Sepofarsen (QR-110) Development Program Update

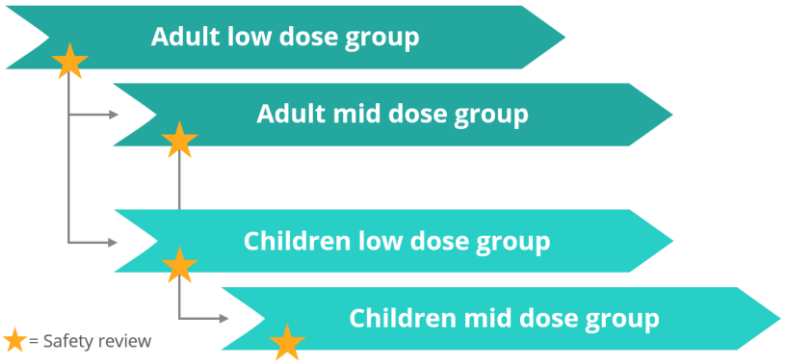
October 2019

ProQR has announced top-line results of a sepofarsen trial (PQ-110-001) in patients who have Leber's congenital amaurosis 10 (LCA10) due to one or two copies of the p.Cys998X mutation in the CEP290 gene.

Summary of the objectives and design of the sepofarsen phase 1/2 trial (PQ-110-001)

The purpose of this trial was to find out if different dose levels of sepofarsen are safe and whether sepofarsen restores/improves vision (efficacy). Participants received intravitreal injections (injection into the eye) with sepofarsen into one eye with the worst vision. The other eye remained untreated. The trial was designed to study different dose levels of sepofarsen in adults and children in a step-wise way. Safety was reviewed before treating the next dose group. The 11 trial participants received sepofarsen for a maximum of 4 times in 12 months.

Clinical trial design



The trial was conducted at three specialized centers with significant expertise in genetic retinal disease:

- University of Iowa, Iowa City, Iowa, U.S.
- Scheie Eye Institute at the University of Pennsylvania, Philadelphia, U.S.
- Ghent University Hospital, Ghent, Belgium

You can find more information about the sepofarsen (QR-110) study at ClinicalTrials.gov

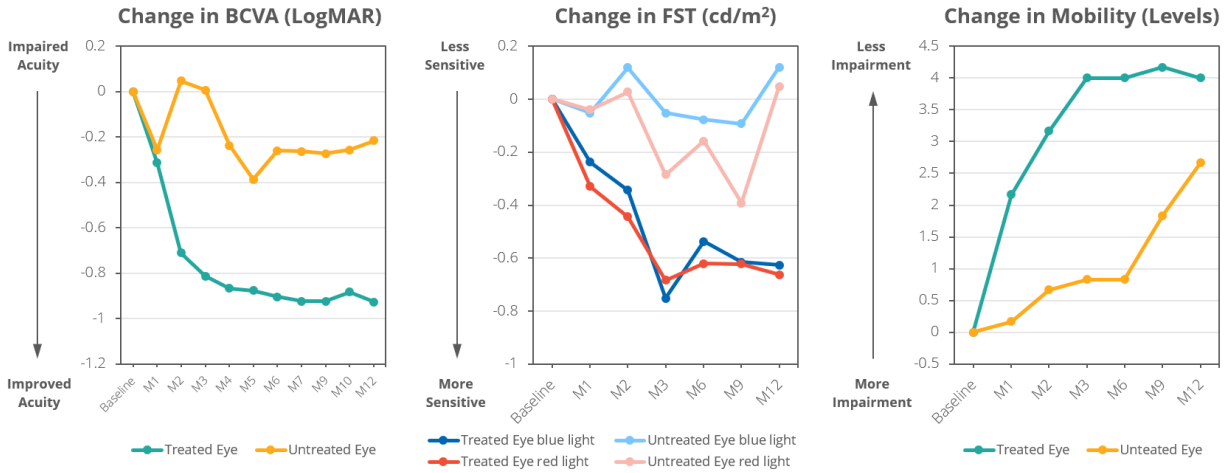
Top-line results of the sepofarsen phase 1/2 trial (PQ-110-001)

The top-line results were encouraging. The majority of participants showed meaningful improvements in visual acuity or functional vision after three months and maintained

that improvement at 12 months. As an example, one participant who was clinically blind at the start of the study could read letters on the standard eye chart after treatment. In the trial, visual acuity was assessed using different eye charts and functional vision was assessed using a series of mobility courses with increasing difficulty and multiple light levels. Improvements in visual function (BCVA) were supported by a significant increase in the ability to detect flashes of red or blue light as determined by the full field stimulus test (FST).

Participants in the low dose group were observed to have the most improvement and this dose had a positive benefit/risk profile. This low dose is being studied in the next clinical trial of sepofarsen, the phase 2/3 trial named Illuminate.

Results for the low dose group (6 participants)
(160µg loading dose with an 80µg maintenance dose)



Eligible patients that complete the trial, are offered the option to continue treatment in the open-label extension trial called "*Insight*".

Next steps for the sepofarsen development program

Based on the positive results from the phase 1/2 trial ProQR started a Phase 2/3 trial called "*Illuminate*" earlier in 2019 and is currently enrolling participants. The trial is expected to initially enroll around 30 patients with LCA10 due to one or two copies of the p.Cys998X mutation in the *CEP290* gene. The trial will study the efficacy and safety of sepofarsen and is being conducted at centers in North America and European countries.

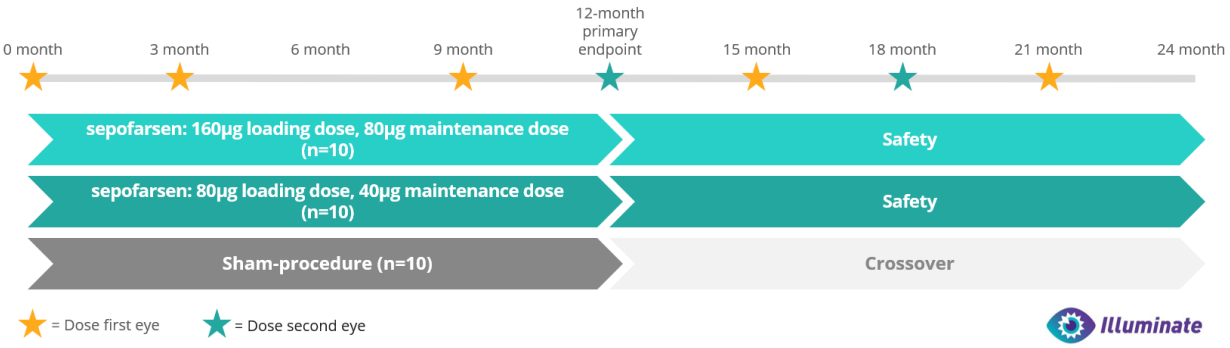
Study participants will be divided into three equal sized groups. All participants will receive sepofarsen during the trial but the dose level and start of dosing differs per group. They will be randomly assigned (like the roll of a dice) to one of the following study groups:

- **Group 1** will receive intravitreal injections (injection into the eye) with dose 1 of sepofarsen.

- **Group 2** will receive intravitreal injections with dose 2 of sepofarsen.
- **Group 3** will receive the sham procedure (intravitreal injection is mimicked but no injection and no study drug are given). For the first 12 months and then receive sepofarsen at one of the two dose levels in the subsequent 12 months

Participants will receive the intravitreal injection with study drug or the sham procedure up to a maximum of 5 times in the chosen(study) eye. This is the eye with the worse vision. The treatment or sham procedure will be given on day 1, in month 3, 9, 15 and 21 of the study.

Illuminate trial design



The ProQR team would like to thank the study participants, their caregivers, and the investigators and their staff for the support in the development of sepofarsen in this trial.

ProQR remains committed to making a significant and positive impact on the lives of those affected by LCA10. We look forward to continued collaboration and support from the LCA community. As the sepofarsen development program advances, we will keep the community updated on our progress. Please visit the website of ProQR for the latest news and future study participation opportunities.

If you have any questions, please consult your treating physician or you can contact ProQR at patientinfo@proqr.com