# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# FORM 6-K

**Report of Foreign Private Issuer**
**Pursuant to Rule 13a-16 or 15d-16 of**
**the Securities Exchange Act of 1934**

**For the month of March 2021**

**Commission File Number: 001-36622**

# PROQR THERAPEUTICS N.V.

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(Address, Including ZIP Code, and Telephone Number,
Including Area Code, of Registrant's Principal Executive Offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

On March 24, 2021, ProQR Therapeutics N.V. (the "Company") issued a press release titled, "ProQR Announces Positive Results from Clinical Trial of QR-421a in Usher Syndrome and Plans to Start Pivotal Trials." A copy of this press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

The Company hereby incorporates by reference the information contained herein into the Company's registration statements on Form F-3 (File No. 333-228251 and File No. 333-248740).

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**PROQR THERAPEUTICS N.V.**

Date: March 24, 2021

By: /s/ Smital Shah
Smital Shah
Chief Financial Officer

**INDEX TO EXHIBITS**

| Number | Description |
| --- | --- |
| 99.1 | Press Release of ProQR Therapeutics N.V. dated March 24, 2021. |

**Exhibit 99.1**

ProQR Announces Positive Results from Clinical Trial of QR-421a in Usher Syndrome and Plans to Start Pivotal Trials

- QR-421a demonstrated a concordant benefit in multiple measures of vision, including best corrected visual activity (BCVA), static perimetry, and retinal imaging (OCT)
- QR-421a observed to be well tolerated with no serious adverse events reported
- Two pivotal Phase 2/3 trials are expected to start by the end of 2021
- Management to host a conference call today at 8:15am EDT

LEIDEN, Netherlands & CAMBRIDGE, Mass., March 24, 2021 -- ProQR Therapeutics N.V. (Nasdaq: PRQR) (the "Company"), a company dedicated to changing lives through the creation of transformative RNA therapies for inherited retinal diseases (IRDs), today announced results from a planned analysis of its Phase 1/2 *Stellar* trial of QR-421a in adults with Usher syndrome and non-syndromic retinitis pigmentosa (nsRP) due to *USH2A* exon 13 mutations. In the trial, QR-421a demonstrated benefit on multiple measures of vision that moved in concordance, including visual acuity, visual fields, and optical coherence tomography (OCT) retinal imaging, after a single dose. QR-421a was observed to be well tolerated with no serious adverse events reported. Based on these findings, the Company plans to advance QR-421a to two parallel pivotal Phase 2/3 trials by year end 2021 – one in early-moderate patients, one in advanced patients.

"We're pleased to have met all the objectives we set for the *Stellar* trial, including determining suitable registration endpoints, the dose, dosing interval, and patient population for the Phase 2/3 pivotal trials," said Aniz Girach, MD, Chief Medical Officer of ProQR, "With just a single dose, QR-421a demonstrated clinical proof of concept with benefit observed in treated eyes compared to the untreated eyes in multiple concordant measures of vision. As expected, we saw benefits in both advanced and early-moderate patients in this slow progressing, debilitating eye disease, allowing us to advance this important investigational therapy for all patients with Usher syndrome and nsRP due to *USH2A* exon 13 mutations. Based on preliminary Regulatory guidance, we plan to submit protocols to advance QR-421a to pivotal testing. This is our second program targeting a severe inherited retinal disease that is moving into pivotal trials, which we believe further validates our RNA therapy platform and our capabilities to design and efficiently take these programs through clinical development."

"The safety profile and efficacy findings for QR-421a are very encouraging," said Robert Koenekoop, MD, MSc, PhD, FRCS(C), FARVO, a clinical-scientist from the Montreal Children's Hospital and Professor of the McGill University Faculty of Medicine and Department of Pediatric Surgery. "Usher syndrome and non-syndromic retinitis pigmentosa due to *USH2A* exon 13 mutations are devastating retinal diseases representing a high unmet medical need, as there are no approved therapies to treat the severe vision loss associated with these diseases. Patients' biggest hope for a therapy is to stop disease progression and prevent vision loss, and these findings suggest that QR-421a has the potential to stabilize vision. I look forward to this exciting program advancing into pivotal trial development."

**Results from the Phase 1/2 trial of QR-421a**

**Safety Data**

QR-421a was observed to be well tolerated at all doses. There were no serious adverse events reported and no inflammation was observed. One patient had worsening of pre-existing cataracts in both the treated and untreated eyes; both were deemed not treatment related by the investigator. One patient had progression of pre-existing cystoid macular edema (CME) that was managed with standard of care. Both cataracts and CME are associated with a high rate of occurrence in the natural history of this disease.

**Efficacy Data**

Given the key differences in baseline characteristics, patients were categorized into “advanced” and “early-moderate” populations based on baseline visual acuity.

In advanced patients, the primary measure of efficacy is BCVA. In early-moderate patients, the primary measure of efficacy is measurement of visual fields by static perimetry. QR-421a-treated patients responded on endpoints consistent with their disease stage in both advanced and early-moderate patient populations after a single injection.

All three doses studied in the *Stellar* trial were observed to be active as predicted by the pre-clinical data. No differences were observed based on patients being homozygous or heterozygous, or having Usher syndrome or non-syndromic retinitis pigmentosa. These findings are consistent with the preclinical data for QR-421a.

Analysis of advanced patients

Visual acuity

Best corrected visual acuity, or BCVA, is a measure of central vision, or sharpness of sight, as measured on an Early Treatment of Diabetic Retinopathy Study (ETDRS) letter chart.

Across all treated patients (n=14), a mean benefit of 6.0 letters was observed at week 48 in the treated eyes compared to the untreated (contralateral) eyes after a single injection.

Among advanced disease patients (n=6), a mean benefit of 9.3 letters was observed at week 48 in the treated eyes as compared to the untreated eyes and the benefit was maintained for >12 months. All six advanced patients had a benefit in the treatment eye, whereas none of the patients in the sham group had a benefit in the treatment eye.

Analysis of early-moderate patients

Static perimetry

Static perimetry assesses visual fields and retinal sensitivity in the peripheral retina.

Across all treated patients, the mean total retinal sensitivity improvement was up to 40dB higher in the treated eyes compared to the untreated eyes, and the benefit was maintained for >6 months after a single injection.

The mean number of retinal locations (loci) that improved by ≥7db in retinal sensitivity demonstrated a benefit in the treated eyes compared to the untreated eyes, with up to a mean of 9 loci in the treated eyes improving by ≥7db .

In early-moderate patients (n=8), up to a mean of 13 loci in the treated eyes improved by ≥7db compared to 7 loci for the untreated eyes at the same timepoint.

Concordant benefits were noted on OCT-based assessment of the Ellipsoid Zone layer, which is an objective evaluation of photoreceptor viability, and other measures of central visual function, such as microperimetry. Sham treated eyes responded similarly to the untreated eyes across all endpoints.

**Pivotal trials**

On the basis of these findings, the Company plans to conduct two pivotal Phase 2/3 clinical trials. Based on initial Regulatory guidance, the Company plans to submit protocols to start two Phase 2/3 trials. Each trial could potentially serve as the sole registration trial depending on the findings. Pending finalization of the study designs with Regulatory authorities, the trials are expected to start before year end 2021. Both trials are expected to be conducted at global centers of excellence.

***Sirius* trial in advanced population**

The "*Sirius*" trial is a Phase 2/3 study that will focus on advanced patients with baseline BCVA ≤20/40. The preliminary design for *Sirius* is a double-masked, randomized, sham-controlled, 24-month, multiple-dose study. The trial is expected to enroll approximately 100 adults with Usher syndrome and nsRP due to *USH2A* exon 13 mutations, including both homozygous and heterozygous patients. The primary endpoint in this trial will be BCVA at 18 months, with potential for an earlier interim analysis. In this three-arm study, two different doses will be studied that will be administered every 6 months, and a third arm will receive sham treatment.

***Celeste* trial in early-moderate population**

In parallel to *Sirius*, the Company plans to start the "*Celeste*" Phase 2/3 trial in early-moderate patients. The preliminary design for *Celeste* is a double-masked, randomized, sham-controlled, 24-month, multiple-dose study. The trial is expected to enroll approximately 100 adults with Usher syndrome and nsRP due to *USH2A* exon 13 mutations. The primary endpoint in this trial will be based on static perimetry at 18 months, with potential for an earlier interim analysis. In this three-arm study, two different doses will be studied that will be administered every 6 months, and a third arm will receive sham treatment.

"There are currently no available treatments for the more than 16,000 patients with Usher syndrome 2A and nsRP due to *USH2A* exon 13 mutations and we are excited about the potential for QR-421a to address this significant unmet need," said Benjamin R. Yerxa, PhD, Chief Executive Officer at the Foundation Fighting Blindness. "We are pleased to see QR-421a advancing to pivotal testing and proud to support the work of ProQR as they advance their pipeline of RNA therapies to potentially help children, adults, and families who are affected by blindness caused by *USH2A* mutations and other rare inherited retinal diseases."

**Conference call**

Management will discuss the data during a **webcasted conference call** today at 8:15 am EDT. The dial-in details for the call are +1 631-510-7495 (US), +31 (0)20 714 3545 (NL), conference ID: 8596733.

An archive of the webcast will be available for approximately 30 days following the presentation date.

**Phase 1/2 *Stellar* trial of QR-421a**

The *Stellar* trial is a randomized, sham-controlled, single ascending dose, global, multicenter, 24-month study. The study includes a total of 20 patients, of which 14 received a single dose of QR-421a and six received a single sham procedure for masking. The 14 QR-421a-treated patients enrolled (mean age of 46 years) varied in their disease stage and were classified as advanced patients (defined as patients with baseline visual acuity of <70 letters, or equivalent to LogMAR 0.3, or worse than 20/40 on a Snellen chart) or early-moderate patients. Six patients had advanced disease and eight patients had early-moderate disease. Three different dose levels were studied. The population also varied in disease characteristics with both Usher syndrome (n=7) and nsRP (n=7) and genetic background with both homozygous (n= 9) and heterozygous (n=5) subjects for *USH2A* exon 13 mutations. The majority of the patients were followed for up to 48 weeks, with one patient followed up to 96 weeks.

**About Usher Syndrome Type 2a and Non-Syndromic Retinitis Pigmentosa**

Usher syndrome is the leading cause of combined deafness and blindness. People with Usher syndrome type 2a are usually born with hearing loss and start to have progressive vision loss during adulthood. The vision loss can also occur without hearing loss in a related disease called non-syndromic retinitis pigmentosa. Usher syndrome type 2a and non-syndromic retinitis pigmentosa can be caused by mutations in the *USH2A* gene. To date, there are no pharmaceutical treatments approved or in clinical development that treat the vision loss associated with mutations in *USH2A*.

**About QR-421a**

QR-421a is a first-in-class investigational RNA therapy designed to address the underlying cause of vision loss in Usher syndrome type 2a and non-syndromic retinitis pigmentosa due to mutations in exon 13 of the *USH2A* gene. QR-421a is designed to restore functional usherin protein by using an exon skipping approach with the aim to stop or reverse vision loss in patients. QR-421a is intended to be administered through intravitreal injections in the eye and has been granted orphan drug designation in the US and the European Union and received fast-track and rare pediatric disease designations from the FDA.

**About ProQR**

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

Learn more about ProQR at www.proqr.com.

**Forward Looking Statements**

This press release contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to", "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions. Such forward-looking statements include, but are not limited to, statements regarding QR-421a, and the clinical development and the therapeutic potential thereof, our other programs and business operations, including timing of commencing clinical trials and enrollment of patients therein, the design of planned trials for QR-421a and the expected regulatory pathway for this product candidate, including the potential for the Sirius and Celeste trials to serve as the sole registration trials in this indication, the expected impact of the COVID-19 on our business operations, including our research and development plans and timelines, and the supply chain for our clinical and development programs. Forward-looking statements are based on management's beliefs and assumptions and on information available to management only as of the date of this press release. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, the risks, uncertainties and other factors in our filings made with the Securities and Exchange Commission, including certain sections of our annual report filed on Form 20-F. These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities by us and our collaborative partners whose operations and activities may be slowed or halted by the COVID-19 pandemic; the likelihood of our clinical programs being executed on timelines provided and reliance on our contract research organizations and predictability of timely enrollment of subjects and patients to advance our clinical trials and maintain their own operations; our reliance on contract manufacturers to supply materials for research and development and the risk of supply interruption from a contract manufacturer; the potential for future data to alter initial and preliminary results of early-stage clinical trials; the unpredictability of the duration and results of the regulatory review of applications or clearances that are necessary to initiate and continue to advance and progress our clinical programs; the ability to secure, maintain and realize the intended benefits of collaborations with partners; the possible impairment of, inability to obtain, and costs to obtain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in research and development; and general business, operational, financial and accounting risks, and risks related to litigation and disputes with third parties. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and we assume no obligation to update these forward-looking statements, even if new information becomes available in the future, except as required by law.

**ProQR Therapeutics N.V.**

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