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 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.
Agenda

1. Introduction
Daniel de Boer

2. Results of Stellar Phase 1/2
Aniz Girach, MD

3. Next steps
Daniel de Boer

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*
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.

Illustrative
Patient baseline disease stage informs endpoints

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

Visual Field
As measured by Static Perimetry

Visual Acuity
As measured by BCVA (Best Corrected Visual Acuity)

Early-moderate disease ↔ Advanced disease

Direction of decline

Visual Field (Degrees)

Age (years)

0 50

BCVA (LogMAR (Snellen))

0 (20/20)
1 (20/200)
2 (CF)
3 (HM)
4 (LP)

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

Enrollment completed; 2\textsuperscript{nd} and final Interim Analysis conducted

\textbf{ProQR Therapeutics}

\textbf{Stellar Phase 1/2 trial}
- Randomized, sham masked, single ascending dose, global multicenter, 24-month study

\textbf{Key endpoints include:}
- Visual acuity (VA): Best-Corrected VA
- Visual field: Static perimetry, microperimetry, dark-adapted chromatic (DAC) perimetry
- Optical Coherence Tomography (OCT) Imaging

\textbf{Goal: to identify for next trial:}
- Registration endpoint(s)
- Dose, dosing regimen
- Population

\textbf{Diagram:}
- Cohort 1: 50 µg (n=4)
- Cohort 2: 100 µg (n=4)
- Cohort 2B: 100 µg Homozygous (n=3)
- Cohort 3: 200 µg Homozygous (n=3)

0 month • 1 month • 3 months • 24 months total

\textbf{Notes:}
- DS = Dose in one eye
- MC = DSMC review
Demographics and disposition

Enrolled Population: n=20

Treated: n=14
- Early-moderate: n=8
  - 12-week follow-up: n=8
  - 24-week follow-up: n=5
  - 36-week follow-up: n=3
  - 48-week + follow-up: n=3
- Advanced: n=6
  - 12-week follow-up: n=6
  - 48-week + follow-up: n=5
  - 36-week follow-up: n=5
  - 24-week follow-up: n=4

Sham: n=6
- 12-week follow-up: n=6
- 24-week follow-up: n=5
- 36-week follow-up: n=5
- 48-week + follow-up: n=4

<table>
<thead>
<tr>
<th>n</th>
<th>Mean age</th>
<th>Mean VA (TE)</th>
<th>Gender</th>
<th>Genotype</th>
<th>Disease stage</th>
<th>Disease type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Early-moderate</td>
<td>advanced nsRP</td>
</tr>
<tr>
<td>QR-421a treated</td>
<td>14</td>
<td>48</td>
<td>66</td>
<td>4</td>
<td>10</td>
<td>64%</td>
</tr>
<tr>
<td>Sham</td>
<td>6</td>
<td>43</td>
<td>68</td>
<td>4</td>
<td>2</td>
<td>17%</td>
</tr>
</tbody>
</table>

Early-moderate disease: baseline VA ≥ 70 letters (20/40)
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

Mean BCVA benefit between treated and untreated eyes
Advanced population (n=6)

- 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

QR-421a Treated eyes minus untreated eyes
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 eyes

Measuring retinal sensitivity in central visual field

Mean change from baseline in microperimetry seeing zones
All QR-421a treated subjects

- 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

Responders by baseline characteristics
at week 48 or last observation carried forward (n=14)

Responders by baseline characteristics and dose
at week 48 or last observation carried forward (n=7)
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

---

**Mean total retinal sensitivity improvement using static perimetry**

All QR-421a-treated patients (n=14)

- **Single dose**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>BL (n=14)</th>
<th>4 (10)</th>
<th>12 (13)</th>
<th>24 (8)</th>
<th>36 (4)</th>
<th>48 (7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total retinal sensitivity (dB)</td>
<td>QR-421a Treated eyes minus Untreated eyes</td>
<td>0</td>
<td>10</td>
<td>20</td>
<td>30</td>
<td>40</td>
</tr>
</tbody>
</table>
Improvement in treated eyes on static perimetry

Measuring retinal sensitivity in peripheral visual field

- 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 ≥7dB 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

Mean change from baseline in BCVA
Advanced population (n=6)
Benefit in vision in treated group, not sham group

Observed in advanced population

Mean change from baseline in BCVA
Advanced population (n=6)
Benefit in vision in treated group, not sham group

Observed in advanced population

Mean change from baseline in BCVA
Advanced population (n=6)

Mean BCVA benefit between treated and untreated eyes
Advanced population (n=6)
Sham in line with untreated eye and natural history

**Ellipsoid zone area:**
% mean change from baseline
All QR-421a treated subjects

**Mean Change from Baseline in BCVA**
Advanced Population

**Mean Number of retinal loci with ≥7dB improvement in static perimetry**
Early-moderate population

QR-421a Treated eyes
Untreated eyes
Sham Treated eyes
Dosing interval identified at 6 months

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

**Ellipsoid zone area:**

% mean change from baseline

All QR-421a treated subjects

<table>
<thead>
<tr>
<th>Weeks</th>
<th>BL</th>
<th>12</th>
<th>24</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>EZ area (%)</td>
<td>-30</td>
<td>-25</td>
<td>-20</td>
<td>-15</td>
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</table>

**Mean Change from Baseline in BCVA**

Advanced Population

<table>
<thead>
<tr>
<th>Weeks</th>
<th>BL</th>
<th>1</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>24</th>
<th>36</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in BCVA (ETDRS letters)</td>
<td>-10</td>
<td>-8</td>
<td>-6</td>
<td>-4</td>
<td>-2</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

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

Early-moderate population

<table>
<thead>
<tr>
<th>Weeks</th>
<th>BL</th>
<th>4</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td># of loci with ≥7dB more</td>
<td>10</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

QR-421a Treated eyes — Untreated eyes — Untreated eyes
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 ≤ 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

- Sepofarsen for LCA10
- QR-421a for Usher Syndrome
- QR-1123 for P23H adRP
- QR-411 for Usher Syndrome
- QR-1011 for Stargardt’s Disease
- QRX-461 for Usher Syndrome
- QRX-136 for LCA10

Other programs for mutations causing IRDs
# Deep pipeline in ophthalmology

*With multiple near-term catalysts*

<table>
<thead>
<tr>
<th></th>
<th>DISCOVERY</th>
<th>PRECLINICAL</th>
<th>PHASE 1/2</th>
<th>PHASE 2/3</th>
<th>NEXT MILESTONE</th>
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<tbody>
<tr>
<td><strong>Sepofarsen (QR-110)</strong></td>
<td></td>
<td></td>
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<td>Completed pivotal enrollment in Q1 2021, <strong>Insight</strong> data update in H2 2021</td>
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<tr>
<td>for LCA10 p.Cys998X</td>
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<tr>
<td><strong>QR-421a</strong></td>
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<td>Phase 2/3 studies to start before year end 2021</td>
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<tr>
<td>for Usher syndrome 2A exon 13</td>
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<tr>
<td><strong>QR-1123</strong></td>
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<td></td>
<td>Interim analysis in <strong>Aurora</strong> trial in 2021</td>
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<tr>
<td>for P23H adRP - <em>discovered by Ionis</em></td>
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<tr>
<td><strong>QR-504a</strong></td>
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<td>Start trial in H1 2021, data in H1 2022</td>
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<tr>
<td>for FECD3</td>
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<tr>
<td>QR-411 for Usher syndrome 2A PE40</td>
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<td><strong>QR-1011</strong></td>
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<td>for Stargardt’s disease c.5461-10T&gt;C</td>
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<td><strong>QRX-461</strong></td>
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<td>for Usher syndrome undisclosed mutation</td>
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<td><strong>QRX-136</strong></td>
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<tr>
<td>for LCA undisclosed mutation</td>
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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

<table>
<thead>
<tr>
<th>2021</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>2022</th>
<th>Q1</th>
<th>Q2</th>
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<tr>
<td>Sepofarsen</td>
<td>Complete enrollment <em>Illuminate</em> in Q1</td>
<td>Start pediatric study in Q2</td>
<td><em>InSight</em> open label extension study data update in H2</td>
<td>Q4 Start pediatric study in 2021</td>
<td>QR-421a USH2A Usher syndrome &amp; RP</td>
<td>QR-1123 RHO RP</td>
<td>QR-504 FECD3</td>
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<tr>
<td>LCA10</td>
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**2021**
- **QR-421a** USH2A Usher syndrome & RP
  - Start pediatric study in 2021
  - *InSight* open label extension study data update in H2
- **QR-1123** RHO RP
  - *Aurora* Interim Analysis in 2021
- **QR-504** FECD3
  - Start *Fuchs Focus* study in H1

**2022**
- **QR-421a** USH2A Usher syndrome & RP
  - Start Phase 2/3 *Celeste* and *Sirius* trials
- **QR-1123** RHO RP
  - **Q1** Start pediatric study in 2021
  - **Q2** *Illuminate* readout H1 2022
- **QR-504** FECD3
  - **Q4** Data from the *Fuchs Focus* study

**Cash runway into 2023**
IT'S IN OUR RNA