QRX-411

Antisense oligonucleotide targeting the PE40 mutation in the USH2A gene for treatment of RP in Usher syndrome type II

Presenter
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ARVO Baltimore 2017

Forward looking statements

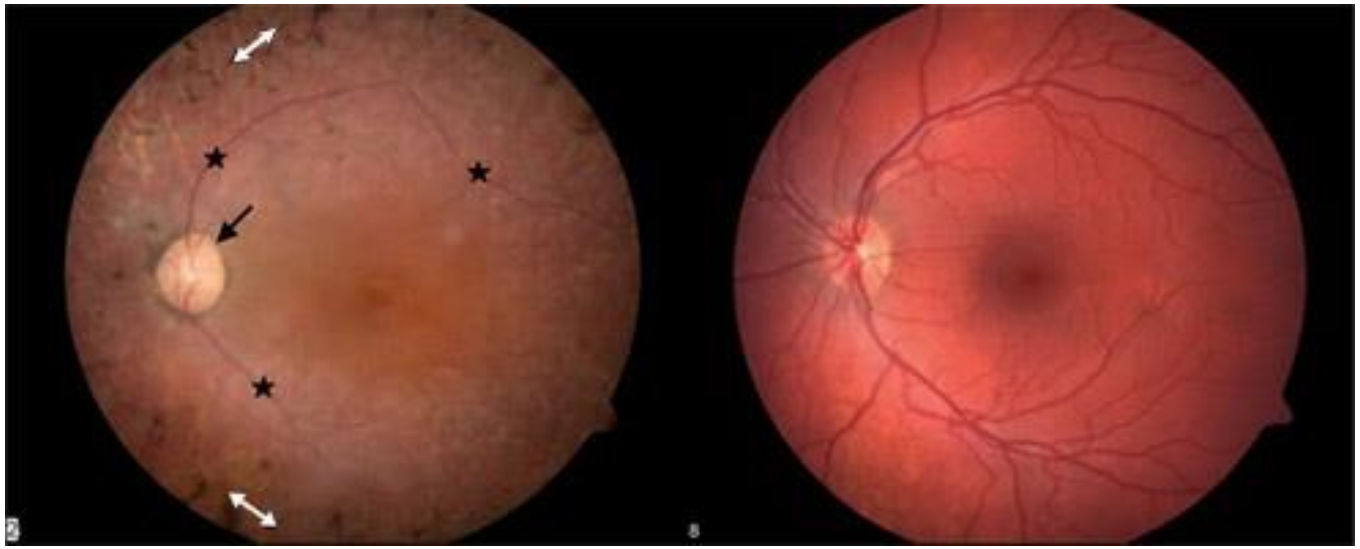
This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including but not limited to, statements regarding our strategy, future operations, future pre-clinical and 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 products, 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 greater detail in the annual report filed on Form 20-F for the year ended December 31, 2016 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.

RP associated with Usher Syndrome

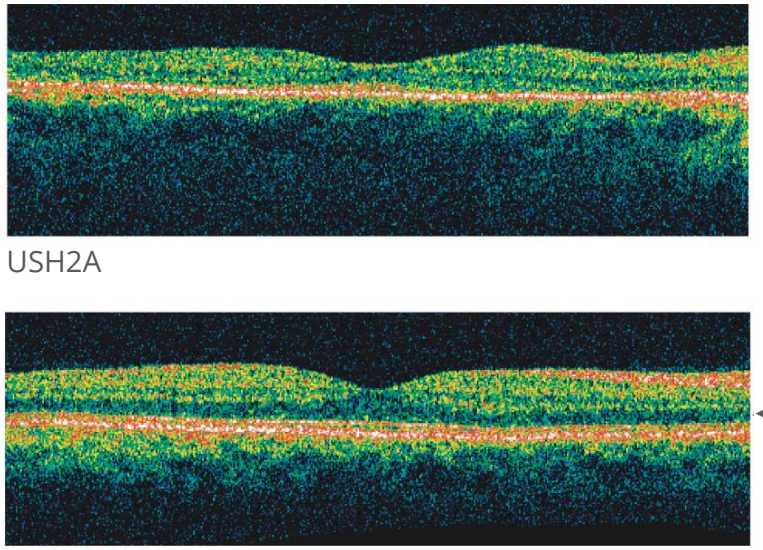
Genetic cause of combined deafness and blindness

Symptoms: Pale optic nerve, thin vessels



USH2A Normal

Degeneration of Outer Nuclear Layer (ONL)



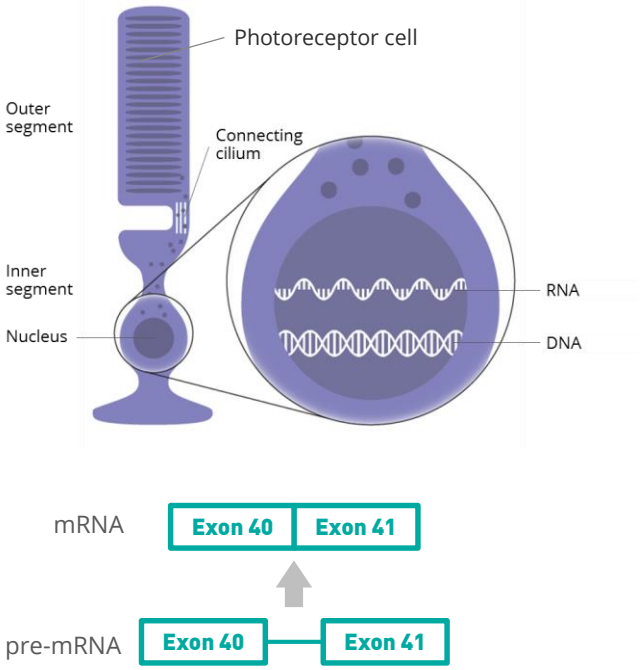
USH2A

Normal

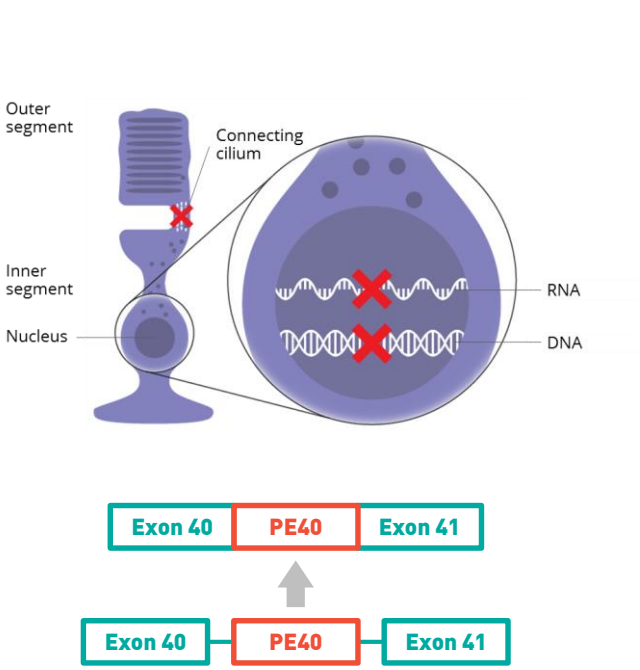
From Sandberg et al. 2008

QRX-411 for RP in Usher Syndrome

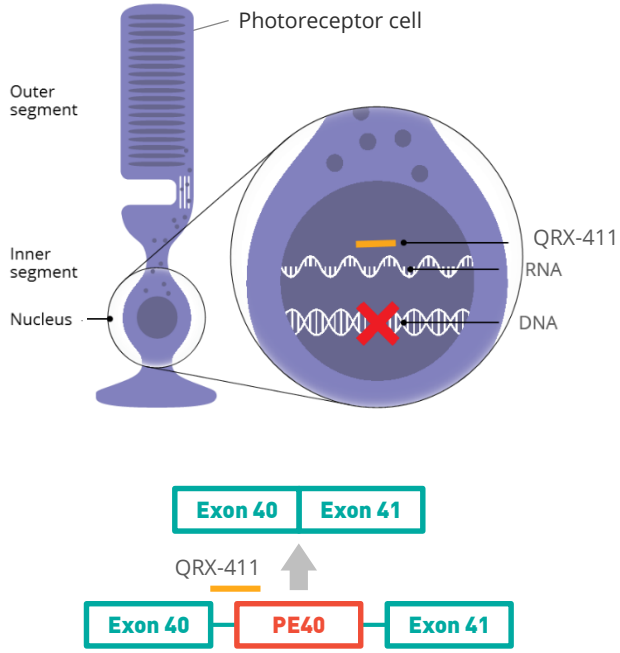
Splice correction for PE40 USH2A mRNA (c.7595-2144A>G mutation)



In wild-type cells
Usherin maintains photoreceptor structure and enables normal protein transport



In PE40 mutant cells
protein Transport
is hampered and the outer segment degenerates



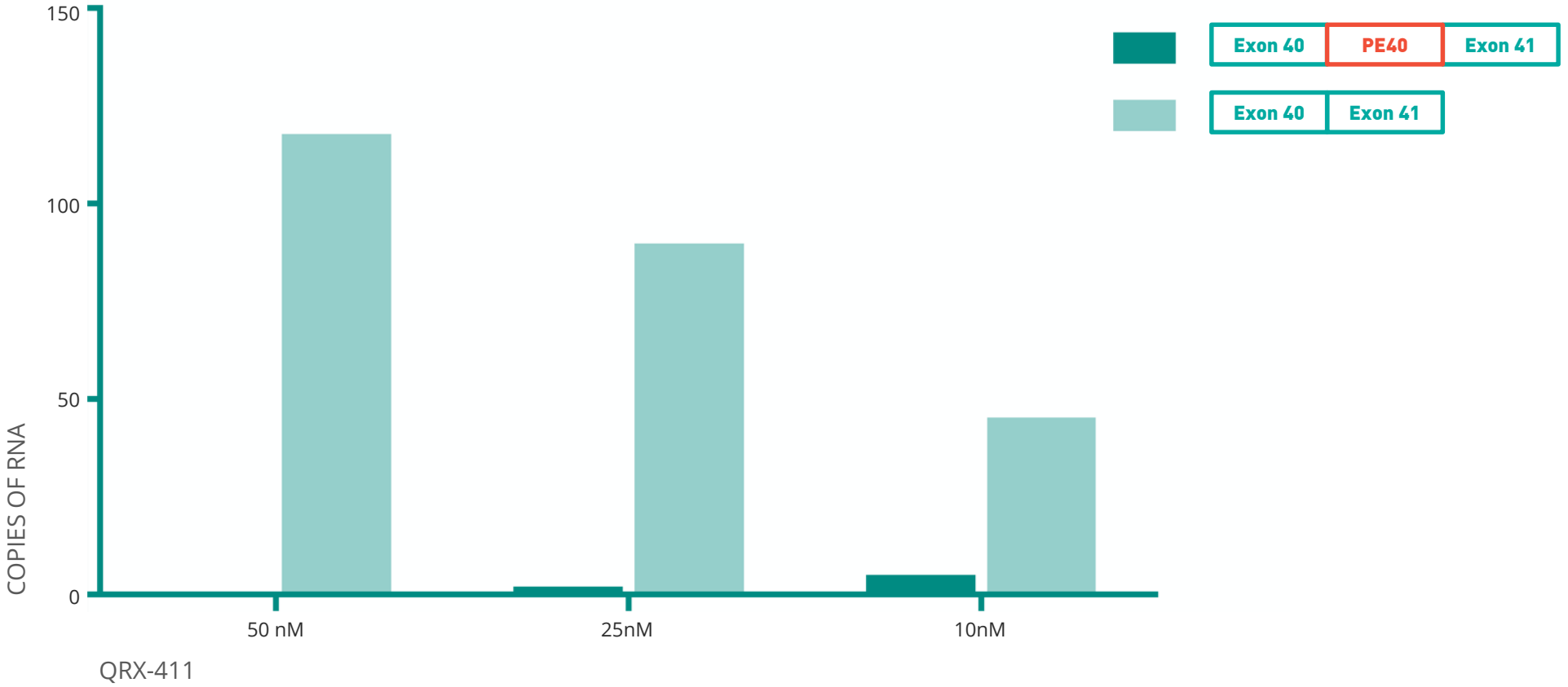
Exclusion of the PE40 region from the mutated mRNA leads to wild-type Usherin protein

QRX-411 overview

- Efficacy data *in vitro* in patient fibroblasts
- Efficacy data in patient-derived optic cups
- *In vivo* localization in mouse retina
- *In vivo* proof of concept in a zebrafish model

QRX-411 restores wild-type RNA in vitro

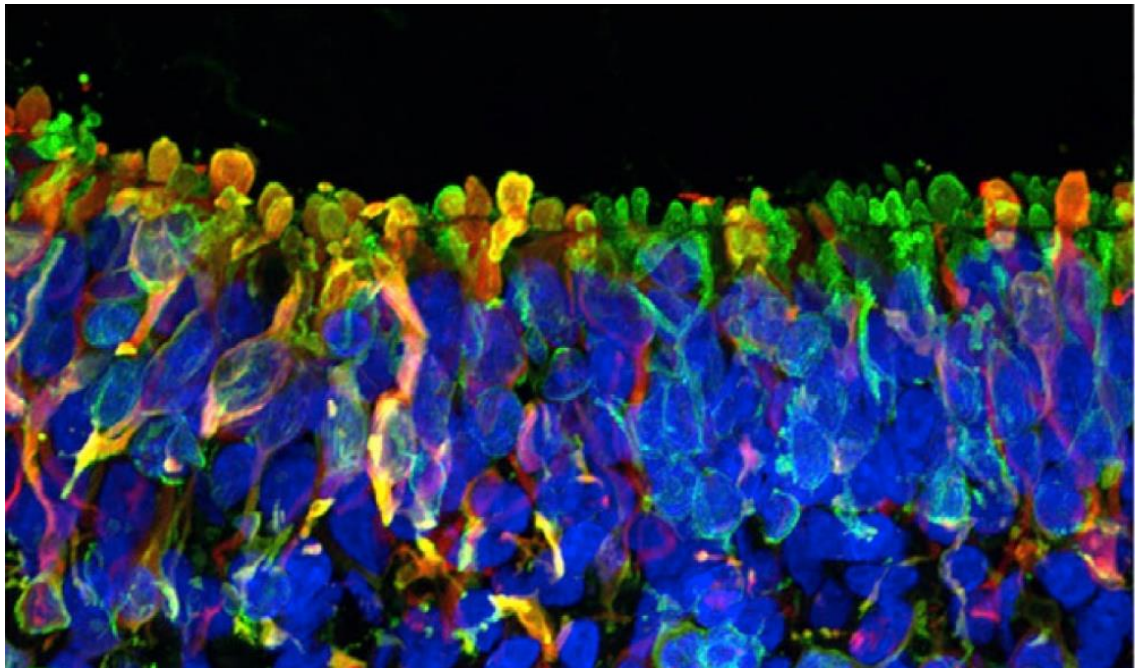
Dose-dependent effect of QRX-411 on WT RNA in patient fibroblasts



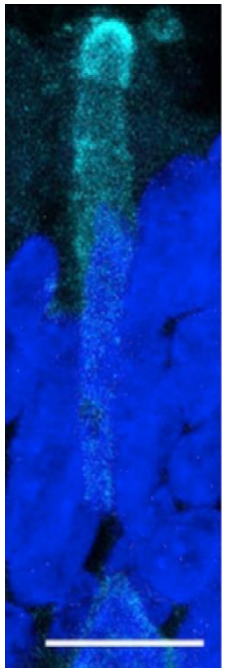
Efficacy testing of QRX-411 in heterozygous patient fibroblasts

Patient-derived iPSC optic cups

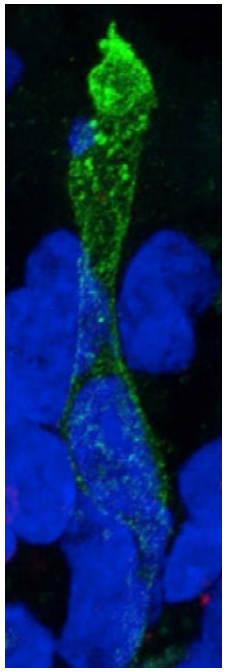
Optic cup is an organoid model containing differentiated photoreceptor cells



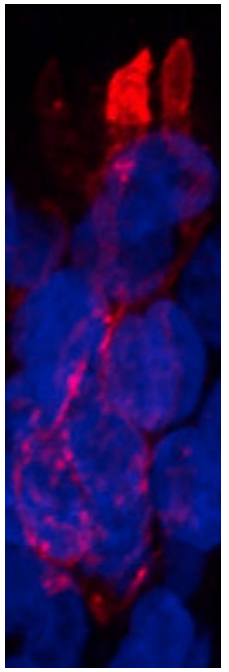
Recoverin cone-arrestin



Detail:
Rhodopsin



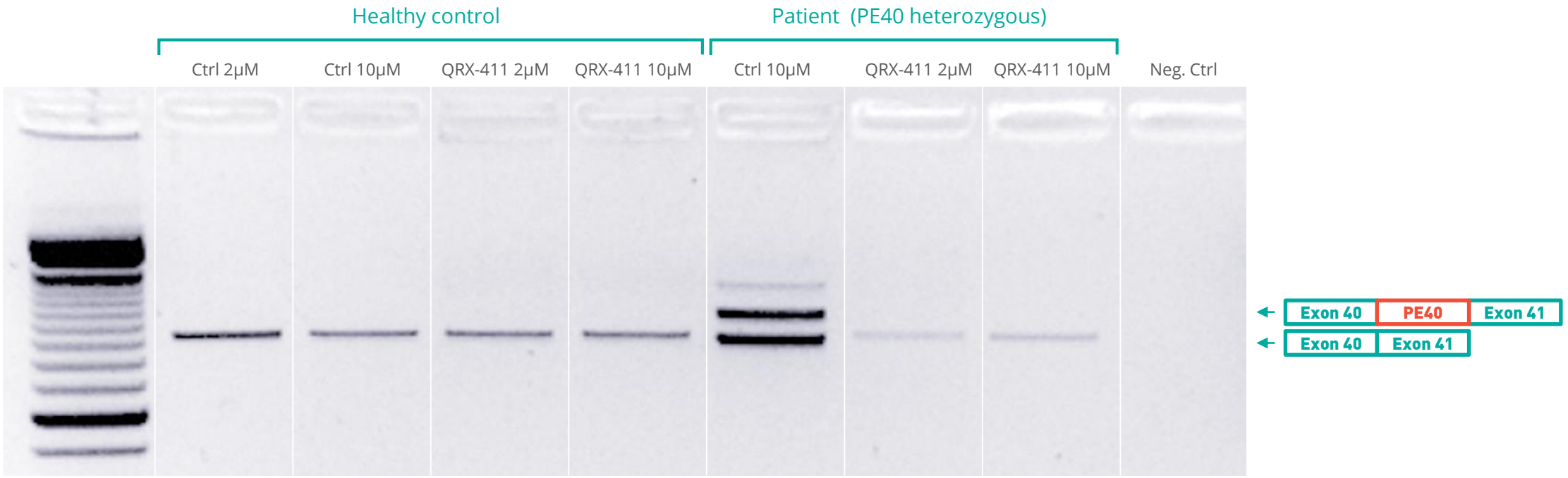
Detail:
L/M-opsin



Detail:
S-opsin

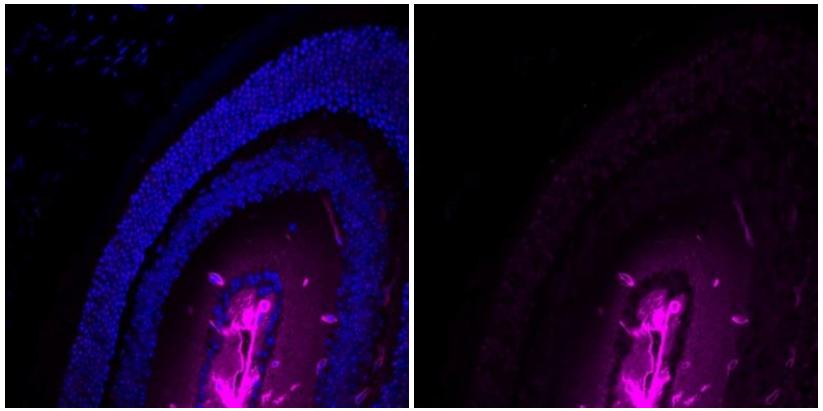
Parfitt et al., 2016

QRX-411 restores WT RNA in patient-derived optic cups

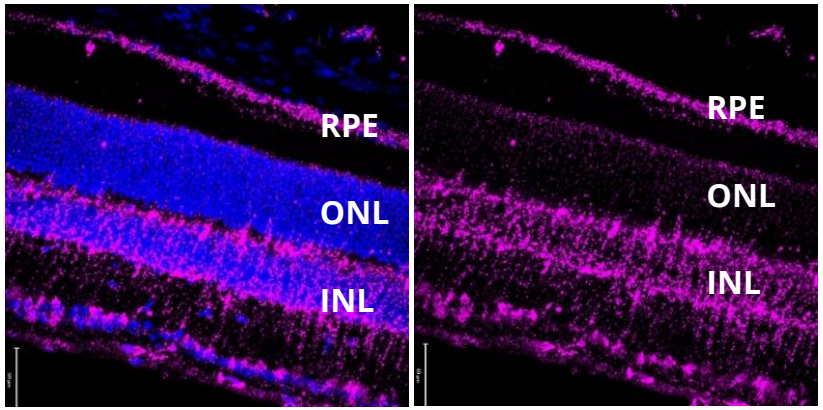


Erwin van Wijk, Radboudumc, Nijmegen, the Netherlands

Efficient delivery of QRX-411 to outer nuclear layer



Immediately post IVT dose

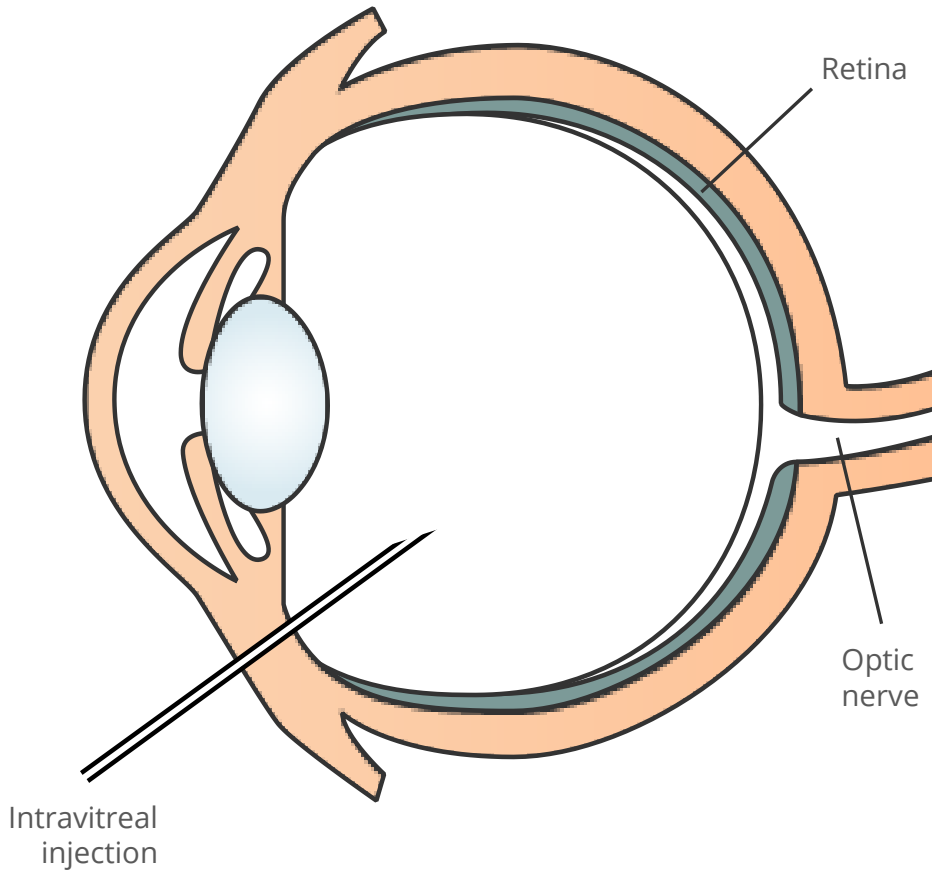


7 days post IVT dose

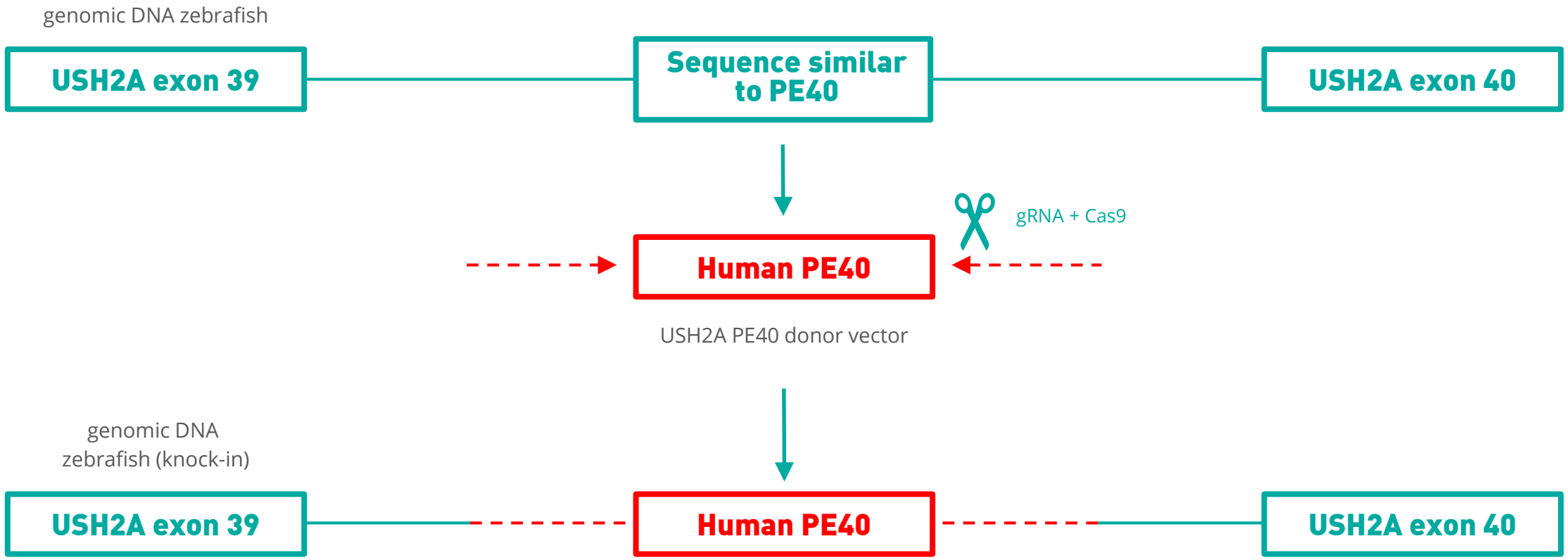
Dose
1µl 25 µg/µl in
C57/Bl6 mice

DAPI

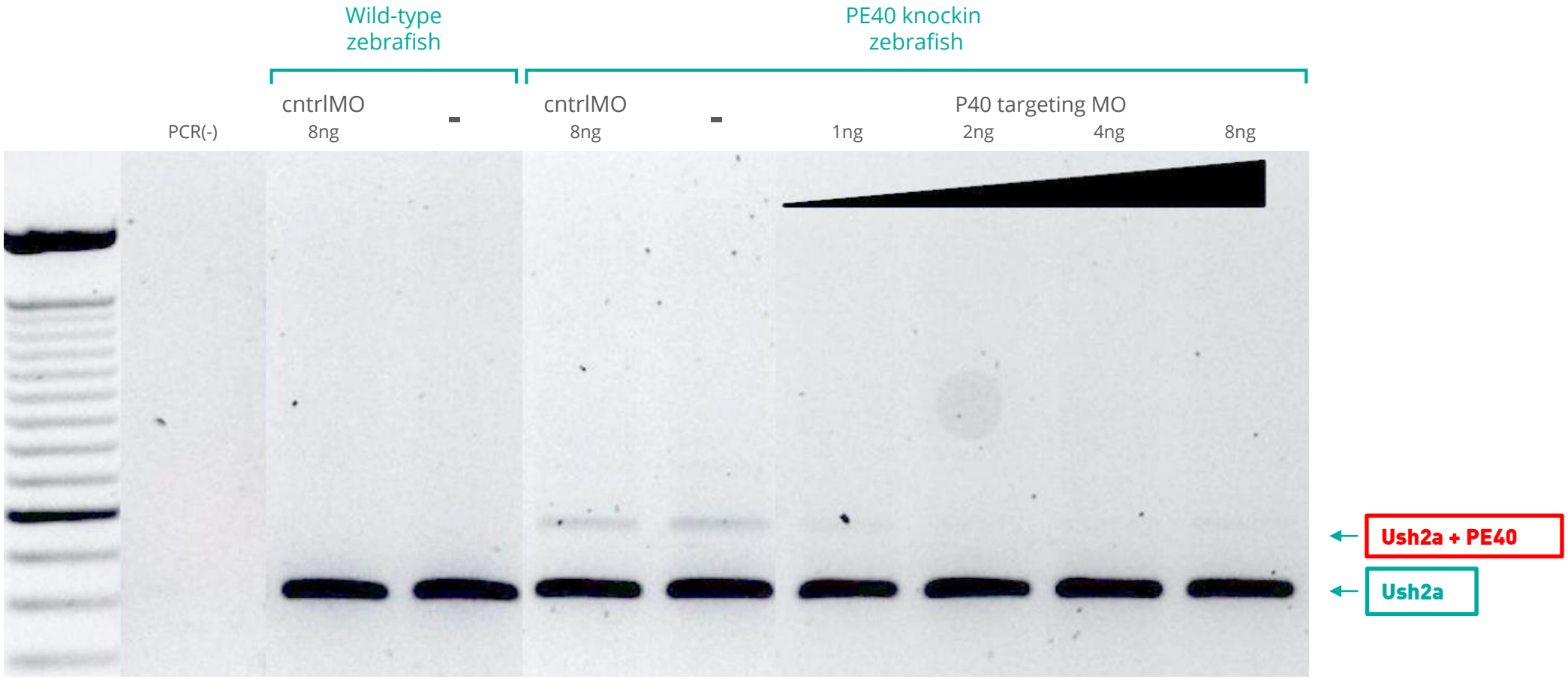
Cy5-QRX-411



Humanized PE40 knock-in zebrafish model



QRX-411 excludes pseudoexon 40 in mutant zebrafish



Erwin van Wijk, Radboudumc, Nijmegen, the Netherlands

Summary: QRX-411 for USH2A PE40

1. mRNA profile restoration

mRNA profile wild-type restoration

2. mRNA profile restoration in eye-cups

mRNA profile shows PE40 Skip in patient–derived eye-cups

3. Local (intravitreal) delivery to the eye

Eye well validated target for oligo's

Efficient delivery to outer nuclear layer in the retina

4. mRNA restoration in fish established

mRNA restoration established

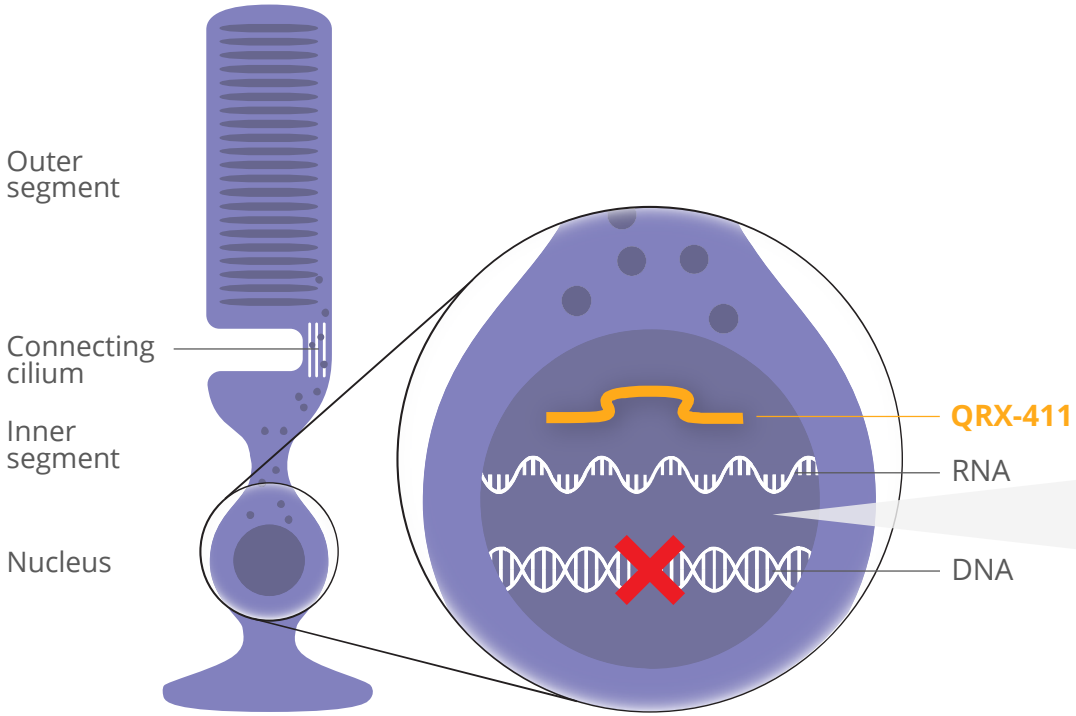
5. Clinical candidate selected

QRX-411 selected as clinical candidate

6. Regulatory

ODD obtained in March 2017 from the European Medical Agency

Summary: QRX-411 for USH2A PE40



QRX-411:

- Single stranded 20-mer RNA oligonucleotide
- P=S and 2'O-Me chemically modified for stability and uptake
- Designed to target c.7595-2144A>G mutation
- IVT-administration

Acknowledgements

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Margo Dona
Erik de Vrieze

Ant Vugler
Ma'ayan Semo

Presentations ProQR at ARVO 2017

USH2A exon 13: Tuesday May 9th, session number 329 at 11:45am by Peter Adamson

LCA 10: Sunday 8:30-10:15; Posterboard Number: 249 - B0280 . More information in clinicaltrials.gov

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