that all securities offered have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference herein and to be a part of this Registration Statement from the date of the filing of such reports and documents. Any report on Form 6-K furnished by the Registrant to the SEC after the date of this Registration Statement (or a portion thereof) is incorporated by reference in this Registration Statement only to the extent that the report expressly states that the Registrant incorporates it (or such portions) by reference in this Registration Statement and it is not subsequently superseded. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained herein or in any subsequently filed document that also is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement.

Item 8. Exhibits.

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

EXHIBIT INDEX

Exhibit Number	Description	Notes
<u>4.1</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).
<u>5.1</u>	<u>Opinion of Allen & Overy LLP, Dutch legal counsel of the Registrant</u>	Filed herewith
<u>23.1</u>	Consent of Deloitte Accountants B.V., Independent Registered Public Accounting Firm of the Registrant	Filed herewith
<u>23.2</u>	<u>Consent of Allen & Overy LLP (included in</u> <u>Exhibit No. 5.1)</u>	=
<u>24.1</u>	<u>Power of attorney (included on the signature pages of this</u> registration statement)	=
<u>99.1</u>	ProQR Therapeutics N.V. Equity Incentive Plan	Incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151)
<u>99.2</u>	Form of Notice of Grant under the ProQR Therapeutics N.V. Equity Incentive Plan	Incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151)
<u>99.3</u>	Form of Notice of Exercise under the ProQR Therapeutics N.V. Equity Incentive Plan	Incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form F-1 (File No. 333-198151)

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 S-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 November 4, 2021.

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-infact 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, this Registration Statement has been signed below by the following persons in the capacities indicated on November 4, 2021.

SIGNATURES	TITLE	DATE
/s/ DANIEL DE BOER Daniel de Boer	Chief Executive Officer and Director, Management Board (Principal Executive Officer)	November 4, 2021
/s/ SMITAL SHAH Smital Shah	Chief Business and Financial Officer (Principal Financial and Accounting Officer)	November 4, 2021
/s/ DINKO VALERIO Dinko Valerio	Chairman, Supervisory Board	November 4, 2021
/s/ ANTOINE BENJAMIN PAPIERNIK Antoine Benjamin Papiernik	Director, Supervisory Board	November 4, 2021
/s/ JAMES SHANNON James Shannon	Director, Supervisory Board	November 4, 2021
/s/ ALISON LAWTON Alison Lawton	Director, Supervisory Board	November 4, 2021
/s/ BART FILIUS Bart Filius	Director, Supervisory Board	November 4, 2021

AUTHORIZED UNITED STATES REPRESENTATIVE

Pursuant to the requirement of the Securities Act of 1933, the undersigned, the duly authorized representative in the United States of the aforementioned Registrant, has signed this Registration Statement on November 4, 2021.

Smital Shah Authorized Representative in the United States

By: /s/ SMITAL SHAH Name: Smital Shah November 4, 2021

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,
 4 November 2021

 Subject
 Legal opinion Dutch law

 Our ref
 0117407-0000001 EUO3: 2006206189.3

Dear Sirs, Madam,

1. We have acted as legal counsel to you, ProQR Therapeutics N.V., a public limited liability company (*naamloze vennootschap*) incorporated under the laws of the Netherlands, with its corporate seat in Leiden (the Netherlands) (the **Company**) on matters of Dutch law in connection with your filing of a registration statement on Form S-8 (the **Registration Statement**) with the U.S. Securities Exchange Commission (the **SEC**) in connection with the registration of the 6,995,064 ordinary shares, nominal value of EUR 0.04 each, in the Company's share capital, to be issued after the date hereof, not exceeding the limitations referred to in the Registration Statement (the Option 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 draft of the Registration Statement dated 4 November 2021;
 - (b) an electronic copy of the registration of the Company in the trade register of the Chamber of Commerce (**Trade Register**, *Handelsregister*) dated 4 November 2021, and confirmed to us by telephone by the Trade Register to be correct on 4 November 2021 (the **Excerpt**);
 - (c) a pdf copy of the written resolution of the Company's supervisory board (the **Supervisory Board**) dated 3 November 2021 (the **Supervisory Board Resolution**);
 - (d) a pdf copy of the written resolution of the Management Board dated 2 November 2021 (the **Management Board Resolution**);
 - (e) the form of the Company's Stock Option Plan as attached as an exhibit to the registration statement on Form F-1 filed by the Company with the SEC on 17 September 2014 (the **Stock Option Plan**);
 - (f) a pdf copy of the internal rules for the Management Board adopted by the Management Board on 23 September 2014 (the **Management Board Rules**);

Allen & Overy LLP is a limited liability partnership registered in England and Wales with registered number OC306763. It is authorised and regulated by the Solicitors Regulation Authority of England and Wales. The term partner is used to refer to a member of Allen & Overy LLP or an employee or consultant with equivalent standing and qualifications. A list of the members of Allen & Overy LLP and of the non-members who are designated as partners is open to inspection at its registered office, One Bishops Square, London E1 6AD.

Allen & Overy LLP or an affiliated undertaking has an office in each of: Abu Dhabi, Amsterdam, Antwerp, Athens, Bangkok, Beijing, Belfast, Bratislava, Brussels, Bucharest (associated office), Budapest, Casablanca, Doha, Dubai, Düsseldorf, Frankfurt, Hamburg, Hanoi, Ho Chi Minh City, Hong Kong, Istanbul, Jakarta (associated office), London, Luxembourg, Madrid, Mannheim, Milan, Moscow, Munich, New York, Paris, Perth, Prague, Riyadh (associated office), Rome, São Paulo, Shanghai, Singapore, Sydney, Tokyo, Warsaw and Washington, D.C. and Yangon.

То

- (g) a pdf copy of the internal rules for the Supervisory Board adopted by the Supervisory Board on 23 September 2014 (the **Supervisory Board Rules**);
- (h) a pdf copy of the recent articles of association (*statuten*) of the Company dated 10 June 2021 (the **Articles of Association**);
- (i) a pdf copy of the deed of incorporation (*akte van oprichting*) of the Company (the **Deed of Incorporation**), as executed by a civil-law notary on 21 February 2012;
- (j) a pdf copy of the deed of conversion and amendment to the articles of association of the Company, pursuant to which deed the Company converted from a B.V. to a N.V. (the **Deed of Conversion**); and
- (k) 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) and (d) are collectively referred to as the **Resolutions**.

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

- 3. We assume:
 - (a) the genuineness of all signatures on the documents referred to in paragraph 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 the Registration Statement has been or shall be filed with the SEC, and shall become effective, in the form referred to in this legal opinion;
 - (d) that the Stock Option Plan is and shall remain effective upon each granting of rights to subscribe for Option Shares (collectively, the "Options" and each, an "Option") and upon each issue of Option Shares pursuant to the exercise of such Options;
 - (e) (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;
 - (f) that at the time of issue of the Option Shares, the Company has not been dissolved (*ontbonden*), granted a moratorium (*surseance verleend*) or declared bankrupt (*failliet verklaard*) (although not constituting conclusive evidence thereof, this assumption is supported by (a) the contents of the Excerpt, (b) an online search in the central insolvency register on 4 November 2021 and (c) information obtained by telephone on 4 November 2021 from the insolvency office (*afdeling insolventie*) of the court in The Hague, the Netherlands);
 - (g) 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;

- (h) 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;
- (i) the Resolutions, including any power of attorney therein have not been and will not be annulled, modified, revoked or rescinded and are in full force and effect as at the date hereof and that the Resolutions have been made with due observance of the statutory requirements and the provisions of the Articles of Association relating to the convening of meetings and the making of resolutions (although not constituting conclusive evidence thereof, failure to observe such provisions is not apparent on the face thereof) and that each factual confirmation and statement in the Resolutions (including any confirmation or statement on conflict of interest (*tegenstrijdig belang*)) is correct;
- (j) that at the time of issue of the Option Shares, the Company will have taken all necessary corporate action required by (i) the Company's articles of association; and (ii) applicable laws of the Netherlands, to (a) issue of the Option Shares and (b) exclude any pre-emption rights with respect to such issuance;
- (k) that at the time of issue of the Option Shares, the authorised share capital of the Company will allow such issue of Option Shares (or the granting of any rights to subscribe for such Option Shares);
- (l) that at the time of issue of the Option Shares, the Option Shares will be issued in the form and manner required by applicable law, the Company's articles of association and its other internal rules and regulations at the time of issue, and otherwise offered to, issued to and accepted by their subscribers in accordance with all applicable laws (including, for the avoidance of doubt, Dutch law);
- (m) that at the time of issue of the Option Shares, the Option Shares will be paid for with due observance of the relevant formalities under all applicable laws (including, for the avoidance of doubt, Dutch law);
- (n) none of the opinions stated in this opinion letter will be affected by any foreign law; and
- (o) 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) The Company is validly existing as a *naamloze vennootschap*.
 - (b) When issued, the Option Shares will have been validly issued, will have been fully paid and will be non-assessable.
- 6. This legal opinion is subject to the following qualifications:
 - (a) The opinions expressed in this legal opinion may be affected or limited by (i) the general defences available to obligors under Netherlands law in respect of the validity and enforceability of agreements; and (ii) the provisions of any applicable bankruptcy (*faillissement*), insolvency, moratorium (*surseance van betaling*), fraudulent conveyance (*Actio Pauliana*), reorganisation and other or similar laws of general application now or hereafter in effect, relating to or affecting the enforcement or protection of creditors' rights.
 - (b) As used in the opinions in paragraph 5 of this opinion letter, the term "non-assessable" which term has no equivalent in Dutch means that a holder of a share will not by reason of merely being such a holder, be subject to assessment or calls by the Company or its creditors for further payment on such share.
 - (c) Under Dutch law, each power of attorney (*volmacht*) or mandate (*lastgeving*), whether or not irrevocable, granted by the Company will terminate by force of law and without notice, upon bankruptcy of the Company. To the extent that the appointment by the Company of a process agent would be deemed to constitute a power of attorney or a mandate, this qualification would apply.
 - (d) This opinion letter does not purport to express any opinion or view on the operational rules and procedures of any clearing or settlement system or agency.
- 7. In this opinion, Dutch legal concepts are expressed in English terms and not in their original Dutch terms. The concepts concerned may not always be identical to the concepts described by the English terms as such terms may be understood under the laws of other jurisdictions. This legal opinion is given on the express basis, accepted by each person who is entitled to rely on it, that this legal opinion and all rights, obligations or liability in relation to it are governed by Dutch law.

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- 8. This legal opinion is given exclusively in connection with our representation of the Company and for no other purpose.
- 9. Notwithstanding the previous sentence, this opinion may be disclosed, quoted, or referred to without our written express consent (i) if such disclosure, quotation or reference without our written consent is required by law, court order or any competent regulatory authority, *provided* that you shall notify us immediately or as soon as otherwise possible after such disclosure, quotation or reference or (ii) to the extent that such disclosure, quotation or reference is required (a) to any of your insurers in respect of any claim or potential claim against you or (b) for evidence in court or similar proceedings in which you are a defendant, *provided*, in each of the events referred to in (a) and (b), that you shall notify us prior to any such disclosure, reference or quotation being made.
- 10. We consent to the filing of this opinion letter as an exhibit to the Registration Statement and also consent to the reference to Allen & Overy LLP in the Registration Statement under the caption "Legal Matters".

Yours faithfully,

/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 S-8 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.

/s/ Deloitte Accountants B.V.

Amsterdam, The Netherlands

November 4, 2021