QR-010
An RNA therapy, restores CFTR function using *in vitro* and *in vivo* models of ΔF508-CFTR

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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.

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QR-010 restores CFTR activity in vitro:

Ussing Chamber

QR-010 restores CFTR activity in vivo:

NPD + SSA

Delivery of QR-010:

Uptake + Biodistribution + Mucus Diffusion
QR-010 Improves CFTR Activity in Primary F508del HBE Cells

The Effect of QR-010 on CFTR Function is Dose-Dependent

QR-010 restores CFTR function in primary F508del HBE cells *in vitro* in a dose-dependent manner.
QR-010 Restores CFTR-Function in F508del-CFTR Mice as Assessed by NPD

Beumer et al. (2014). Ped Pulm 49(S38):227-228. (NACFC 2014)
QR-010 Restores CFTR-Function in F508del-CFTR Mice in a Dose-Dependent Manner

Beumer et al. (2014). Ped Pulm 49(S38):227-228. (NACFC 2014)
Pulmonary Administration of QR-010 Restores CFTR Function in the Salivary Glands of F508del-CFTR Mice

Beumer et al. (2014). Ped Pulm 49(S38):227-228. (NACFC 2014)
Pulmonary Delivery of QR-010 Results in Systemic Exposure.

QR-010 is Taken up by the Airway Epithelium

Negative Control  (Cy5)  24hrs  48hrs  3 days  7 days  14 days

Cy5-labeled QR-010 in Red – DAPI in Blue

Cy5-Labeled QR-010 Diffuses Through CF-like Mucus

Cy5-labeled QR-010 in red. Calcein stained cells (GFP antibody in Green). Pictures were taken every 2 seconds.
Fast Diffusion of Cy5-labeled QR-010 Through CF-like Mucus

- Within minutes the max. Cy5 signal is reached at the HBE cell layer.
Conclusions

• QR-010 results functional restoration of CFTR activity in:
  ✓ Primary F508del HBE cells as assessed by Ussing chamber.
  ✓ F508del-CFTR mice as assessed by NPD
  ✓ F508del-CFTR mice as assessed by SSA.

• Pulmonary administration of QR-010 shows body-wide distribution and uptake in extra-pulmonary organs.

• QR-010 diffuses quickly through CF-like mucus
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