

FOUNDATION FIGHTING BLINDNESS AND THE RETINAL DEGENERATION FUND



An update on some pipeline candidates that received Foundation funding.

BY BEN SHABERMAN, MA, MS

The most challenging aspect of therapy development for the eye is advancing a treatment into a clinical trial. Crossing the threshold from the lab into the clinic requires significant investment as well as regulatory expertise, knowledge of good manufacturing processes, and risk tolerance.

In 2018, the Foundation Fighting Blindness launched a venture philanthropy investment arm called the Retinal Degeneration (RD) Fund to help companies and researchers advance promising treatments for inherited retinal diseases (IRDs) into and through early-stage human studies. The targeted IRDs include retinitis pigmentosa (RP), Usher syndrome, and Stargardt disease. As a global leader in driving research for IRD treatments and cures, the nonprofit brings unparalleled scientific expertise and credibility to the projects that it funds.

"The Foundation has been a research-funding leader in the IRD space for nearly 50 years, which is very attractive to potential investors," Benjamin Yerxa, PhD, chief executive officer at the Foundation, told me in an interview. "Our investment in a project often serves as a seal of approval for our potential partners. We also bring clinical development expertise to the efforts, which is valuable to small

R&D teams in start-up companies emerging from academic settings."

The goal of the RD Fund is to demonstrate early proofs of concept for emerging therapies to attract much larger investments from biotech and pharmaceutical companies for later-stage human studies, which hopefully lead to regulatory approval.

"If through our RD Fund investment we can show safety and evidence of efficacy in a phase 1/2 trial and reduce risk, then large companies are more inclined to take on the development effort and, ultimately, the commercialization process," Dr. Yerxa said.

Currently, the RD Fund has allocated about 75% of its \$72 million fund to eight investments. A few examples are outlined below.

ProQR Therapeutics: RNA Therapies

Based in the Netherlands, ProQR develops RNA therapies for rare diseases. The company has three emerging therapies, all of which are antisense oligonucleotides (AONs) in clinical trials for the treatment of IRDs. AONs are small, single-stranded DNA fragments designed to mask or correct mutations in RNA. They are administered via intravitreal injection.

The Foundation is investing \$7.5 million in development of the candidate QR-421a, an AON therapy

that is being evaluated in the STELLAR trial, a phase 1/2 dose-escalation clinical trial for patients with mutations in exon 13 of the *USH2A* gene, which can cause Usher syndrome type 2A and nonsyndromic RP. In an interim report on the QR-421a clinical trial, ProQR said that two of eight participants had improvements in functional and structural measures.¹

The company also has a phase 2/3 clinical trial under way to evaluate sepo-farsen, an AON therapy that targets a mutation (c.2991+1655A>G in Intron 26) in the gene *CEP290*, which causes Leber congenital amaurosis 10 (LCA 10). In the phase 1/2 clinical trial evaluating sepo-farsen, four of six participants demonstrated vision improvements.²

In late 2019, ProQR launched an AON clinical trial for people with RP caused by the *P23H* mutation in the gene *RHO*, but no results have been reported.

Nacuity Pharmaceuticals: Antioxidative Treatment

Based in Fort Worth, Texas, Nacuity Pharmaceuticals is developing an oral antioxidant candidate known as NPI-001, which is designed to slow vision loss in patients with IRDs such as RP and Usher syndrome. In May 2020, the company launched a phase 1/2 clinical trial in Australia to evaluate the safety of NPI-001. Researchers in

the study SLO-RP, will enroll at least 48 patients with Usher syndrome and follow them for 2 years. If results for SLO-RP are favorable, Nacuity plans to launch clinical trials in 2021 to evaluate NPI-001 in patients with RP in the United States and Australia.

The Foundation is investing \$7.5 million in NPI-001 development and providing scientific consulting for the clinical trial and therapy development. Dr. Yerxa is on Nacuity's board of directors.

SparingVision: Neuroprotection for RP

In most patients with RP, vision loss begins in rod cells. As a result, night and peripheral vision are affected first. However, over time, central vision and visual acuity are often affected due to loss of cone cells. Researchers from the Institut de la Vision in Paris identified a protein produced by rod cells that preserves cone cells. Researchers have begun to develop a gene therapy to express this protein, aptly named rod-derived cone viability factor, or RdCVF. The goal of the treatment is to preserve cone cells in patients with RP, Usher syndrome, and other related conditions. This therapy is designed to work independently of the mutated gene that underlies the IRD in question. The company plans to launch a clinical trial of the RdCVF gene therapy in 2021.

The Foundation is investing \$7.9 million (€7 million) in development of this gene therapy. ■

1. Interim Findings of QR-421a Phase 1/2 Clinical Trial for Usher Syndrome and nsRP [press release]. ProQR Therapeutics; Leiden, Netherlands, and Cambridge, Massachusetts; March 2020.

2. ProQR Announces Positive Top-Line Results from the Phase 1/2 Study of Sepofarsen in LCA10 Patients [press release]. ProQR Therapeutics; Leiden, Netherlands, and Cambridge, Massachusetts; October 10, 2019.

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Details about the Foundation's RD Fund
can be accessed at [RDFund.org](https://www.rdfund.org).