FOUNDATION FIGHTING BLINDNESS

# USHER SYNDROME RESEARCH ADVANCES

## Usher Syndrome Gene Therapy Clinical Trial Underway

The first-ever gene therapy for Usher syndrome is in a Phase I/IIa clinical trial at the Foundation-funded Casey Eye Institute, Oregon Health & Science University (OHSU), in Portland, and the Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts in Paris, France. The UshStat® treatment is being developed by Sanofi, and designed to halt vision loss in people affected with Usher syndrome type 1B, which is caused by defects in the MY07A gene. Based on results in lab studies, researchers believe a single UshStat treatment may last several years, perhaps a lifetime. FFB is funding the Paris site of the clinical trial and funded lab research that made the human study possible.

## Advancement of Usher 1C Gene Therapy

Uwe Wolfrum, PhD, at Johannes Gutenberg University of Mainz in Germany, is developing a gene replacement therapy for people with Usher syndrome type 1C. The treatment is designed to work by delivering copies of healthy USH1C genes to the retina to replace those that are defective and causing vision loss. He is also developing a pig model of Usher syndrome type 1C for testing his therapy in preparation for a future clinical trial. The project is funded by the Foundation Fighting Blindness.

## Emerging Therapies to 'Read Through' Usher Syndrome Gene Defects

Kerstin Nagel-Wolfrum, Ph.D., at Johannes Gutenberg University of Mainz in Germany, is developing compounds designed to "read-through" certain mutations (defects) in Usher syndrome genes such as USH2A, USH1C, and USH2C. By reading through the mutations, the cells of the retina can function normally, thereby preventing or slowing vision loss. She will test the compounds in mouse and pig models to help move them toward a clinical trial. The Foundation Fighting Blindness previously funded Uwe Wolfrum, PhD, for research for "read-through" technology.

## jCyte Stem-Cell Therapy Moves into Phase IIb Clinical Trial for RP/Usher Syndrome

The stem-cell therapy company jCyte is launching a Phase IIb clinical trial of its therapy for people with retinitis pigmentosa (RP). The 85-participant study is being led by Henry Klassen, MD, PhD. The treatment involves intravitreal injection of retinal progenitor cells

(RPCs), which are stem cells that have partially developed into the retinal cells that make vision possible. Based on lab studies, researchers believe the treatment can preserve and potentially rescue the patient's existing photoreceptors, thereby saving and possibly restoring vision. Administration of the treatment does not require surgery and can be performed in minutes in an outpatient setting. The RPCs are injected into the vitreous, the gel-like substance in the middle of the eye. Twenty-eight patients were enrolled in the safety-oriented Phase I/IIa trial for the treatment, which began in June 2015. Dr. Klassen says safety results from that trial have been encouraging.

### ReNeuron's Stem-Cell Therapy Performs Encouragingly in Phase 2 Clinical Trial

ReNeuron, a stem-cell development company in the United Kingdom, has reported that three patients with retinitis pigmentosa (RP) have been treated with its stem-cell therapy in its Phase 2 clinical trial taking place at Massachusetts Eye and Ear Infirmary (MEEI). All have shown vision improvements shortly after treatment. The treatment involves the injection of human retinal progenitor cells (hRPCs) — stem cells that have partially developed into photoreceptors — underneath the patient's retina. Based on results from preclinical studies, researchers believe the injected hRPCs will integrate into the retina and fully develop into photoreceptors, replacing those lost to disease, thereby restoring vision. FFB funded previous research that made this trial possible. The emerging therapy might also benefit people with Usher syndrome.

### Company Formed to Advance RP Drug into a Clinical Trial

The Foundation Fighting Blindness Clinical Research Institute (FFB-CRI) announced an investment of up to $7.5 million to advance a promising, emerging drug for retinitis pigmentosa (RP), and potentially Usher syndrome, into and through a Phase II clinical trial. Known as N-acetylcysteine-amide (NACA), the molecule is designed to slow vision loss by protecting retinal cells from oxidative stress. In previous FFB-funded lab studies at Johns Hopkins University, NACA slowed retinal degeneration in rodent models of RP.

### Optogenetic Therapy for Advanced RP and Usher Syndrome in Clinical Trial

RetroSense Therapeutics reported that three participants have received injections of its potential optogenetic therapy, known as RST-01, in a Phase I/II clinical trial. The patients were given the lowest dose of RST-01, and no adverse ocular events were observed. The treatment is designed to provide vision to people who are completely blind from conditions such as retinitis pigmentosa and Usher syndrome. The therapy works

by bestowing light sensitivity to ganglion cells in patients who have lost all of their photoreceptors. The Foundation funded earlier lab research that helped make this clinical trial possible. In September 2016, RetroSense was acquired by the pharmaceutical company Allergan.

### SparingVision Formed to Advance Sight-Saving Protein for RP

The development of a vision-saving treatment for people with retinitis pigmentosa (RP), and potentially Usher syndrome, is getting a major boost thanks to the formation of the French biotech SparingVision to move it into a clinical trial and out to the international marketplace. A spin-off of the Institut de la Vision, SparingVision was established to clinically develop and commercialize a protein known as rod-derived cone-viability factor (RdCVF). The emerging therapy performed well in several previous lab studies funded by the Foundation Fighting Blindness. Scientists demonstrated that RdCVF prevented or slowed the degeneration of cones, the cells in the retina that provide central and color vision and enable people to read, drive, and recognize faces. RdCVF is naturally secreted by rods, the retinal cells that provide night and peripheral vision.

### FFB Launches RUSH2A Natural Study for People with USH2A Mutations

FFB's Clinical Research Institute (CRI) is launching a natural history study for people with mutations in the USH2A gene, which are leading causes of Usher syndrome and retinitis pigmentosa. A major goal of the study, known as RUSH2A, is to better understand the course of vision loss in people with USH2A mutations, so that researchers can design successful clinical trials for potential therapies and identify patients for the treatment studies. More than 100 patients will be enrolled at approximately 20 sites in the US, Canada, and Europe.