ProQR Update and Additional Sepofarsen *Illuminate* Trial Analyses

April 2022

ProQR has announced the completion of an in-depth strategic review designed to deliver on our commitment to advance RNA therapies for diseases with high unmet need. We are also publishing an update on our sepofarsen program, following a comprehensive analysis of the data from the Phase 2/3 *Illuminate* trial in people with *CEP290*-mediated Leber congenital amaurosis 10 (LCA10).

ProQR update

Based on the outcomes of this strategic review, ProQR will prioritize the following strategic objectives:

1. **Genetic eye diseases** – explore development path for selected ophthalmology programs subject to Regulatory feedback from European Medicines Agency (EMA) and US Food & Drug Administration (FDA).
2. **RNA editing technology** – accelerate development of the Axiomer® RNA base-editing technology platform, including initial focus on liver, the Central Nervous System (CNS) and the eye.

ProQR ended 2021 with €187.5 million of cash and cash equivalents on its balance sheet and expects this, together with expense reductions resulting from a corporate restructuring and the strategic update announced today, will fund operations into 2025, and through several milestones, including the potential readout of the modified Phase 2/3 *Sirius* trial of ultevursen.

ProQR will reduce expenses through the following portfolio prioritization and restructuring initiatives:

- Focus the ultevursen (QR-421a) program for USH2A-mediated Usher syndrome and retinitis pigmentosa on a single Phase 2/3 *Sirius* trial with the potential addition of an interim/futility analysis in 2023. Updates on planned adjustments to the *Sirius* trial considering the findings related to sham control will be provided after alignment with regulatory authorities.
- Suspend development of QR-1123 for autosomal dominant retinitis pigmentosa and QR-504a for Fuchs endothelial corneal dystrophy.
- Suspend all other IRD-related research activities.
- Reduce the workforce by approximately 30%, which will include the departure of our Chief Scientific Officer Naveed Shams, MD, PhD, expected to be effective in Q2.

"We believe deeply in the promise of RNA therapies, the Company's pioneering efforts in this field, and ProQR employees. These are the right steps to take to offer the best opportunity to create long-term value for all of our stakeholders, including our shareholders whom we thank for their support, and the communities we aim to serve."

Dinko Valerio, co-founder and Chairman of ProQR's Supervisory Board.

"These have been extremely difficult decisions to make as we position the business to drive long-term growth and value. I want to thank the employees separating from ProQR for their significant contributions toward our mission. I also want to acknowledge the disappointment that many in the eye disease community may feel today, particularly individuals and families living with autosomal dominant retinitis pigmentosa and Fuchs endothelial corneal dystrophy as we wind down our programs for these indications."

Daniel A. de Boer, Founder and CEO of ProQR Therapeutics.

Sepofarsen update

Following the top-line data announcement in **February 2022 that *Illuminate***, ProQR's pivotal Phase 2/3 trial of sepofarsen in LCA10, did not meet the primary endpoint of Best Corrected Visual Acuity (BCVA) at month 12 compared to a sham procedure control group, comprehensive post-hoc analyses of the trial and trial conduct were undertaken which revealed:

No technical errors in the trial conduct, data handling, or the medicine product used.

The overall safety profile of sepofarsen was consistent with earlier trials.

When the effect in the sepofarsen treated eye was compared to the untreated eye in the same patient, at month 12, a benefit in vision was observed. This effect was not observed in the control group that received a sham treatment.

Other endpoints showed similar effect when comparing treatment to untreated eye, including Full Field Stimulus Testing (FST).

These findings were supported by the patient reported outcomes analysis, based on the Patient Global Impressions-Change (PGI-C) that demonstrated that 61% of patients in the treatment groups reported an improvement in vision, as well as by Visual Function Questionnaire 25 (VFQ-25).

Overall, the post-hoc analyses showed that the efficacy seen with sepofarsen when comparing the active treatment and sham eyes to their corresponding untreated contralateral eyes across BCVA, FST, and other endpoints, including PROs, is more consistent with the

results seen in earlier trials, where the untreated contralateral eye was used as the control.

Based on these results, ProQR will focus on the following core activities related to sepofarsen:

In Q3, ProQR plans to meet with the EMA and FDA to discuss these data from the *Illuminate* trial. Following this discussion, ProQR will share an update in Q3 or early Q4.

ProQR currently plans to continue *Illuminate*, which is a 2-year study, the *Brighten* pediatric study, and the *Insight* open-label extension study, until further Regulatory guidance, after which next steps will be determined.

"These post-hoc analyses show an encouraging efficacy signal when comparing the active treatment and sham eyes to their corresponding contralateral eyes across multiple endpoints and are consistent with feedback received from the investigators. In prior interactions, EMA preferred the use of the contralateral eye as a control, however the protocol was ultimately harmonized globally to use a parallel sham group based on US regulatory requirements. While we were disappointed by the outcome of the primary analysis, we believe that these post-hoc analyses and the observation that approximately a third of the patients benefited across multiple concordant endpoints in this trial, in combination with the high unmet need in LCA10, warrants a discussion with the regulators."

Aniz Girach, MD, Chief Medical Officer of ProQR Therapeutics

Data from the *Illuminate* trial will be presented at the upcoming Seventh Annual Retinal Cell and Gene Therapy Innovation Summit, April 29, 2022, and the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, May 1-4, 2022.

Axiomer® RNA editing platform technology

ProQR will accelerate the development of its Axiomer® RNA editing platform and pipeline activities and expand into areas beyond the eye, including initially liver and CNS.

"We are focusing our strategy on accelerating our Axiomer® RNA-base editing platform technology, and a select pipeline of RNA therapies for inherited retinal diseases as we remain committed to developing RNA therapies for patients with high unmet need. ProQR has a strong cash position with runway into 2025, and we look forward to continued progress with the business, including providing an update following our discussions in Q3 with the EMA and FDA, and sharing details of our development plans for Axiomer® in the second half of 2022."

Daniel A. de Boer, Founder and CEO of ProQR Therapeutics.

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