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ProQR Announces Top-Line Results from Phase 2/3 Illuminate Trial of Sepofarsen in CEP290-mediated LCA10

- Study did not meet primary endpoint nor notable secondary endpoints – no benefit observed in either treatment arm versus sham
- Additional analyses to be conducted and presented at a future medical congress
- Sepofarsen continues to be generally well tolerated
- Strong cash position provides runway into mid- to late-2024
- ProQR Management to host conference call today at 8:15am EST

LEIDEN, Netherlands & CAMBRIDGE, Mass., Feb. 11, 2022 (GLOBE NEWSWIRE) -- ProQR Therapeutics N.V. (Nasdaq: PRQR) (the "Company"), a company dedicated to changing lives through the creation of transformative RNA therapies for genetic eye diseases, today announced its pivotal Phase 2/3 *Illuminate* trial of sepofarsen for the treatment of *CEP290*-mediated Leber congenital amaurosis 10 (LCA10) did not meet its primary endpoint of Best Corrected Visual Acuity (BCVA) at Month 12.

"Given the results observed in earlier studies of sepofarsen, the *Illuminate* trial results are unexpected and disappointing, especially for people living with LCA10," said Daniel A. de Boer, Founder and CEO of ProQR Therapeutics. "ProQR was founded with the goal of developing RNA therapies for patients with high unmet medical need, and we will continue to advance our robust pipeline of therapies for genetic eye disease. We are deeply grateful to all of the participants, their supporters, and investigators who participated in the *Illuminate* study."

"LCA10 is a devastating, very difficult-to-treat retinal disease resulting in blindness, for which there are no therapies," said Dr. Bart Leroy, Head of the Ophthalmology Department at Ghent University Hospital and Professor of Ophthalmology and Ophthalmic Genetics at Ghent University, Ghent, Belgium and Attending Physician for Ophthalmic Genetics and Retinal Degenerations at The Children's Hospital of Philadelphia. "We will continue to work with ProQR to understand the data as they work to advance therapies for inherited retinal diseases."

Illuminate, a randomized, sham-controlled trial, enrolled 36 participants aged eight years or older with genetically confirmed LCA10 due to the c.2991+1655A>G (p.Cys998X) mutation in the *CEP290* gene, at 14 study sites in 9 countries. Participants were randomized to three equal groups (1:1:1) of the target registration dose sepofarsen (160 µg/80 µg loading dose/maintenance doses), a low dose of sepofarsen for masking (80 µg/40 µg loading dose/maintenance doses), or sham procedure, with sepofarsen administered via intravitreal injection and the sham procedure mimicking an injection with no drug or injection given.

Key findings from the top-line results:

- At Month 12, the mean change from baseline in BCVA in the 160/80 µg dose group was -0.11 logMAR (p=0.96), in the 80/40 µg group -0.13 logMAR (p=0.97), and in the sham group -0.12 logMAR. P values are treatment group vs. sham, ANCOVA.

- For secondary endpoints full-field stimulus test (FST) and mobility, there was also no difference between the treated and sham groups in the top-line analysis.

- Sepofarsen was observed to be generally well-tolerated. Consistent with the findings observed in the Phase 1/2 trial, cataracts, CME, and retinal thinning were observed.

“This was not the outcome we had hoped for and we share in the disappointment many are feeling in the community,” said Benjamin R. Yerxa, Chief Executive Officer at the Foundation Fighting Blindness. “We will continue to work alongside ProQR to learn more from the ongoing analyses and as they work to advance RNA therapies to potentially help children, adults, and families who are affected by rare genetic eye diseases.”

Conference call and webcast details

Company management will host a call today at 8:15am EST. The live and archived webcast of the presentation will be accessible through this **webcast link**, or through the Events page of the Company’s website. The dial-in details for the call are +1 631-510-7495 (US) and +31 (0) 20 714 3545 (NL), conference ID: 8159878. The archived webcast will be available for approximately 30 days following the presentation date.

About Leber Congenital Amaurosis 10 (LCA10)

Leber congenital amaurosis (LCA) is the most common cause of blindness due to genetic disease in children. It consists of a group of diseases of which LCA10 is the most frequent and one of the most severe forms. LCA10 is caused by mutations in the *CEP290* gene, of which the c.2991+1655A>G (p.Cys998X) mutation has the highest prevalence. LCA10 leads to early loss of vision causing most people to lose their sight in the first few years of life. To date, there are no treatments approved that treat the underlying cause of the disease. Approximately 2,000 people in the Western world have LCA10 because of this mutation.

About Sepofarsen

Sepofarsen (QR-110) is an investigational RNA therapy designed to restore vision in Leber congenital amaurosis 10 due to the c.2991+1655A>G mutation (p.Cys998X) in the *CEP290* gene. The mutation leads to aberrant splicing of the mRNA and non-functional CEP290 protein. Sepofarsen is designed to enable normal splicing, resulting in restoration of normal (wild type) *CEP290* mRNA and subsequent production of functional CEP290 protein. Sepofarsen is intended to be administered through intravitreal injections in the eye and has been granted orphan drug designation in the United States and the European Union and received fast-track designation and rare pediatric disease designation from the FDA as well as access to the PRIME scheme by the EMA.

About ProQR

ProQR Therapeutics is dedicated to changing lives through the creation of transformative RNA therapies for the treatment of severe genetic rare diseases such as Leber congenital amaurosis 10, Usher syndrome and retinitis pigmentosa. Based on our unique proprietary RNA repair platform technologies we are growing our pipeline with patients and loved ones in mind.
Learn more about ProQR at **www.proqr.com**.

FORWARD-LOOKING STATEMENTS

This press release contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to", "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions. Such forward-looking statements include, but are not limited to, statements regarding our product candidates, including sepofarsen (QR-110) and the clinical development and the therapeutic potential thereof, statements regarding our pipeline of programs targeting inherited retinal dystrophies, our other programs and business operations, and our financial position and cash runway. Forward-looking statements are based on management's beliefs and assumptions and on information available to management only as of the date of this press release. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, the risks, uncertainties and other factors in our filings made with the Securities and Exchange Commission, including certain sections of our annual report filed on Form 20-F. These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities by us and our collaborative partners whose operations and activities may be slowed or halted by the COVID-19 pandemic; the likelihood of our clinical programs being executed on timelines provided and reliance on our contract research organizations and predictability of timely enrollment of subjects and patients to advance our clinical trials and maintain their own operations; our reliance on contract manufacturers to supply materials for research and development and the risk of supply interruption from a contract manufacturer; the potential for future data to alter initial and preliminary results of early-stage clinical trials; the unpredictability of the duration and results of the regulatory review of

applications or clearances that are necessary to initiate and continue to advance and progress our clinical programs; the ability to secure, maintain and realize the intended benefits of collaborations with partners; the possible impairment of, inability to obtain, and costs to obtain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in research and development; our ability to maintain and service our loan facility with Pontifax and Kreos; general business, operational, financial and accounting risks; and risks related to litigation and disputes with third parties. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and we assume no obligation to update these forward-looking statements, even if new information becomes available in the future, except as required by law.

Cautionary Note on Future Updates

The statements contained in this press release reflect our current views with respect to future events, which may change significantly as the global consequences of the COVID-19 pandemic rapidly develop. Accordingly, we do not undertake and specifically disclaim any obligation to update any forward-looking statements.

ProQR Therapeutics N.V.

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