### 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

September 5, 2018

#### **PROQR THERAPEUTICS N.V.**

Zernikedreef 9 2333 CK Leiden The Netherlands

Tel: +31 88 166 7000 (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 x Form 40-F o

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): o

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): o

On September 5, 2018, ProQR Therapeutics N.V. (the "Company") issued a press release titled, "ProQR Announces Positive Interim Results from Phase 1/2 Clinical Trial of QR-110 in LCA10 Patients, and Plans to Start a Phase 2/3 Pivotal Trial." 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 statement on Form F-3 (File No. 333-207245).

In addition, the Company presented interim results from its Phase 1/2 clinical trial of QR-110 in LCA10 patients during a webcasted conference call. A copy of the presentation is attached hereto as Exhibit 99.2 and is incorporated herein by reference. In addition, the Company presented interim results from its Phase 1/2 clinical trial of QR-110 in LCA patients at the previously announced International Symposium for Retinal Degeneration.

	INDEX TO EXHIBITS
Number	Description
99.1 99.2	ProQR Announces Positive Interim Results from Phase 1/2 Clinical Trial of QR-110 in LCA10 Patients, and Plans to Start a Phase 2/3 Pivotal Trial. Presentation for webcasted conference call.

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: September 5, 2018

By: /s/ Smital Shah

Smital Shah Chief Financial Officer

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#### ProQR Announces Positive Interim Results from Phase 1/2 Clinical Trial of QR-110 in LCA10 Patients, and Plans to Start a Phase 2/3 Pivotal Trial

QR-110 demonstrated rapid and sustained improvement in vision in the majority of subjects, as measured by visual acuity and mobility course

#### QR-110 was well-tolerated with no serious adverse events

#### A Phase 2/3 pivotal trial is expected to start in the first half of 2019

Management to host a conference call today at 8:15 a.m. ET

LEIDEN, Netherlands & CAMBRIDGE, Mass., Sept. 5, 2018 — ProQR Therapeutics N.V. (Nasdaq:PRQR), a company dedicated to changing lives through the creation of transformative RNA medicines for the treatment of severe genetic rare diseases, today announced results from a planned interim analysis of its Phase 1/2 trial of QR-110 in patients with Leber's congenital amaurosis 10 (LCA10) due to the p.Cys998X mutation in the *CEP290* gene. LCA10 typically leads to childhood blindness and has no available treatment options. In the trial, QR-110 demonstrated rapid and sustained improvement in vision in patients with LCA10, as measured by visual acuity and the mobility course performance, as well as being well-tolerated with no serious adverse events recorded. Results from this interim analysis were presented earlier today at the Retinal Degeneration 2018 meeting in Killarney, Ireland, by principal investigator Artur Cideciyan, Ph.D., research professor of ophthalmology at the Scheie Eye Institute, University of Pennsylvania.

"The results of this interim analysis are encouraging and met our decision criteria to stop enrollment in this study and progress to a pivotal Phase 2/3 trial," said David Rodman, M.D., executive vice president of research and development of ProQR. "We observed a clinically meaningful improvement in vision in the treated eye as measured by both mechanistic and potential registration endpoints. Consistent with predictions based on our patient derived optic-cup models, improvement in visual function was observed as early as two months after treatment and was maximal and stable by three months and thereafter. We are very grateful to the study participants, their caregivers, and the investigators and their staff for the support in the development of QR-110 in this trial."

Thaddeus P. Dryja, M.D., professor of ophthalmology at Harvard Medical School and Massachusetts Eye and Ear and member of the National Academy of Sciences, commented, "These results are the first human data to evaluate the clinical utility of RNA-based therapeutics in a human photoreceptor disease, particularly one with a severe unmet medical need. While a confirmatory trial will be required to establish the full potential of QR-110 in LCA10, these results suggest that therapeutic oligonucleotides have the potential to be broadly applicable to a wide spectrum of inherited retinal disorders."

Based on the emerging findings from the Phase 1/2 trial, the Company agreed with the FDA to submit a protocol to progress to a pivotal Phase 2/3 trial. In light thereof, the originally planned interim analysis at six months treatment was accelerated to the point when eight patients had reached three months of treatment. Given comparable activity was observed in the first two dose levels, the trial did not escalate up to the high dose and trial enrollment has stopped, in anticipation of the start of a Phase 2/3 trial.

#### Results from the interim analysis

Efficacy data: Approximately 60% of subjects showed a clinically meaningful response in visual acuity and mobility course endpoints at three months of treatment and there was general concordance across the endpoints. Efficacy signals were observed within two months with maximal benefits seen within two to three

months post treatment initiation. A secondary analysis assessing all available data demonstrated that observed effects on efficacy were durable beyond three months

Visual acuity: In the majority of patients, there was a substantive overall improvement in best corrected visual acuity (BCVA) as assessed by the Berkeley Rudimentary Vision Test (BRVT) and the Early Treatment of Diabetic Retinopathy Study (ETDRS) eye chart. At three months of treatment, the mean improvement (and standard error of mean, SEM) was -0.67 LogMAR (SEM 0.32) with 62.5% of subjects showing an improvement of greater than -0.3 LogMAR from baseline, which is considered clinically meaningful. The mean change in the contralateral eye was 0.02 LogMAR (SEM 0.05).

Mobility course: Effects on visual acuity correlated with effects on mobility. In the majority of patients there was a substantive overall improvement in functional visual performance as assessed using a series of mobility courses at increasing difficulty and multiple light intensities. At three months of treatment, the mean improvement in navigating the mobility course was 2.6 levels (SEM 1.2) with 57.1% of subjects improving by more than 2.0 levels, which is regarded as clinically meaningful. The mean change in the contralateral eye was 1.36 (SEM 1.04).

Full field stimulus test (FST): Improvements in visual function were supported by a meaningful increase in the ability to detect flashes of red or blue light as determined by the FST. After three months of treatment mean improvement in red light sensitivity was -0.74 log Cd/m<sup>2</sup> (SEM 0.35) and improvement in blue light sensitivity was -0.91 log Cd/m<sup>2</sup> (SEM 0.38).

Ocular Instability (OCI): Additionally, the majority of patients improved on nystagmus (involuntary eye movements in low vision patients), with a mean change of log -0.14 mm (SEM 0.08) in OCI.

Safety: Out of the 10 subjects dosed in the study, one subject has received all four doses and three have received three doses, representing a combined total of more than 1,500 treatment days. So far QR-110 was well tolerated with no serious adverse events related to treatment or procedure. All data and safety monitoring committee (DSMC) reviews were completed with no restrictions on further dose escalation or pediatric dosing.

#### Start of Phase 2/3 pivotal "ILLUMINATE" trial

The Company has agreed with the FDA to submit a protocol to start a Phase 2/3 trial that could serve as the sole registration trial, to be called "ILLUMINATE". The preliminary design for "ILLUMINATE" is a double-blind, controlled, 12month study. The trial is expected to initially enroll 30-40 patients with LCA10 due to one or two copies of the p.Cys998X mutation and could be adaptively repowered. The primary endpoints in this trial are expected to include the mobility course and visual acuity, among others. The trial is expected to be conducted at centers in North America and select European countries. Pending discussions on the design of the study with the FDA in 2018, the trial is expected to start in the first half of 2019. In parallel to the pivotal Phase 2/3 trial, the Company plans to start a trial in patients <6 years old.

#### Conference call

Management will discuss the data during a webcasted conference call today at 8:15 a.m. ET. The live webcast can be accessed here. The dial-in details for the call are +1-877-407-3982 or +1-201-493-6780 (international), conference ID: 13682382.

An archive of the webcast (available for 30 days) can be accessed here.

About the PQ-110-001 Phase 1/2 trial

A total of 12 patients were screened, of which 10 subjects were dosed, have been in the trial for at least one month and are included in the interim analysis. All 10 patients were enrolled in either the 80 µg dose cohort (160 µg loading dose) or 160 µg dose cohort (320 µg loading dose) in the treated eye, with the other eye remaining untreated. Based on the safety profile the DSMC approved further dose escalation if needed. However, given indications of comparable activity in the first two dose groups, the decision was made to defer

further dose escalation. Enrollment has been completed and patients in the trial will complete the 12-month treatment and observation period and subsequently will have the option to participate in "INSIGHT", an open-label extension study including the possibility of receiving treatment in the second eye.

PQ-110-001 is an open-label trial that has been designed to enroll children (age 6 - 17 years) and adults ( $\geq$  18 years) who have LCA10 due to one or two copies of the p.Cys998X mutation in the CEP290 gene. Patients are receiving four intravitreal injections of QR-110 into one eye; one injection every three months. The trial is being conducted at three specialized centers with significant expertise in genetic retinal disease: the University of Iowa, Iowa City, Iowa, U.S., the Scheie Eye Institute at the University of Pennsylvania, Philadelphia, U.S., and the Ghent University Hospital, Ghent, Belgium.

The primary objectives of the PQ-110-001 trial are safety and tolerability. Secondary objectives include pharmacokinetics, as well as restoration/improvement of visual function and retinal structure through ophthalmic endpoints, such as visual acuity (BCVA), mobility course, full field stimulus testing (FST), ocular instability (OCI), optical coherence tomography (OCT), and pupillary light reflex (PLR). Changes in quality of life in the trial subjects are also being evaluated.

#### About QR-110

QR-110 is a first-in-class investigational RNA-based oligonucleotide designed to address the underlying cause of Leber's congenital amaurosis 10 due to the p.Cys998X mutation (also known as the c.2991+1655A>G mutation) in the CEP290 gene. The p.Cys998X mutation is a substitution of one nucleotide in the pre-mRNA that leads to aberrant splicing of the mRNA and non-functional CEP290 protein. QR-110 is designed to restore normal (wild-type) CEP290 mRNA leading to the production of normal CEP290 protein by binding to the mutated location in the pre-mRNA causing normal splicing of the pre-mRNA. QR-110 is intended to be administered through intravitreal injections in the eye and has been granted orphan drug designation in the United States and the European Union and received fast-track designation by the FDA.

#### About Leber's Congenital Amaurosis 10

Leber's congenital amaurosis (LCA) is the most common cause of blindness due to genetic disease in children and consists of a group of diseases of which LCA10 is the most frequent and one of the more severe forms. LCA10 is caused by mutations in the CEP290 gene, of which the p.Cys998X mutation is the most common. LCA10 leads to early loss of vision causing most people to lose their sight in the first few years of life. To date, there are no treatments approved or other products in clinical development that treat the underlying cause of the disease. Approximately 2,000 people in the Western world have LCA10 because of this mutation.

#### About ProQR

ProQR Therapeutics is dedicated to changing lives through the creation of transformative RNA medicines for the treatment of severe genetic rare diseases such as Leber's congenital amaurosis 10, dystrophic epidermolysis bullosa and cystic fibrosis. Based on our unique proprietary RNA repair platform technologies we are growing our pipeline with patients and loved ones in mind. \*Since 2012\*

#### 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," "should," "will," "would" and similar expressions. Such statements include those relating to QR-110 and the clinical development and

therapeutic potential thereof, including our PQ-110-001 clinical trial of QR-110 and statements regarding release of clinical data, including that from our PQ-110-001 trial. 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. 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.

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# INTERIM RESULTS QR-110 PHASE 1/2 TRIAL IN LCA10

Investor conference call

**Nasdaq**: PRQR

Date: September 5, 201

### **Forward looking statements**

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including but not limited to, statements regarding our strategy, future operations, future preclinical and clinical trial plans and related timing of trials and results, research and development, future financial position, future revenues, projected costs, prospects, therapeutic potential of our product candidates, plans and objectives of management, are forwardlooking statements. The words "aim," "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements represent our management's beliefs and assumptions only as of the date of this presentation. We may not actually achieve the plans, intentions or expectations

disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those that may be described in greater detail in the annual report filed on Form 20-F for the year ended December 31, 2017 that we have filed with the U.S. Securities and Exchange Commission (the "SEC") and any subsequent filings we have made with the SEC. We have included important factors in the cautionary statements included in that annual report, particularly in the Risk Factors section, and subsequent filings with the SEC that we believe could cause actual results or events to differ materially from the forward-looking statements that we make.



### Welcome and introduction

by Smital Shah

### Phase 1/2 interim results and future development of QR-110

by David Rodman, MD

### **Next steps in Ophthalmology** By Daniel de Boer



Smital Shah Chief Financial Officer



David Rodman, MD Executive Vice President of Research & Development



Daniel A. de Boer Chief Executive Officer

ProQR - Interim Results QR-110 Phase 1/2 Trial



# Phase 1/2 interim results and future development of QR-110

by David Rodman Executive Vice President of Research and Development

# QR-110 for LCA10



ProQR - Interim Results QR-110 Phase 1/2 Trial

# Clinical study design – PQ-110-001

Open label, multiple dose, dose escalation study, Phase 1/2



1 loading dose & 3 maintenance doses over 1 year:

- 160 μg loading dose / 80 μg maintenance dose
- 320 µg loading dose / 160 µg maintenance dose

#### Observation of early efficacy at low and mid dose led to:

- Accelerated interim analysis
- · No escalation to the high dose

- Up to twelve p.Cys998X LCA10 patients; adults and children (≥6yrs)
- · Intravitreal injections in one eye
- Participating sites: major sites in EU (UGhent) and US (UPenn, Ulowa)
- Primary endpoints:
  - Safety, tolerability
- Secondary endpoints and exploratory efficacy:
- Visual acuity, mobility course, FST, OCI, pharmacokinetics, OCT, PRO, ERG, pupilometry
- IND and CTA (BE)
- Orphan drug designation in EU and US
- FDA Fast-track designation
- Plan to start a pivotal Phase 2/3 ILLUMINATE trial in H1 2019 with parallel pediatric study

ProQR – Interim Results QR-110 Phase 1/2 Tria

## **Interim results summary**

### The trial met its primary and secondary objectives

- ✓ Safe and well tolerated in >1500 subject treatment-days analyzed
- Mechanistic proof-of-concept confirmed by improvement in FST
- Clinical proof-of-concept confirmed by BCVA and supported by improvement in mobility course
- The four analyzed outcome measures showed concordant improvement
- Enrollment has been completed
- 12 month data in all subjects is expected in H2 2019
- Plan to start a Phase 2/3 trial in H1 2019
  - Double-blind, controlled, dose range finding adaptive design
  - Could serve as the sole pivotal registration trial
  - Parallel trial in pediatric <6 years old

ProQR - Interim Results QR-110 Phase 1/2 Trial

### **Baseline Demographics**

Pediatric and adult patients (8-44 age range), with severely impaired vision

Sex	2 <sup>nd</sup> CEP290 Allele	Age / Group	Baseline VA (logMAR)	Treated Eye	Dose (µg)
Μ	c.2506_2507delGA	19 / A	LP / LP	RE	160/80
Μ	c.4723A>T	41 / A	LP / LP	RE	160/80
Μ	c.5668G>T	44 / A	2.3 / 2.4	LE	160/80
F	c.4438-3delC	16 / P	2.5 / 2.5	RE	160/80
Μ	c.6277delG	8 / P	1.9 / 2.1	LE	160/80
F	c.3167_3168insA	21 / A	LP / LP	RE	320/160
F	c.4723A>T	27 / A	1.1 / 0.7	RE	320/160
F	c.4393C>T	24 / A	LP / LP	RE	320/160
М	c.6277delG	10 / P	1.9 / 1.4	RE	320/160
F	c.547_550delTACC	15 / P	LP / LP	RE	320/160
F	c.2991+1655A>G	14 / P	0.6/0.6	-	320/160

# **Disposition and Safety Results**

10 subjects enrolled, no early terminations or SAEs

# doses       0       1       2       3       4         Safety findings:	Screened 12	Subjects         1         2         4         3         1				
Dosed 10 Safety findings:		# doses 0 1 2 3 4				
Safety findings:	Dosed 10					
> 1 month follow-up 10		Safety findings:				
<ul> <li>∠ 1 month follow-up 10</li> <li>Generally well tolerated with occasional mi AEs related to injection, typical to IVT.</li> </ul>	$\ge$ 1 month follow-up 10 ≥ 3 month follow-up 8	<ul> <li>Generally well tolerated with occasional mild AEs related to injection, typical to IVT.</li> </ul>				
• No SAEs.	-	• No SAEs.				
$\geq$ 5 month follow-up 6 • No early discontinuations.	$\geq$ 5 month follow-up 6	<ul> <li>No early discontinuations.</li> <li>Independent DSMC agreed that there were no safety concerns.</li> </ul>				
<ul> <li>≥ 6 month follow-up 4</li> <li>Independent DSMC agreed that there were no safety concerns.</li> </ul>	≥ 6 month follow-up 4					

ProQR - Interim Results QR-110 Phase 1/2 Trial

## **Top Line Efficacy Results**

Concordant improvement in all outcome measures

	Direction of improvement	Responder threshold	Change from baseline at Month 3 Mean (SEM)	
			Treated	Untreated
Visual Acuity (ETDRS/BRVT) – LogMAR (n=8)	↓= improved	<u>&gt;</u> -0.3	-0.67 (0.32)	0.02 (0.05)
Mobility Course – level (n=7)	↑ = improved	<u>&gt;</u> 2	2.57 (1.19)	1.36 (1.04)
Full field stimulus red (FST red) - cd/m2 (n=7)	↓= improved		-0.74 (0.35)	-0.23 (0.18)
Full field stimulus blue (FST blue) - cd/m2 (n=7)	↓= improved		-0.91 (0.38)	-0.02 (0.11)
Nystagmus tracking (OCI) - Log <sub>10</sub> mm (n=7)	↓= improved		-0.14 (0.08)	-0.04 (0.06)

# **Best Corrected Visual Acuity (BCVA)**

Majority of subjects had clinically meaningful improvement

3 Months mean (SEM) and Median



ProQR - Interim Results QR-110 Phase 1/2 Trial

### **BCVA effect was maintained for at least 6 months**



# **Mobility Course for LCA10**

- Large dynamic range to accommodate lower visual acuity.
- Measures functional visual performance using a series of courses at increasing difficulty and multiple light intensities.
- $\geq$  2 levels considered meaningful.



Backlit Room Exit at 10% and 100% backlighting intensity (Ora, Inc. BRE™)



High-Contrast Room Exit at 1, 50, 400 lux (Ora, Inc. HCRE™)



High-Contrast Visual Navigation Challenge at 1, 4, 10, 50, 125, 250, 400 lux (Ora, Inc. HCVNC<sup>™</sup>)



Low-Contrast Visual Navigation Challenge at 1, 4, 10, 50, 125, 250, 400 lux (Ora, Inc. LCVNC<sup>™</sup>)

#### Grading scores:

Course	Light level	Score
Fail all co	0	
BRE	100% LED	1
BRE	10% LED	2
HCRE	400 lux	3
HCRE	50 lux	4
HCRE	1 lux	5
HCVNC	400 lux	6
HCVNC	250 lux	7
HCVNC	125 lux	8
HCVNC	50 lux	9
HCVNC	10 lux	10
HCVNC	4 lux	11
HCVNC	1 lux	12
LCVNC	400 lux	13
LCVNC	250 lux	14
LCVNC	125 lux	15
LCVNC	50 lux	16
LCVNC	10 lux	17
LCVNC	4 lux	18
LCVNC	1 lux	19

ProQR - Interim Results QR-110 Phase 1/2 Trial

### Video slide placeholder

### Mobility Course Improved at month 3 and month 6



### **Change in BCVA tracks with change in Mobility**



#### All available datapoints Month 3 and Month 6

## Full Field Stimulus Test (FST)

Measured with blue and red light



ProQR - Interim Results QR-110 Phase 1/2 Trial

### **Ocular instability (OCI)** Measuring nystagmus (involuntary eye movement)



Mean change from baseline through month 6



### Example of restoration of anatomy detected by OC1

Normal retina



EZ line in normal retina shows outer segments by EZ-line, as detected by OCT

### LCA10 retina



EZ line in missing in LCA10 retina due to lack of of outer segments

**Restoration of EZ-line in subject** 



#### ProQR - Interim Results QR-110 Phase 1/2 Trial

## Summary of Phase 1/2 interim analysis

- QR-110 was safe and well tolerated.
- Approximately 60% of subjects demonstrated improvement in BCVA and performance on mobility course.
- Improvement was seen within two months of the first dose and has been maintained throughout ongoing dosing and monitoring.
- Improvement in physiological endpoints including full field stimulation test and ocular instability was also observed.
- General concordance between all 4 endpoints

### Preliminary design pivotal Phase 2/3 trial



Visual Acuity (ETDRS, BRVT)

Expected to start in H1 2019

Mobility course

regulatory feedback

trial in <6 years old

Planning to start pediatric

- Double-blind, controlled, 12-month, dose range finding study in adaptive design
- Could serve as the sole registration trial
- Sites in US and select EU countries
- 30+ patients >6 years old
- Multiple IVT injections initially in one eye

ProQR - Interim Results QR-110 Phase 1/2 Trial

# Next steps in Ophthalmology

by Daniel A. de Boer Chief Executive Officer

# **ProQR** inherited blindness platform



ProQR - Interim Results QR-110 Phase 1/2 Trial

### **QR-110 interim data summary**

### The Phase 1/2 trial met its primary and secondary objectives

- ✓ Safe and well tolerated in >1500 subject treatment-days analyzed
- Mechanistic proof-of-concept confirmed by improvement in FST
- Clinical proof-of-concept confirmed by visual acuity and supported by improvement in mobility course
- The four analyzed outcome measures showed concordant improvement
- Plan to start a Phase 2/3 trial in H1 2019
  - Double-blind, controlled, dose range finding adaptive design
  - Could serve as the sole pivotal registration trial
  - · Parallel trial in pediatric at age of diagnosis



ProQR - Interim Results QR-110 Phase 1/2 Trial

