
**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.

**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 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") announced results from a planned analysis of its Phase 1/2 *Stella* trial of QR-421a in adults with Usher syndrome and non-syndromic retinitis pigmentosa (nsRP) due to *USH2A* exon 13 mutations using a webcasted conference call. A copy of the presentation 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](#)

[Presentation for webcasted conference call](#)



QR-421A STELLAR

Trial results

March 24, 2021



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, 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, research and development, future financial position, future revenues, projected costs, prospects, therapeutic potential of our product candidates, plans and objectives of management, are forward-looking 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 are based on management's beliefs and assumptions and on information available to management only as of the date of this presentation. 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; 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, or 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.

Agenda

1. Introduction

Daniel de Boer

3. Next steps

Daniel de Boer

2. Results of *Stellar* Phase 1/2

Aniz Girach, MD

4. Q&A

Daniel de Boer, Aniz Girach and Smital Shah



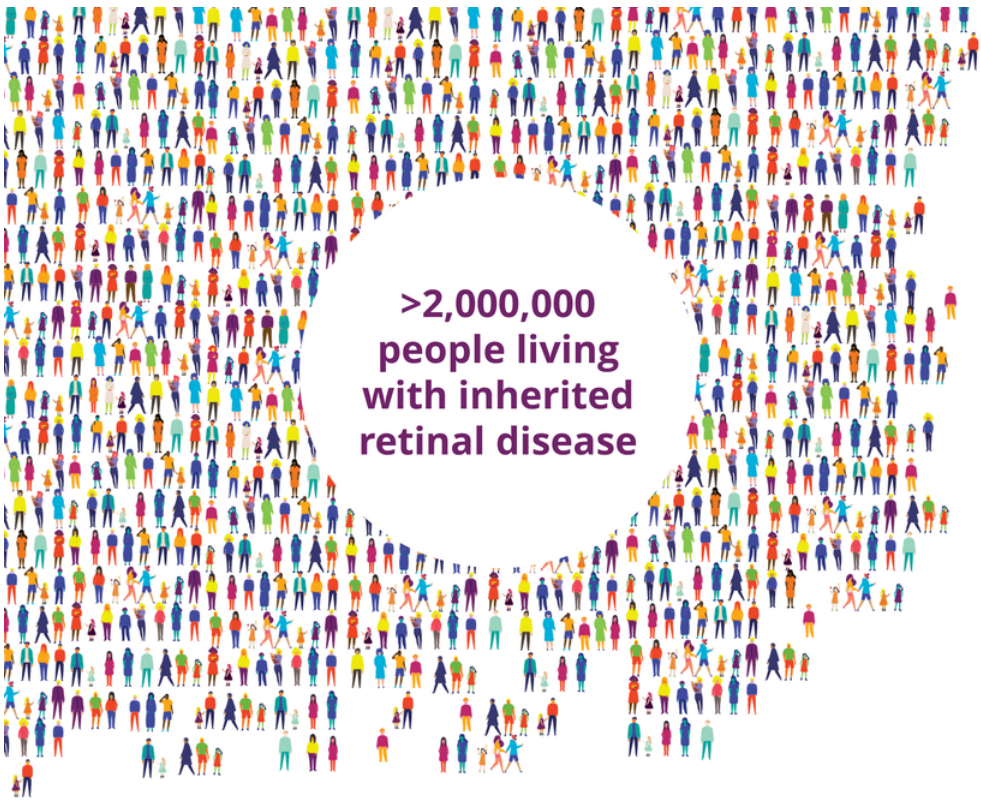
Daniel de Boer
*Founder and
Chief Executive Officer*



Aniz Girach, MD
Chief Medical Officer



Smital Shah
*Chief Business
& Financial Officer*



**>2,000,000
people living
with inherited
retinal disease**

**Very few
have a
treatment**



The impact of *USH2A* mediated vision loss



This video is not available in the pdf. Please [register](#) to watch the full presentation.

Results of *Stellar* Phase 1/2 Trial

By Aniz Girach, MD, Chief Medical Officer

ProQR Therapeutics

QR-421a for Usher syndrome and non-syndromic retinitis pigmentosa (nsRP)

- Potential first-in-class RNA therapy
- QR-421a targets Exon 13 mutations in Ush2a (>16,000 patients)
- QR-421a aims to prevent patients from going blind
- \$7.5M co-funding from Foundation Fighting Blindness

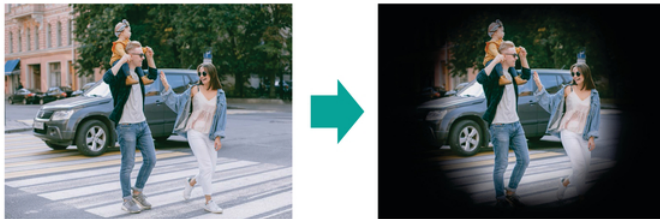


Usher syndrome / non-syndromic retinitis pigmentosa (nsRP) are slow progressing

QR-421a targets early-moderate and advanced disease

Early-moderate disease

Losing visual field from the outside-inward



Advanced disease

Losing visual acuity (VA)

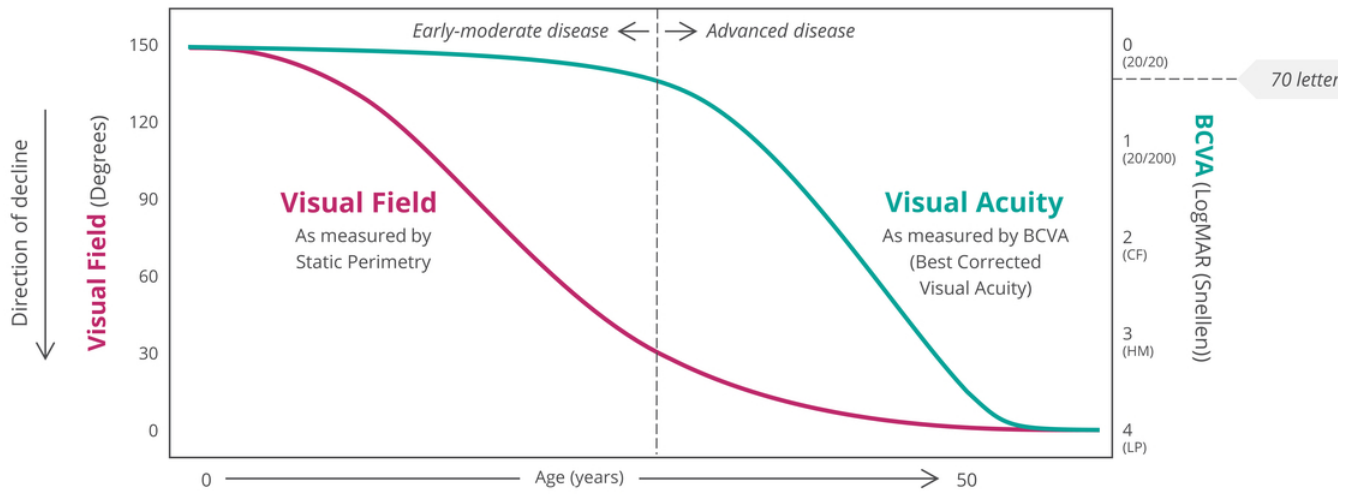


Progression rate varies from patient to patient;
best control is the patient's other, untreated eye

Illustrati

Patient baseline disease stage informs endpoint:

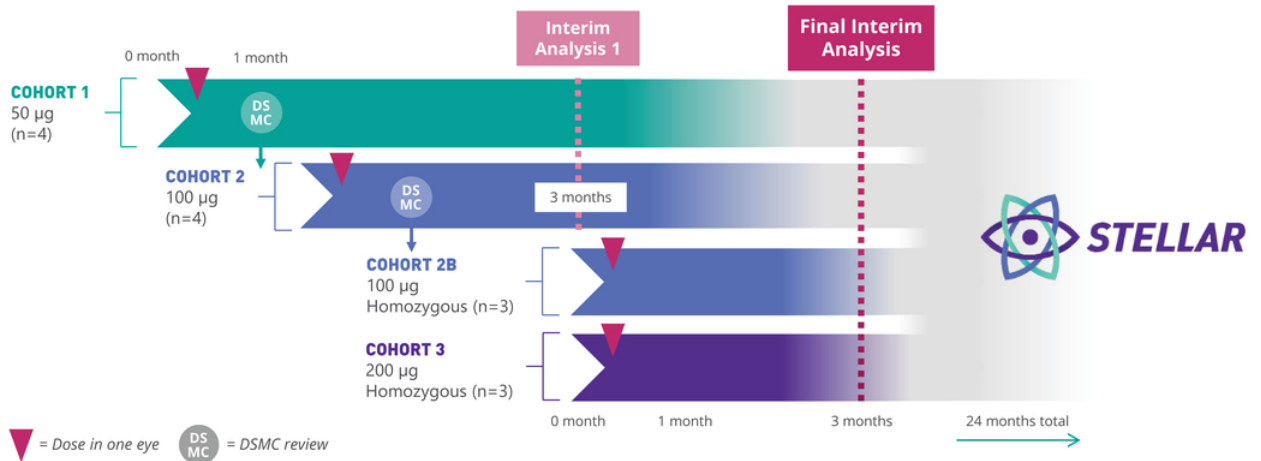
VA of less than 70 letters (20/40) at baseline is advanced disease



Illustrati

QR-421a Phase 1/2 trial in Usher & nsRP

Enrollment completed; 2nd and final Interim Analysis conducted



Stellar Phase 1/2 trial

- Randomized, sham masked, single ascending dose, global multicenter, 24-month study

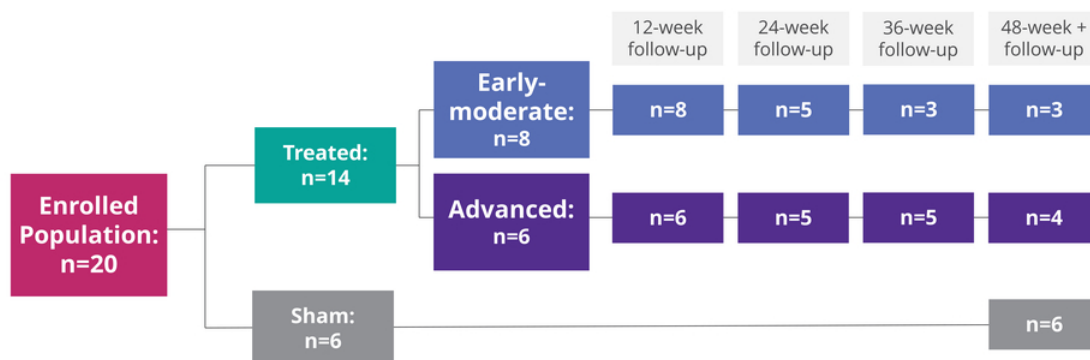
Key endpoints include:

- **Visual acuity (VA):** Best-Corrected VA
- **Visual field:** Static perimetry, microperimetry, dark-adapted chromatic (DAC) perimetry
- **Optical Coherence Tomography (OCT) Imaging**

Goal: to identify for next trial:

- **Registration endpoint(s)**
- **Dose, dosing regimen**
- **Population**

Demographics and disposition



	n	Mean age	Mean VA (TE)	Gender		Genotype		Disease stage		Disease type	
				Male	Female	Homo-zygous	Hetero-zygous	Early-moderate	advanced	nsRP	Usher syndrom
QR-421a treated	14	48	66	4	10	64%	36%	57%	43%	50%	50%
Sham	6	43	68	4	2	17%	83%	67%	33%	67%	33%

Early-moderate disease: baseline VA \geq 70 letters (20/

Summary of trial results

- **Trial met its key objectives**
 - ✓ Well tolerated with no serious adverse events
 - ✓ Clinical proof of concept established
 - ✓ Best Corrected Visual Acuity (BCVA) in advanced patients
 - ✓ Static Perimetry in early-moderate patients
 - ✓ Concordant improvements in multiple other endpoints
 - ✓ Identified key information to take the program forward:
 - ✓ Registration endpoint
 - ✓ Dose and dose interval
 - ✓ Optimal study population
- **Plan to start Phase 2/3 pivotal trials by YE 2021**

QR-421a was well tolerated

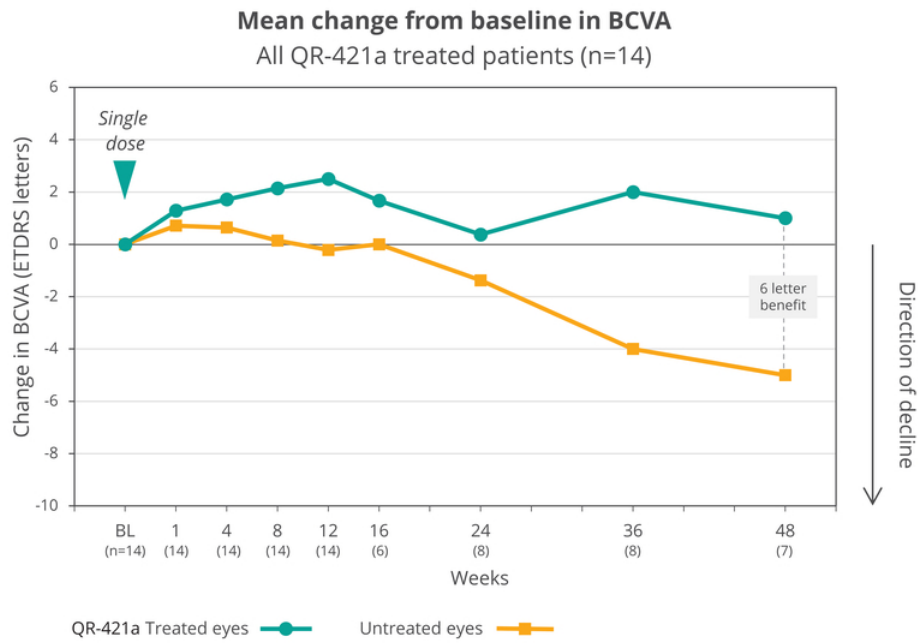
- **QR-421a was well tolerated in >3,700 subject follow up days**
- **No SAEs, no inflammation**
- Cataracts occur in >30% patients in natural history of disease
 - 1 patient had worsening of pre-existing cataracts in both the treated and untreated eye with cataract extractions in both eyes
 - Deemed not treatment related by Investigator
- Cystoid Macular Edema (CME) known to occur as part of natural history of disease in >30% of the patients
 - No new occurring cases of CME during study
 - 1 patient with CME at baseline progressed during study, classified as mild, managed with standard of care

Advanced population efficacy results

Population with progressed visual acuity loss

BCVA stabilization in treated eye

Mean 6 letter benefit at week 48

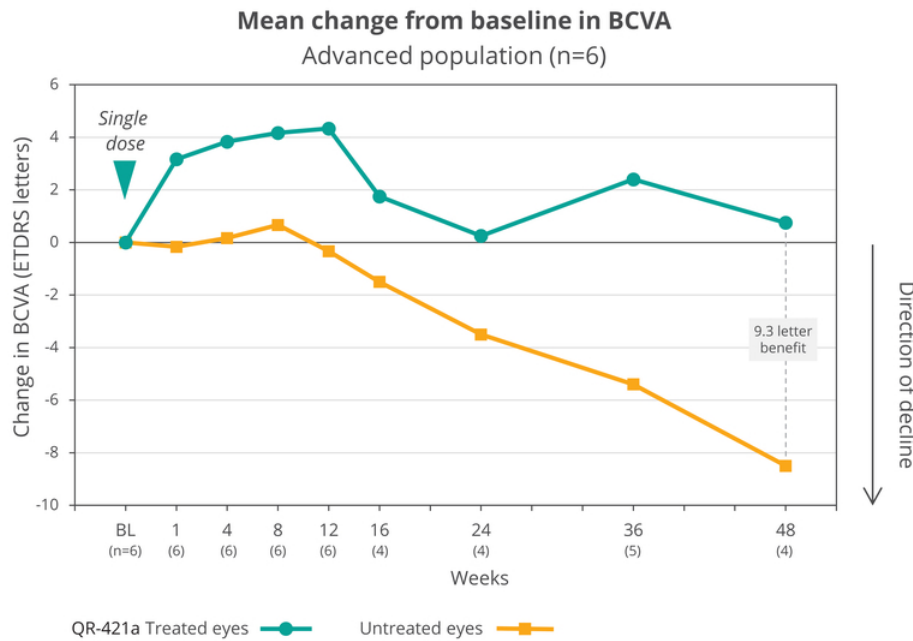


- Stabilization of vision observed in treated eye vs decline in untreated eye in all patients
- 6 letter benefit at week 48, after single dose
- Sustained effect is consistent with the long half-life of QR-421a



BCVA stabilization driven by advanced population

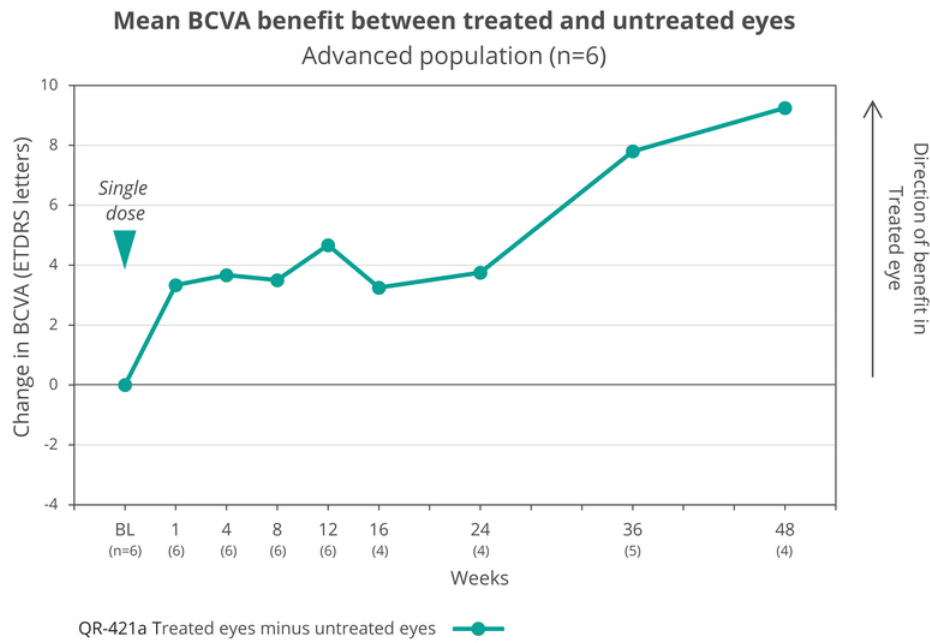
Mean 9.3 letter benefit at week 48



- BCVA response is driven by advanced disease population
- Stabilization of vision in treated eye after single dose
- Deterioration of untreated eye in line with expected natural history of disease
- Mean 9.3 letter benefit at week 48 in the advanced population
- Sustained effect is consistent with the long half-life of QR-421a



Benefit in BCVA in advanced population

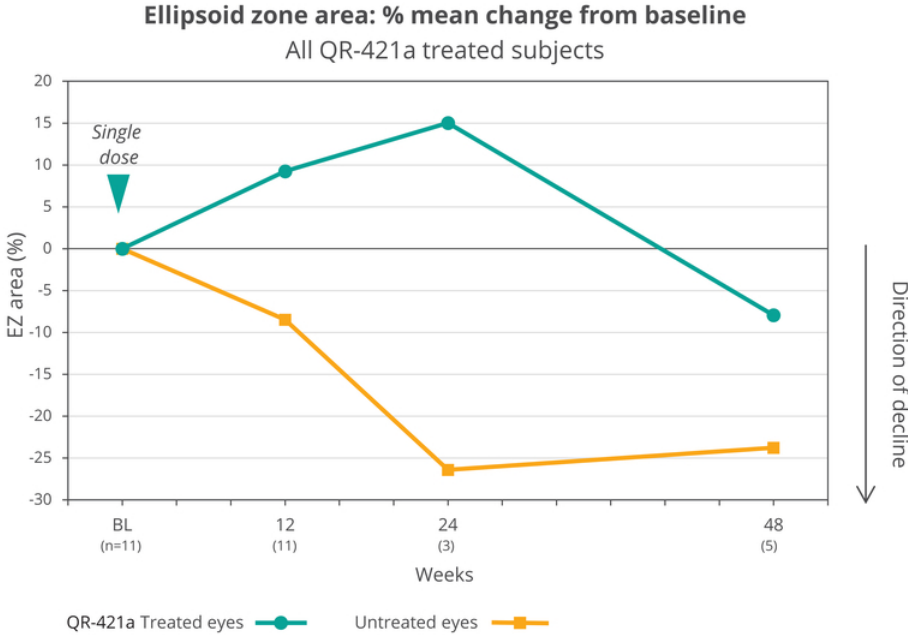


- Difference between treated and untreated eyes demonstrate BCVA benefit in advanced patients
- Response is consistent with disease state
- 9.3 letter benefit at week 48 in the advanced population



Stabilization of retinal structure in treated eyes

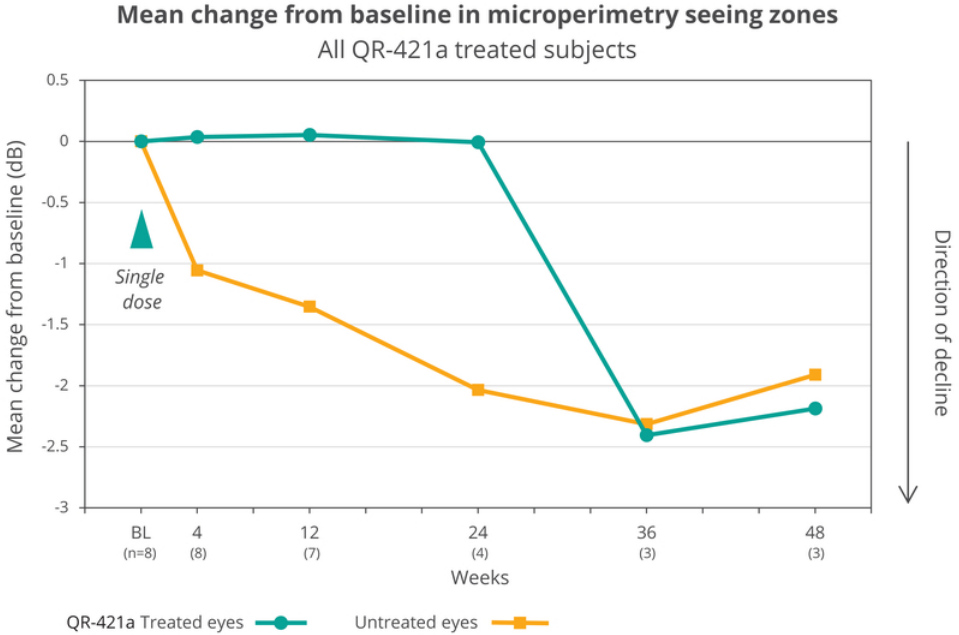
Measured by OCT based Ellipsoid Zone (EZ) in the central macular area



- Stabilization in the treated eyes out to 48 weeks, after single dose
- Deterioration in untreated eyes in line with natural history
- Benefit on OCT provides objective validation of response on BCVA and other endpoints

Stabilization of microperimetry in treated eye

Measuring retinal sensitivity in central visual field

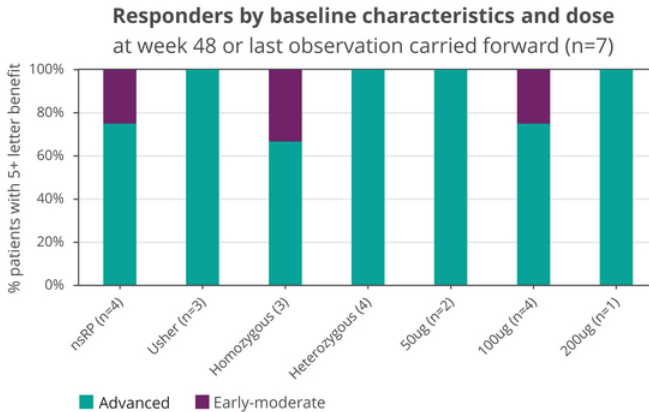
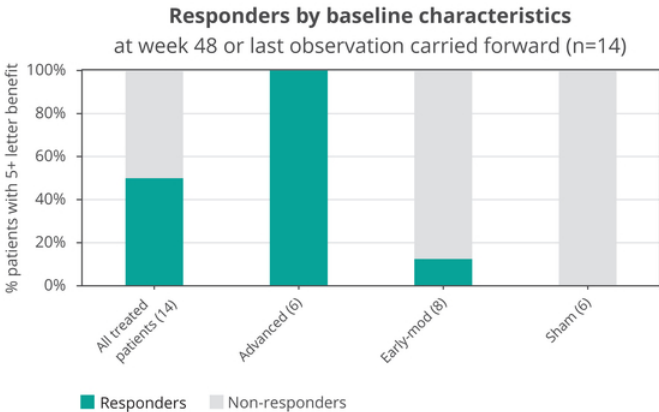


- Stabilization in the treated eyes out to week 24, after single dose
- Durability of response in line with half life of QR-421a
- Steady decline in untreated eye over same period

BCVA selected as primary endpoint for advanced population

- ✓ **Patient population identified**
 - ✓ 100% of the advanced patients were responders
 - ✓ No difference between homozygous and heterozygous genotype
 - ✓ No difference between Usher and nsRP

- ✓ **Dose for next trial identified**
 - ✓ No difference between different dose levels, consistent with preclinical data
 - ✓ All tested doses were active providing great flexibility for dose selection

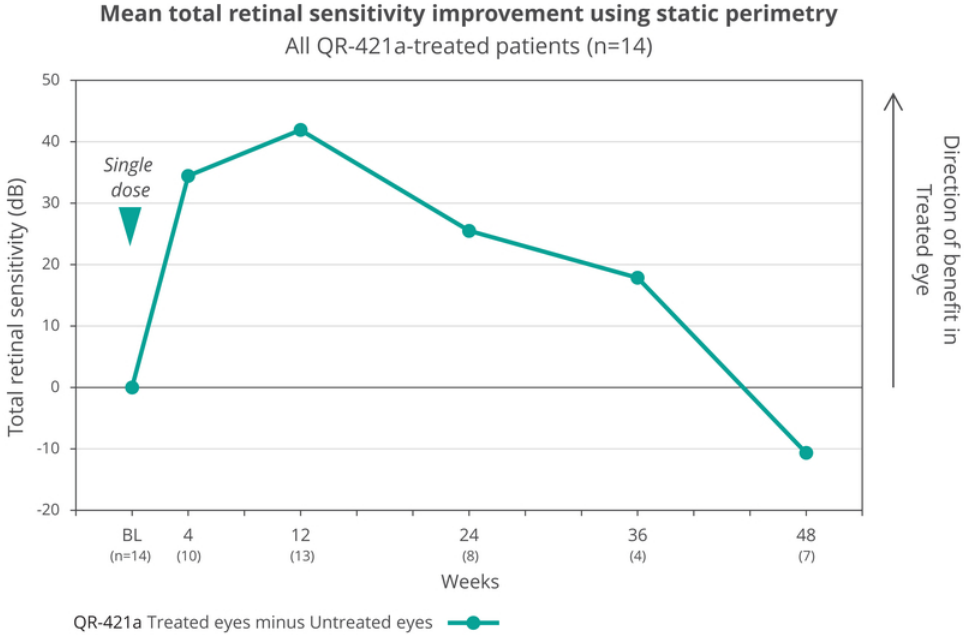


Early-moderate population efficacy results

Population with visual field loss, but minimal visual acuity loss

Visual field: Benefit on retinal sensitivity

Improvement measured by static perimetry after single dose



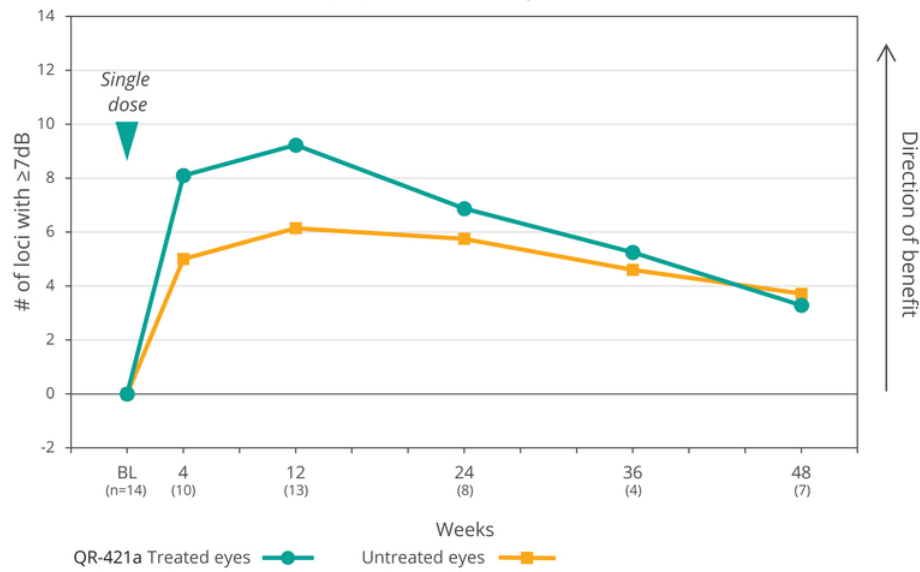
- Analysis: total retinal sensitivity improvement difference between treated and untreated eyes change from baseline
- Benefit observed in treated eyes after single dose
- Benefit sustained for >6 months

Improvement in treated eyes on static perimetry

Measuring retinal sensitivity in peripheral visual field

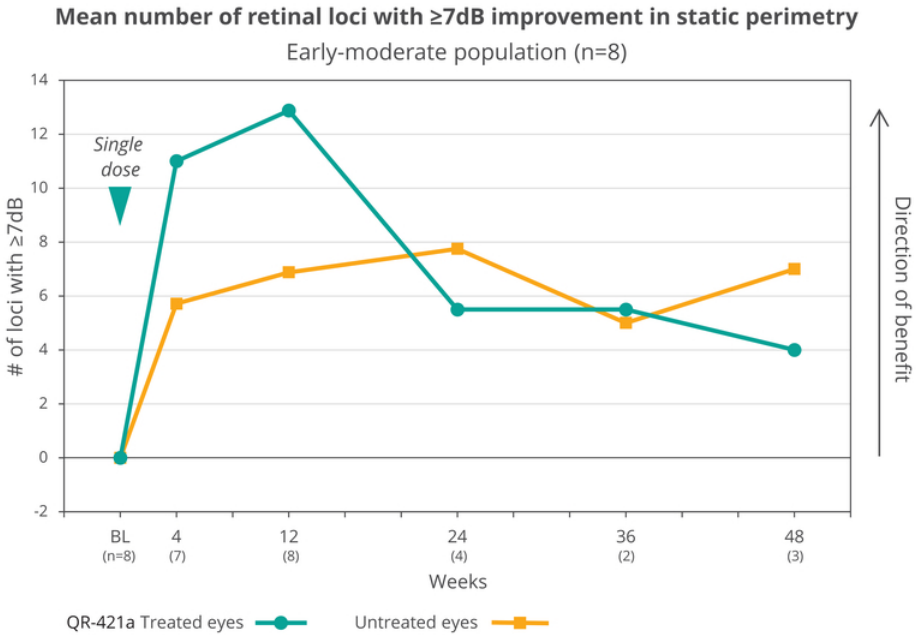
Mean number of retinal loci with ≥ 7 dB improvement in static perimetry

All QR-421a treated patients



- Benefit observed in treated eyes vs untreated eyes
- Benefit sustained for 9+ months after single dose
- Static perimetry improvement in line with approvable endpoint threshold

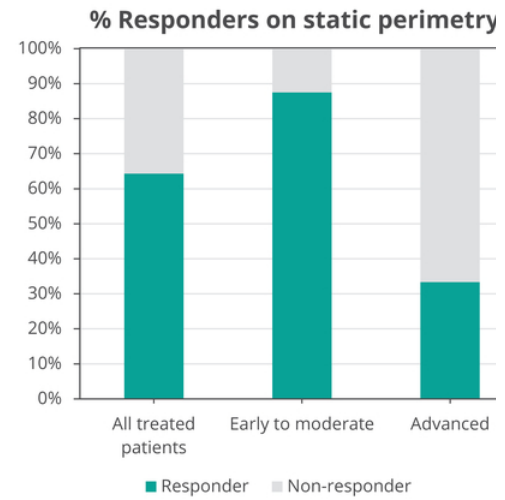
Static perimetry improvement driven by early-moderate population



- Benefit observed in treated eyes vs untreated eyes after single dose
- Magnitude greater in early-moderate population
- Static perimetry improvement in line with approvable endpoint threshold

Static perimetry selected as primary endpoint for early-moderate population

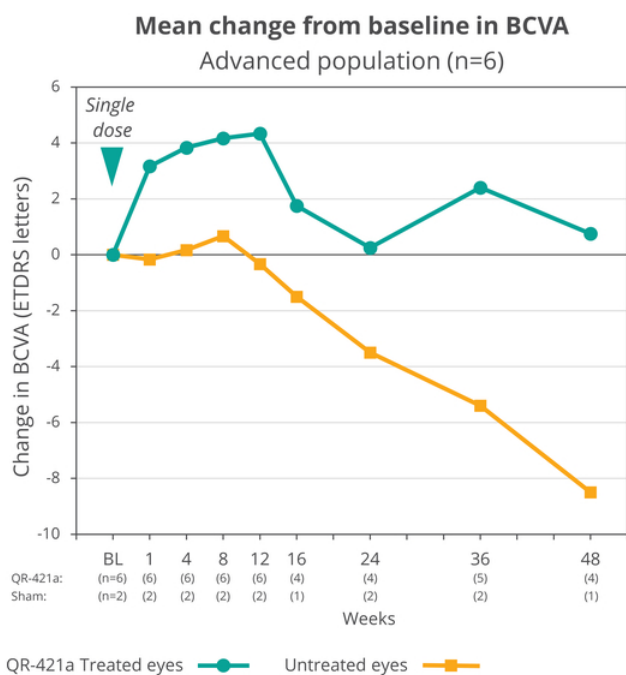
- ✓ Benefit in mean total retinal sensitivity improvement observed in all treated eyes
- ✓ 7dB analysis in all treated group crossed threshold for regulatory approval with a more pronounced benefit in early-moderate patients
- ✓ Effect consistent with half-life with benefit lasting for 24 weeks post a single-dose
- ✓ Static perimetry selected as primary endpoint in early-moderate population



Responder = subject with more retinal loci improved by ≥ 7 dB in the treated eye than in the untreated eye at week 12

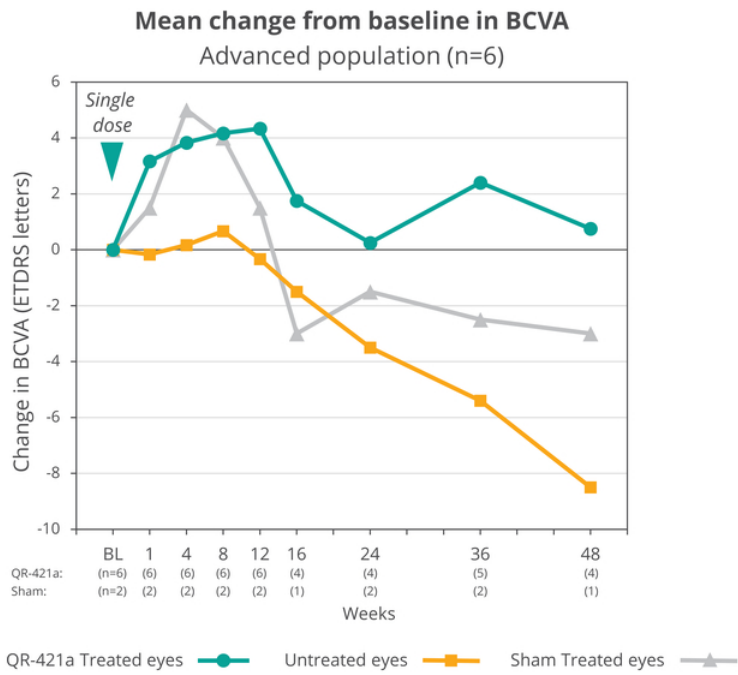
Benefit in vision in treated group, not sham group

Observed in advanced population



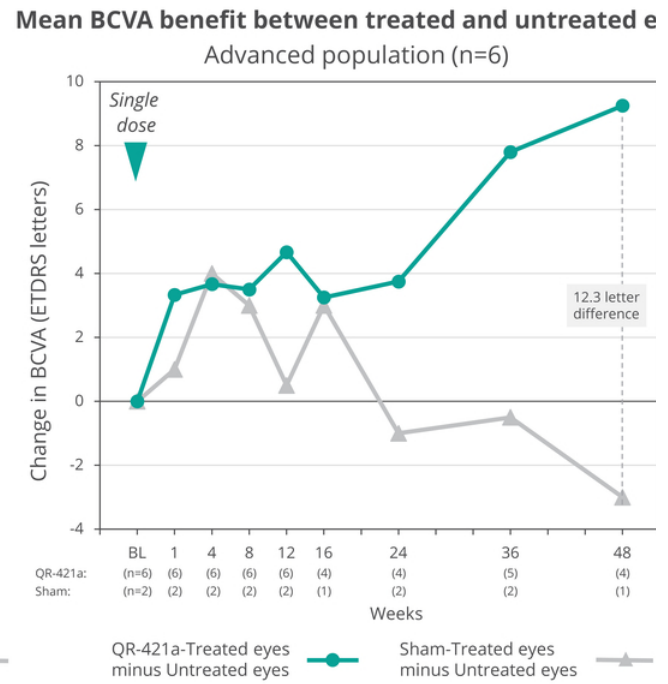
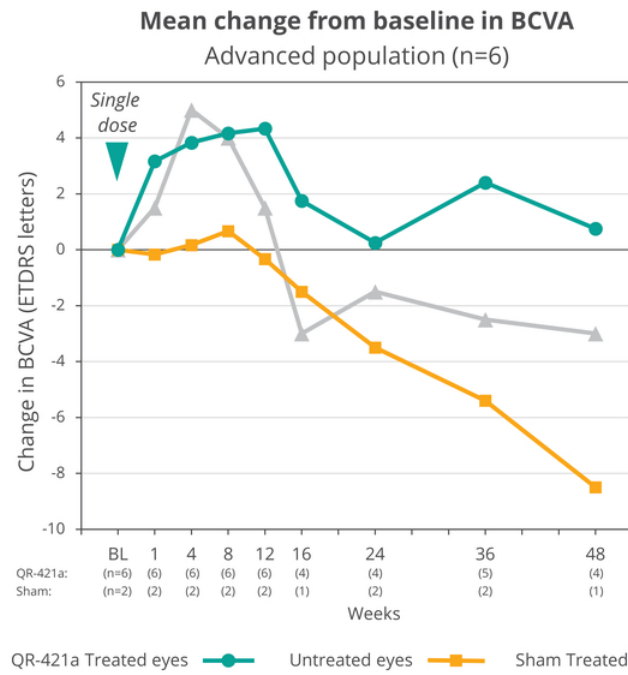
Benefit in vision in treated group, not sham group

Observed in advanced population

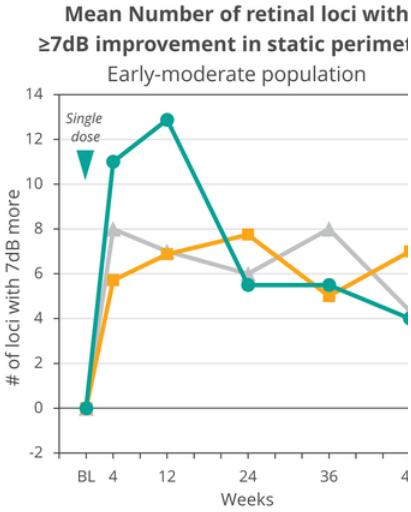
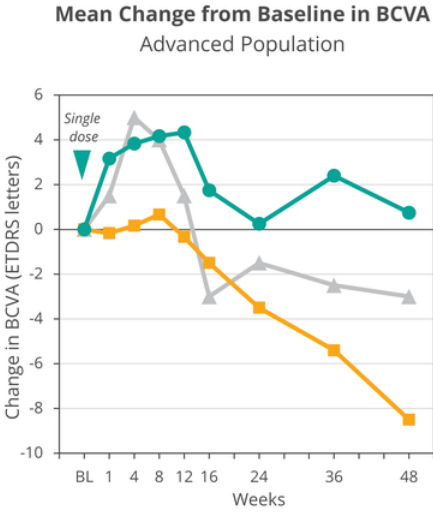
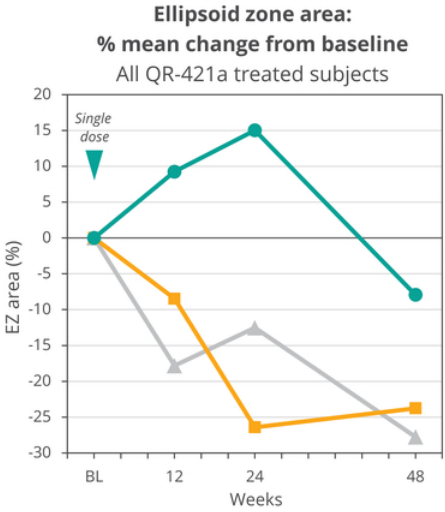


Benefit in vision in treated group, not sham group

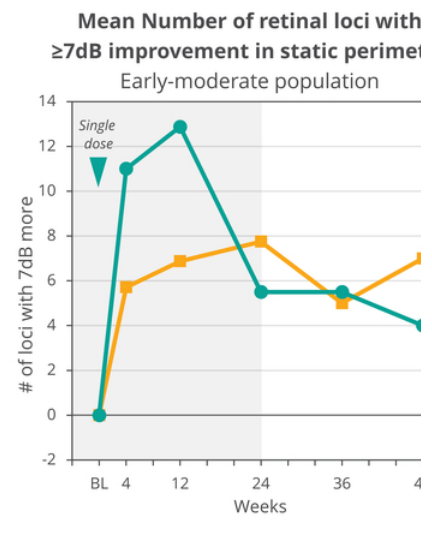
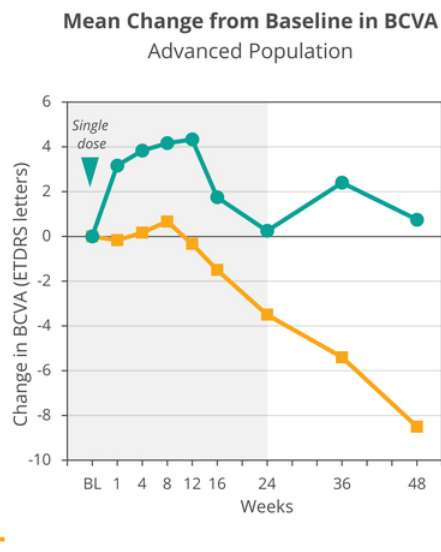
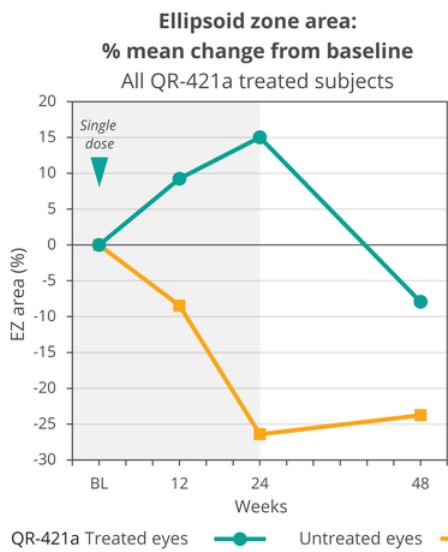
Observed in advanced population



Sham in line with untreated eye and natural history



Dosing interval identified at 6 months



QR-421a Treated eyes —●— Untreated eyes —■—

- Effect sustained for approx. 6 months across endpoints
- Durability in line with half-life and pre-clinical modeling

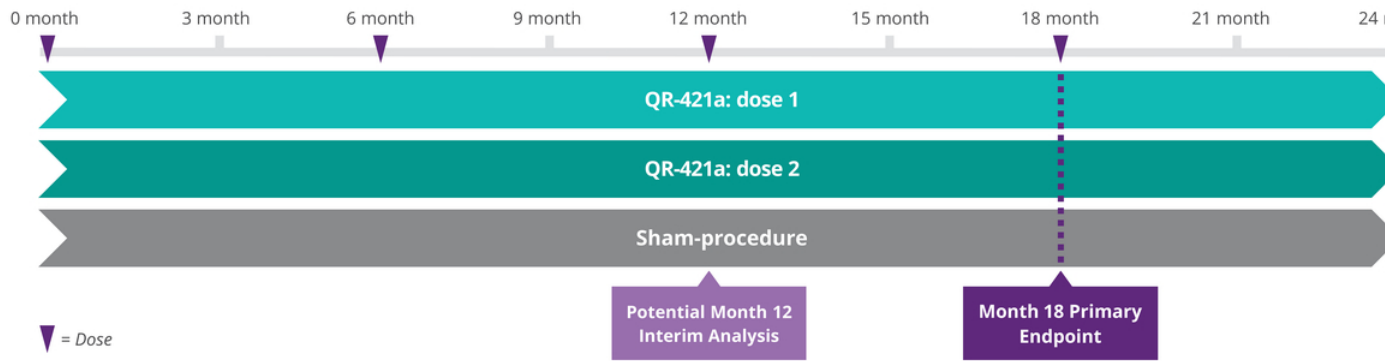
- Redosing interval established at 6 Months

Summary of Phase 1/2 results

- ✓ **QR-421a was well tolerated**
- ✓ **Clinical proof of concept established, consistent with baseline disease, after single dose**
 - ✓ Advanced disease: 100% of patients had a BCVA benefit, 0% in sham group
 - ✓ Early-moderate population: Improvement on Static Perimetry
 - ✓ Supported by key secondary endpoints:
 - ✓ Stabilization of EZ area on OCT imaging (objective measurement)
 - ✓ Stabilization of Microperimetry-based retinal sensitivity
 - ✓ Dose range and dose interval established
- **All information acquired in *Stellar* to design Phase 2/3 studies:**
 - *Sirius* clinical study: a Phase 2/3 study in *advanced patients*
 - *Celeste* clinical study: a Phase 2/3 study in *early-moderate patients*

QR-421a planned Phase 2/3 for Advanced Patients

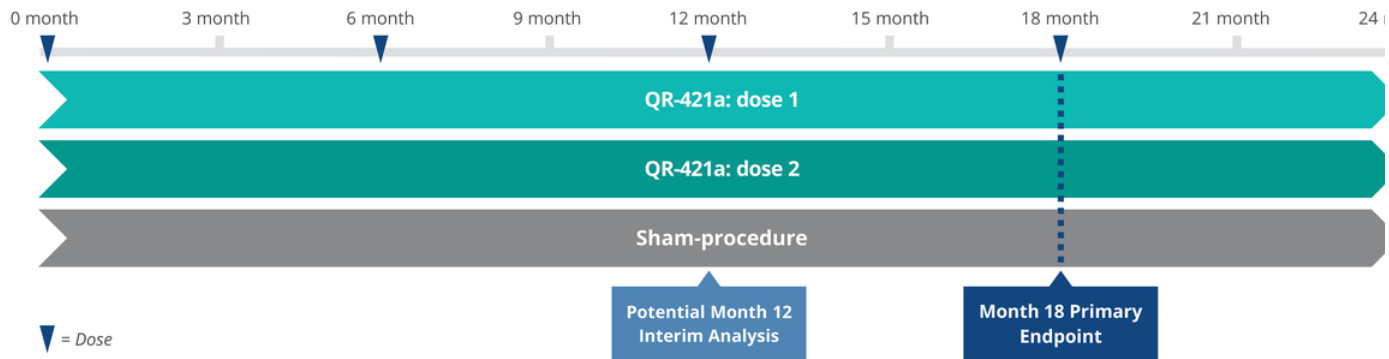
Preliminary design, to be agreed with regulators



- Double-masked, randomized, sham controlled, 24-month, multiple dose study
- Population:
 - Approx. 100 patients
 - Homozygous and heterozygous, Usher and nsRP
- Baseline BCVA \leq 20/40
- Primary endpoint: Visual Acuity
- Key secondary endpoint: OCT, Mobility course, Perimetry
- **Anticipated start of trial: YE 2021**

QR-421a planned Phase 2/3 for Early-Moderate patients

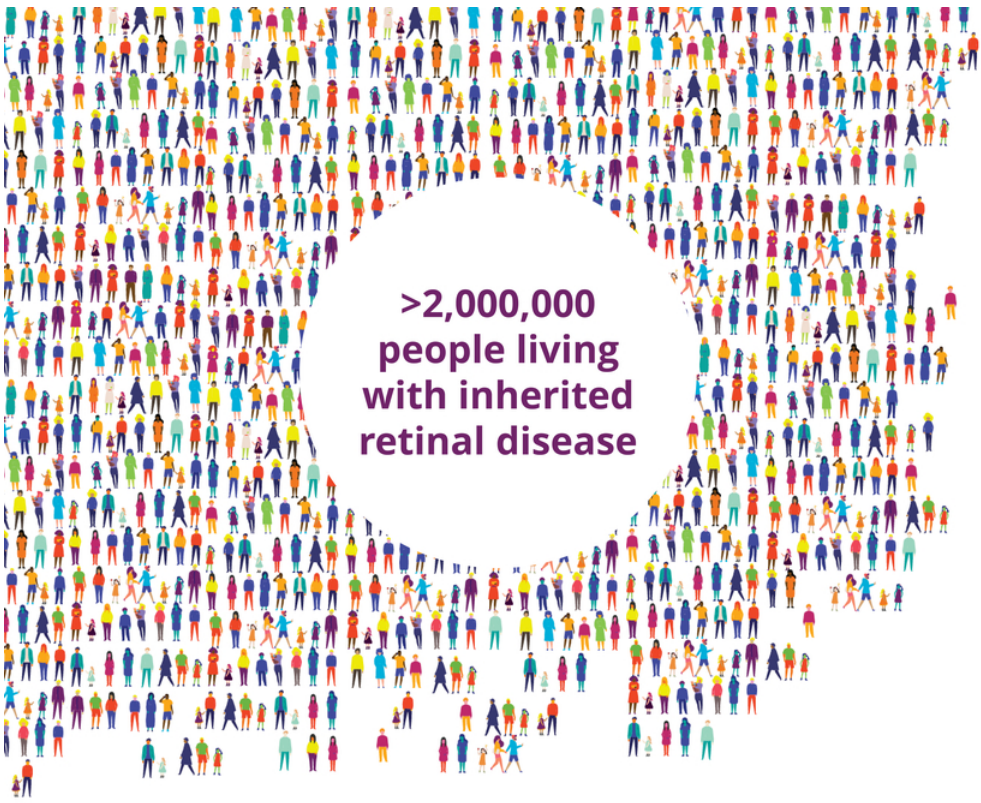
Preliminary design, to be agreed with regulators



- Double-masked, randomized, sham controlled, 24-month, multiple dose study
- Population:
 - Approx. 100 patients
 - Homozygous and heterozygous, Usher and nsRP
- Primary endpoint: Static Perimetry
- Key secondary endpoint: Mobility course, BCVA, OCT
- **Anticipated start of trial: YE 2021**

Next steps

By Daniel A. de Boer, Chief Executive Officer

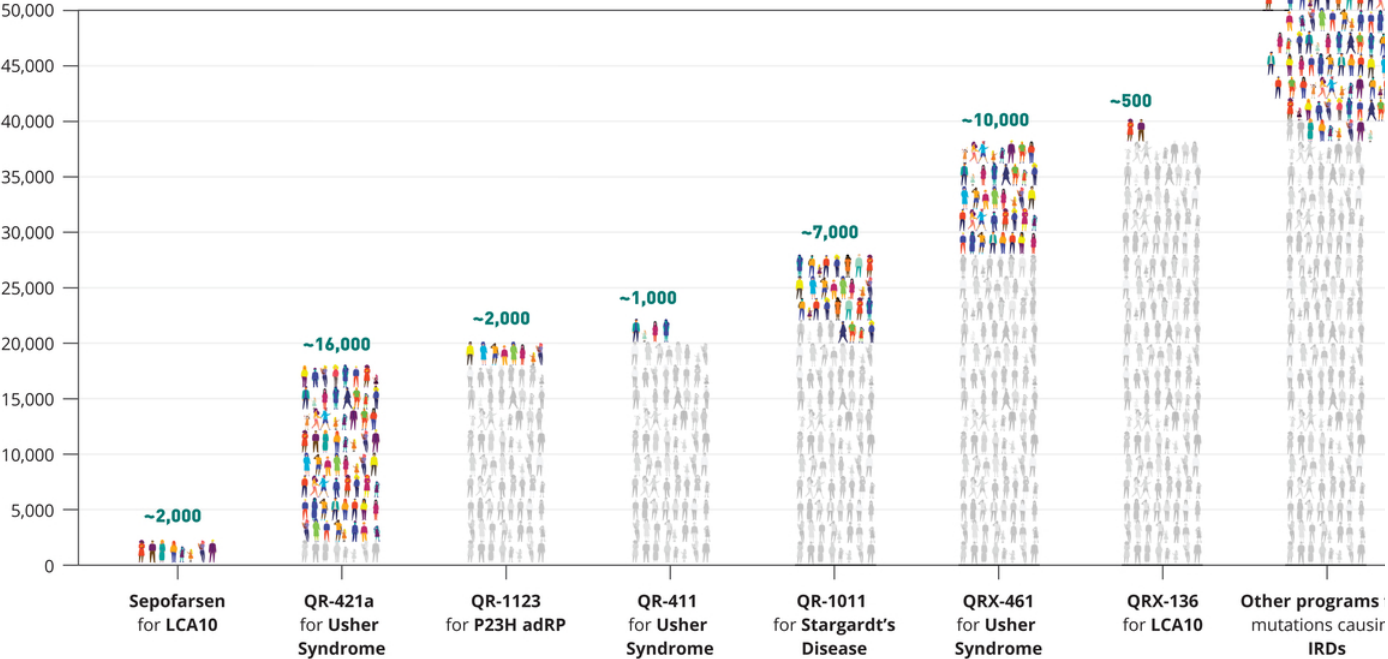


**>2,000,000
people living
with inherited
retinal disease**

**Very few
have a
treatment**



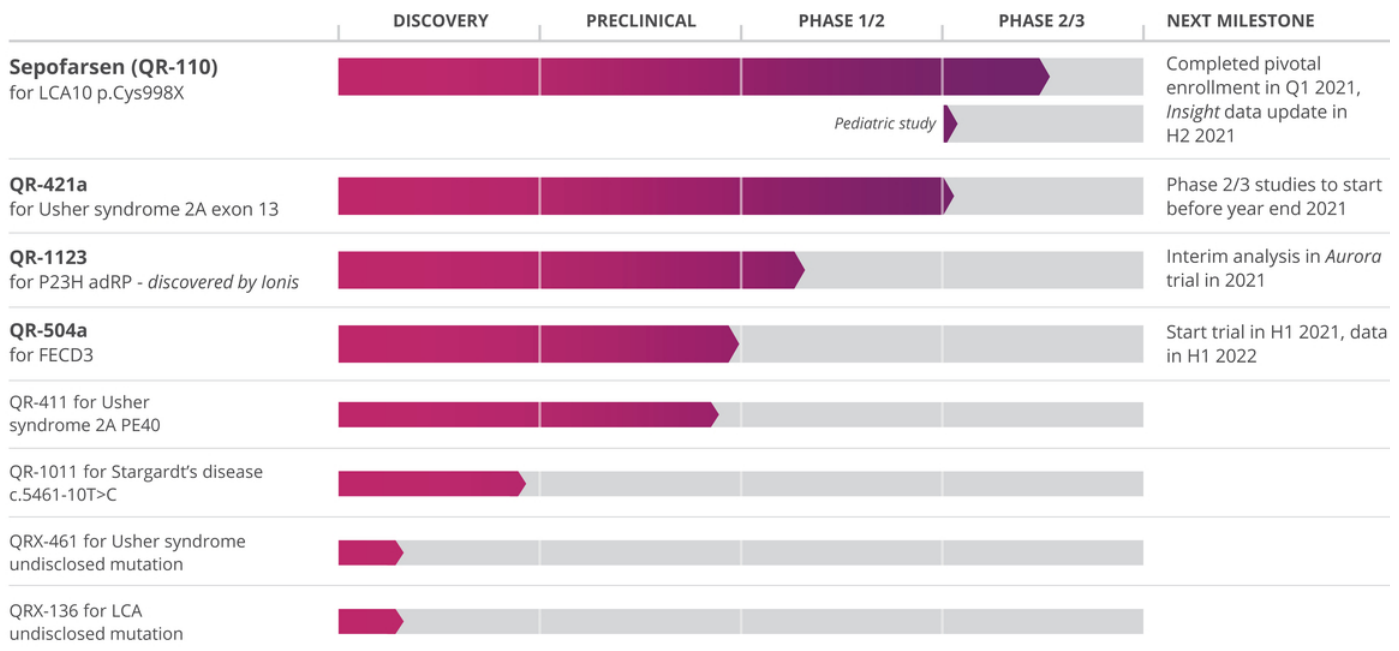
Investigational RNA therapies in pipeline for >100,000 IRD patients



ProQR Therapeutics

Deep pipeline in ophthalmology

With multiple near-term catalysts



ProQR Inherited Retinal Disease Strategy

Mutation specific medicines for IRDs



Patient focused

- >2,000,000 patients worldwide without a treatment
- Large unmet need
- Engagement with patient communities globally



Proven discovery engine

- >50 molecules in pipeline for IRD causing mutations
- Validated scientific platform
- Favorable therapeutic profile in IRD: long half life, IVT administration



Strong translational platform

- Predictive translational platform based on human retinal organoids
- *In vitro/in vivo* correlation



Integrated clinical development

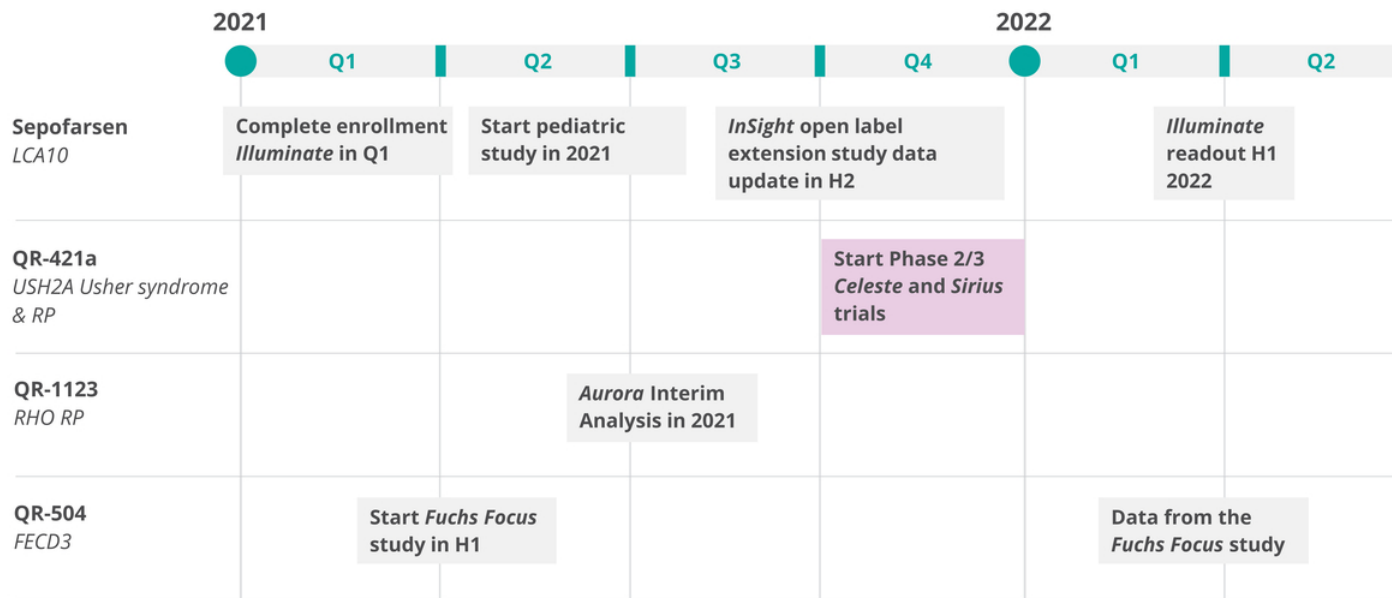
- Deep network in IRD specialist clinical sites in Europe and Americas
- Vast experience in ophthalmic development



Synergistic commercial infrastructure

- ~35 specialist sites across EU and US see >80% of the patients
- Specialized sites see patients with all different IRDs
- Allowing for cross-portfolio synergies
- IVT administration provides access advantage

Full catalyst calendar



Cash runway into 2023



Q&A



**IT'S IN
OUR RNA**
