QR-010 penetrates the CF-like mucus barrier *in vitro* and *in vivo*.
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 statements regarding our strategy, future operations, future pre-clinical and clinical trial plans, future financial position, future revenues, projected costs, prospects, 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 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 our filings made with the Securities and Exchange Commission, including certain sections of our annual report filed on Form 20-F, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make.
QR-010; 33 mer ssRNA oligonucleotide

ΔF508

Reversal of cystic fibrosis phenotype in a cultured ΔF508 cystic fibrosis transmembrane conductance regulator cell line by oligonucleotide insertion
In vivo delivery:
• In vivo biodistribution is similar in WT mice and betaENaC over-expressing mice with a CF lung phenotype

In vitro delivery and stability:
• QR-010 diffuses rapid through CF-like mucus after single and repeated nebulization
• QR-010 remains stable in CF sputum
• QR-010 is stable in the presence of CF lung bacteria
• QR-010 is stable in the presence of clinically relevant levels of CF standard-of-care
Respiratory: QR-010 for cystic fibrosis

**GLP Tox**
- 28 days in mice
- No DLT up to high dose (30mg/kg) for 28 days in monkeys

**Functional Restoration of CFTR Response**
- Two in vitro models:
  - MQAE
  - Ussing Chamber
- Up to 80% restoration of wild-type CFTR response in two independent ΔF508 mouse assays:
  - Saliva Secretion assay
  - Nasal Potential Difference assay
- Work around mode of action ongoing

**PQ-010-001 Phase 1b Clinical Study**
- Data readout mid / late 2016:
  - Safety & Tolerability + Exploratory Efficacy Endpoints
  - 64 homozygous ΔF508
  - Nebulized delivery into the lung

**PQ-010-002 Proof of Concept Clinical Study**
- Data readout mid / late 2016:
  - Nasal Potential Difference
  - 8 homo- 8 heterozygous ΔF508
  - Local delivery into the nose

**Inhaled Administration to the Lung**
- In vitro CF mucus penetration
- Similar biodistribution between wild-type and mice with CF lung phenotype
QR-010: *In vitro*
QR-010: Airway surface layer

Potential barrier

QR-010 diffuses rapid through normal and CF–like mucus

Video of QR-010 diffusion through an in vitro mucus layer. Video is sped up ~10 fold from real time. Green indicates calcein stained cells and QR-010 is in red.
QR-010 diffusion speed unchanged by repeated nebulization

**Diffusion speed in CF-like mucus after repeated nebulisation**

<table>
<thead>
<tr>
<th># nebulisation</th>
<th>Diffusion speed (μm/second)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1x</td>
<td>0.4</td>
</tr>
<tr>
<td>2x</td>
<td>0.5</td>
</tr>
<tr>
<td>5x</td>
<td>0.5</td>
</tr>
</tbody>
</table>

(1.5 week time frame)

n.s.
QR-010 levels remain stable in CF patient sputum

QR-010 stability in CF sputum

Percentage QR-010 compared to t=0

10 µg/ml QR-010

100 µg/ml QR-010

Incubation time (hrs)

No significant differences found
QR-010 is stable in the presence of CF lung bacteria

QR-010 stability and uptake/binding with CF micro-organisms

No significant differences found
QR-010 is stable in the presence of clinically relevant levels of CF standard-of-care therapies.
QR-010: *In vivo*
QR-010: betaENaC mice (Scnn1b-Tg)

Introduction

In vivo biodistribution is similar in WT and betaENaC over-expressing mice with a CF lung phenotype
Conclusions

• QR-010 diffuses rapidly through CF-like mucus, and is unaffected by repeated nebulization
  • Size (~3nm) and charge of QR-010 (highly negative) allows diffusion

• QR-010 levels remain stable in:
  • patient CF sputum for at least 48 hrs
  • in the presence of CF prevalent lung microorganisms for at least 24 hrs, and in vitro uptake/binding to bacteria is not an issue.
  • in the presence of clinically relevant levels of inhaled CF standard of care for at least 24 hrs

• In vivo biodistribution is unaffected by the CF lung phenotype
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Study locations

North America

- Penn State Milton S. Hershey Medical Center, Hershey, PA
- Texas University Southwestern Medical Center, Dallas, TX
- University of Washington Medical Center, Seattle, WA
- Nationwide Children’s Hospital, Columbus, OH
- Stanford University, Palo Alto Stanford, CA
- Medical University of South Carolina, Charleston, SC
- University of Kansas Medical Center, Kansas City, KS
- Massachusetts General Hospital Cystic Fibrosis Clinical Research Center, Boston, MA
- Boston Children’s Hospital, Boston, MA
- University of Calgary, Calgary, Alberta, Canada
- Northwestern University Depart of Medicine – Pulmonary and Critical Care, Chicago, IL
- National Jewish Health, Denver, CO
- Cincinnati Children’s Hospital, Cincinnati, OH
- University of Alabama, Birmingham, AL

Europe

- Fakultní nemocnice v Motole, Praha, Czech Republic
- Universitair Ziekenhuis Leuven, Leuven, Belgium
- Universitair Ziekenhuis Brussel, Brussel, Belgium
- Trust-Wolfson Northern Ireland Clinical Research Facility and Queens University Belfast, Belfast, Ireland
- Royal Brompton Hospital – Adult Cystic Fibrosis Centre, London, England
- Bispebjerg Universitetshospital, København, Danmark
- Klinikum der Universität München, München, Germany
- Charite Universitätsmedizin Berlin, Berlin, Germany
- Centro di Ricerche Cliniche - Azienda Ospedaliera Universitaria Integrata di Verona, Verona, Italy
- Hôpital Necker – Enfants Malades, Paris, France
- CHU de Nantes – Hôpital Nord Laennec (HGRL) – Pneumologie, Nantes, France