

FDA Approves Spark's Vision-Restoring Gene Therapy

Spark Therapeutics' vision-restoring RPE65 gene therapy has received marketing approval from the U.S. Food and Drug Administration, becoming the first gene therapy to gain regulatory approval in the U.S. for the eye or any inherited condition. Known as LUXTURNA™ (voretigene neparvovec), the gene therapy restored vision in a clinical trial for people between the ages of 4 and 44 with Leber congenital amaurosis (LCA) caused by mutations in the gene RPE65. Study participants with severe vision loss reported putting away their navigational canes, seeing stars, being able to read, and recognizing faces of loved ones. Vision restoration has persisted for at least three years. The treatment is also designed to work for people with retinitis pigmentosa (RP) caused by RPE65 mutations. FFB invested about \$10 million in more than a decade of lab research that made possible the RPE65 gene therapy clinical trial at the Children's Hospital of Philadelphia (CHOP).

Gene Therapy for LCA1 (GUCY2D Mutations)

Investigators from the Universities of Pennsylvania and Florida have

demonstrated efficacy for gene therapy in two mouse models of LCA1 — one rich in cones, the other rich in rods. Based on an adeno-associated virus, the treatment provided profound improvement in vision, which has persisted for eight months thus far. Patients with LCA1 have also been identified and characterized in preparation for a human study. The investigators are working to gain authorization from the U.S. Food and Drug Administration to launch a clinical trial. A partnership with the pharmaceutical company Genzyme has been established to advance the treatment.

Gene Therapy for LCA6 (RPGRIP1 Mutations)

A research team from Massachusetts Eye and Ear Infirmary is developing a gene therapy based on an adeno-associated virus for LCA caused by RPGRIP1 mutations. Future plans include generating a clinical-grade gene-therapy vector for toxicology studies, and ultimately, a clinical trial. Dr. Eric Pierce's clinic has also identified seven families with RPGRIP1 mutations. An earlier study showed that gene therapy rescued degenerating rods and cones in a mouse model of the condition.

Leber Congenital Amaurosis: Research Advances, Continued

ProQR Doses First Participant in Its LCA10 (CEP290) Therapy Clinical Trial

ProQR, a biotech company in the Netherlands, has reported vision improvements for patient in a Phase 1/2 clinical trial for QR-110, a therapy for people with Leber congenital amaurosis 10 (LCA10), which is caused by the p.Cys998X mutation in the CEP290 gene. The mutation is estimated to affect about 2,000 people in the Western world. The company is now moving the therapy into a Phase 2/3 trial. The treatment, known as an antisense oligonucleotide, is delivered through an injection into the vitreous, the gel-like substance in the middle of the eye. It works like a piece of genetic tape to mask the mutation.

CRISPR Therapy in Development for LCA10 (CEP290 Mutations)

Editas Medicine, a company developing gene-editing treatments, has received authorization from the US Food and Drug Administration to launch a clinical trial for its emerging CRISPR/Cas9 therapy for people with a mutation in the gene CEP290, which causes Leber congenital amaurosis 10 (LCA10). LCA causes severe vision loss or blindness at birth. The treatment, EDIT-101, targets a specific mutation, "c.2991+1655A>G" in intron 26, of the CEP290 gene. The gene-editing therapy uses a cut-and-paste technology known as CRISPR/Cas9 to correct defective copies of CEP290. (The long-hand for this technology is: Clustered, Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein 9.) CRISPR, which comes from the immune system in strep bacteria, locates the region in the gene that needs correction. Cas9 is the molecular scissors that cuts out the mutation.