HOPE in FOCUS
Seeing a cure for blindness
Supporting the LCA and rare retinal disease community

SEEING HOPE | Newsletter

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HOPE IN FOCUS MAKES $300,000 PLEDGE FOR LCA TREATMENTS

By Rosanne Smyle

The big news just keeps coming: Fresh off the rebranding from Sofia Sees Hope to Hope in Focus, we are pleased to announce a pledge to raise $300,000 by 2025 to fund LCA research and therapies.

"This is a lot of money for a small organization like ours," Co-Founder and President Laura Manfre said. "It is the biggest commitment we have made to date."

Individual contributions and donations to the organization go 100 percent toward funding research and LCA therapies, Manfre said. Meanwhile, grant funding and corporate support fuel the organization's advocacy, outreach, and education programs.

The news comes in conjunction with the Foundation Fighting Blindness recently announcing the formation of a new company called Opus Genetics

that will help move LCA therapy research forward from clinical trials to federally approved treatments for people living with LCA and other retinal degenerative diseases.

For perspective, no treatments existed when Hope in Focus began in 2014; now five or six LCA treatments are moving forward, along with LUXTURNA® gene therapy already having earned federal approval in 2017 to help improve vision in people living with LCA2 (RPE65). ***Continued on page 2***

Big News for LCA5 and LCA13 Patients with Launch of Opus Genetics

By Rosanne Smyle

The Retinal Degeneration Fund (RD Fund), the venture arm of the Foundation Fighting Blindness, recently launched Opus Genetics, a patient-focused gene therapy company initially concentrating on advancing research into two forms of Leber congenital amaurosis: LCA5 (Lebercilin) and LCA13 (RDH12).

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"Getting the research from the lab to the patient community is a huge lift," Manfre said. "It's complicated.

"There are many parties involved, from regulatory bodies to industry to investors to the patient community. It's a significant event, and while we have several LCA treatments that look promising for clinical trials in humans, this is a big gap to close. I'm very excited for Opus Genetics, as it was created to help close that gap."

Laura Manfre

In late September, the Foundation's venture arm, known as the Retinal Degeneration Fund (RD Fund), launched Opus Genetics, a patient-first, science-driven gene therapy company tackling manufacturing obstacles standing in the way of treatments for ultra-rare blinding conditions.

Foundation CEO Ben Yerxa, PhD, said he was excited from the perspectives of the Foundation and the new company.

"We see a lot of opportunity to develop new therapeutics in this space," he said. "It starts with early translational research, it starts with genetic testing, and then once we figure that out, it's time to develop therapeutics."

Yerxa, CEO of the RD Fund and Acting CEO of Opus, said he was happy to be working with Hope in Focus.

"We think you're the best in the business when it comes to creating community, and without that community, those who are affected and the families, we can't do our job.

"So just thank you for pulling it together and being with us. We're here for you and we're rooting for you, and we appreciate everything you do to support us, and stay tuned: More to come."

Benjamin Yerxa, PhD

The pledge by Hope in Focus marks a milestone in our fundraising efforts to drive LCA research forward.

"I'm very excited for our goal of raising $300,000 in support of treatments for LCA, and I hope that our donors and supporters will be too," said Manfre. "Not only will we be able to support early stage research for LCA treatments, but with Opus Genetics, we will actually be able to make an impact in getting those treatments to the people who need them."

Big News for LCA5 and LCA13 Patients with Launch of Opus Genetics

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The RD Fund led the $19 million in seed financing, with participation from the Manning Family Foundation and Bios Partners.

Opus Genetics is the first spin-out company internally conceived and launched by the RD Fund to further the Foundation's mission. The RD Fund aims at rapidly driving research toward preventions, treatments, and cures for the entire spectrum of retinal degenerative diseases.

Opus Co-Founders include Jean Bennett, MD, PhD, the F.M. Kirby Emeritus Professor of Ophthalmology at the Perelman School of Medicine at the University of Pennsylvania, and a lead researcher into the first and, so far, only gene therapy federally approved for an inherited condition or a form of LCA.

She is joined by Junwei Sun, Chief Administrator of Penn's Center for Advanced Retinal Ocular Treatments (CAROT), and Eric Pierce, MD, PhD, the William F. Chatlos Professor of Ophthalmology at Harvard Medical School and Massachusetts Eye and Ear.

First-of-its-Kind Model

Ben Yerxa, PhD, CEO of the Foundation and its RD Fund, and acting CEO of Opus, described the venture and thanked investors.

"Opus is a first-of-its-kind model for patient-focused therapeutic development," Yerxa said in a news release.

"... Opus is uniquely positioned to bring experts, resources, and patients together to efficiently advance ocular gene therapies for small groups of patients that to date have been neglected.

"We're grateful for our fellow investors and supporters who share our commitment to realizing the promise of improving vision for people with devastating sight-limiting diseases and look forward to building upon the pioneering work of Dr. Bennett, Mr. Sun and Dr. Pierce, and expanding our pipeline with more programs soon."

Dr. Bennett said she has dedicated her career to the research and development of treatments for blinding diseases.

"I'm eager to continue to build on this work with the RD Fund, an organization that understands the science and is deeply ingrained in the patient community," she said in the news release.

"Founding Opus enables us to progress with our first two programs in Leber congenital amaurosis, while building an engine to move additional treatments toward the patients who need them."

The company also is co-founded and managed by Rusty Kelley, PhD, Peter Ginsberg, and Jason Menzo; they also form the RD Fund's management team. The Board of Opus is composed of Yerxa, Kelley, and Bennett.

LCA5 and LCA13 Targeted for Treatments

The new company's lead program, OPGx-001, will address mutations in the LCA5 gene, which encodes the lebercilin protein. LCA5 is one of the most severe forms of LCA and affects about 1 in 1.7 million people.

Opus's second program, OPGx-002, will focus on restoring protein expression and halting functional deterioration in patients with retinal dystrophy caused by mutations in the retinal dehydrogenase gene, known as LCA13 (RDH12). This disease affects 1 in 288,000 people. Preclinical research shows potential for each of these novel ways to restore structure and function. Opus expects to file an Investigational New Drug (IND) application for the LCA5 research (OPGx-001) in early 2022.

The U.S. Food and Drug Administration's IND program is how a pharmaceutical company obtains permission to start human clinical trials and to ship an experimental drug across state lines before approving a marketing application for the drug.

Families Welcome News of Opus Genetics Launch

By Rosanne Smyle

Allison Galloway feels cautiously excited about a new genetics company prioritizing research into her children's form of Leber congenital amaurosis known as LCA13 (RDH12).

"I would say I'm excited, but I don't put all my eggs in one basket," the Colorado mother said of the news to bring a treatment closer to market. Her children, Logan and Zoe, both live with LCA13.

"Many times, we think we made progress and then we had some studies done and invested money, and the researcher never progressed with the research."

Now, a new gene therapy company called Opus Genetics plans to target two forms of LCA. The company's research into LCA13 will focus on restoring protein expression and halting functional deterioration in patients with retinal dystrophy caused by mutations in the retinal dehydrogenase gene RDH12. LCA13 affects 1 in 288,000 people. Opus also will concentrate on research into LCA5, which encodes the lebercilin protein and affects about 1 in 1.7 million people.

The Retinal Degeneration Fund (RD Fund) of the Foundation Fighting Blindness led the $19 million in seed financing for Opus, based in Raleigh, N.C.

Motivated Parents

Opus comes amid efforts by the Galloways and a network of motivated parents to raise money, invest in research, and advocate for genetic testing to help drive studies forward to find a treatment for LCA13.

Allison, a nurse practitioner and founder of a women's health practice, and her husband, Michael, a VP of Finance, are part of a non-profit that parents of LCA13 patients founded more than 11 years ago called RDH12 Fund for Sight (www.RDH12sight.org).

Michael, Allison, Zoe, and Logan Galloway

"We work with scientists around the world to fund research. We support each other even if we live in the U.S., Italy, Australia, or Saudi Arabia. We try to advocate the importance of all children diagnosed with a rare disease to get genetic testing. Without it, we would have never known what our children had, let alone how to cure it."

A mutation in the RDH12 gene means an inability for the body to create a simple enzyme called retinal dehydrogenase, which helps in the cleaning and health of the eyes. LCA13 is an autosomal recessive gene defect that appears when each parent has a mutation on the same gene in the same place.

Doctors genetically diagnosed Logan at age 3. Now 10, he is a fifth grader who loves everything technology. Logan loves to ski and is fluent in braille. While his vision is fairly stable, he lost some of his field of vision over the years and his night blindness is severe, his mom said.

When Logan was 5 and Zoe was 3, one day at dinner, Allison noticed her daughter's eye started to bounce from side to side.

"I immediately knew what it meant," she said. "A nystagmus means that the eye is weak and sick. I didn't need the gene results to know that not only did my son have LCA, but my beautiful little girl did too. A 6 percent chance."

Doctors genetically diagnosed Zoe also at age 3. Now 8, she is a third grader who loves painting, clay modeling, reading, writing, and riding horses. Her vision is much better than Logan's, and while it has also been fairly stable, she has lost some over the years.

RDH12 Natural History Study

The children took part in an RDH12 Natural History study by Drs. Tomas S. Aleman, Katherine E. Uyhazi, and Jean Bennett, among a host of other researchers, at the Perelman Center for Advanced Medicine at the University of Pennsylvania.

Logan and Zoe were among 21 patients, ages 2 to 17 years old, from 14 families, who underwent exams, imaging, and numerous studies to track details about the gene's structure and function, and the progression of the disease across a range of patients with the RDH12 mutation. Natural History studies often serve as a critical part in designing clinical trials eventually involving testing on humans.

The journal Retina published results of this segment of the study in an article titled "RDH12 Mutations Cause a Severe Retinal Degeneration with Relatively Spared Rod Function."

Allison and Michael attended the Hope In Focus 2019 LCA Family Conference in Philadelphia, where panels of researchers, including Drs.

Aleman and Bennett, shared their study results among an audience of patients, care givers, advocates, scientists, and leaders in biotechnology and the regulatory process.

The Galloways and others in the RDH12 group have been disappointed in the past. In one instance, a biotechnology company announced they were moving forward with RDH12 trials.

"Nothing happened. We're emotionally battered, so we tend to have a little reluctance until it's actually occurring."

Regarding Opus's plans to drive LCA13 research forward to a viable treatment, Allison said, "While we're excited, we can't get all our hopes up. As a board member of the RDH12 Fund for Sight, we have other coals in the fire to keep the research going if this doesn't progress. But we are hopeful that this is our time, and this study is an answer to our hopes and dreams.

"We're trying to be part of this study financially because we owe it to our kids and affected members to not be left behind like we have in the past," she said.

"We have fought too hard and for too long to keep watching them lose their sight."

What is Hope in Focus?

We are a community of support, advocacy and education. We fund research around the globe that has resulted in clinical trials for treatments for blindness caused by inherited retinal disease. We pave the way for many families to receive genetic testing and counseling.

Thank you to all who make it possible for us to keep hope in focus for the Leber congenital amaurosis community!

HELP US CONTINUE OUR WORK TO ADVANCE TREATMENTS FOR LCA.

This year, we have three great ways you can support our work!

1. **GIVE CHANGE** - Donate your change from everyday purchases to Hope in Focus. We've partnered with Harness to make it possible for you to round up the change on your bank and credit card purchases to the nearest dollar, and donate that change to Hope in Focus. It's a small amount that gets rounded up, and it makes a big difference to us. We hope you will give it a try — our team has already and it's easy! Just visit **www.hopeinfocus.org** and look for the "Offer Spare Change" tab in the bottom right corner.

2. **AMAZON SMILE** - When you shop at **smile.amazon.com**, Amazon donates 0.5% of your eligible purchases — at no cost to you. Simply log in to your account on smile.amazon.com and select Hope in Focus as your charity of choice.

3. **DONATE NOW** - 100% of the contributions we receive from individual donors goes to research and the development of LCA therapies. Visit **www.hopeinfocus.org**, or send a check to Hope in Focus, P.O. Box 705, Ledyard, CT 06339

However you decide to donate, we are grateful for your support as we continue our work to advance treatments for blindness for individuals who are living with Leber congenital amaurosis. Together we are making a real difference.

HOPE in FOCUS

Seeing a cure for blindness

Vision Improvements Reported for Two LCA10 Patients in Phase 1/2 Clinical Trial for Editas' CRISPR/Cas9 Treatment

By Ben Shaberman
Senior Director, Scientific Outreach & Community Engagement

FOUNDATION FIGHTING BLINDNESS

At the XIXth International Symposium on Retinal Degeneration (RD2021), Mark Pennesi, MD, PhD, Oregon Health & Science University, reported that two of three participants in the mid-dose group of Editas' BRILLIANCE Phase 1/2 clinical trial for its LCA 10 CRISPR/Cas9 treatment showed improvements in vision. Known as EDIT-101, the emerging gene-editing therapy is the first of its kind to be administered directly to the human body.

One participant in the BRILLIANCE trial had improvements in best corrected visual acuity (BCVA, the ability to read lines on an eye chart) sustained for six months and in the ability to navigate a mobility course at the sixth month after treatment. Also, the participant showed a positive trend in retinal sensitivity (as measured by a full field stimulus threshold test or FST).

Another participant had stable BCVA at three months and a notable improvement in retinal sensitivity at six weeks that continued to improve through the third month.

Dr. Pennesi said that no serious adverse events were observed. Safety data were reported for a total of six participants — two in the low dose group and four in the mid-dose group.

"We are encouraged by these early results of safety and efficacy and look forward to additional data as the trial moves forward," said Ben Yerxa, PhD, chief executive officer at the Foundation Fighting Blindness. "CRISPR/Cas9 is a promising, emerging technology for addressing inherited retinal diseases and we are excited by its potential."

The EDIT-101 gene-editing technology is designed to locate and remove a specific mutation (c.2991+1655A>G in Intron 26) in the CEP290 gene. The treatment works like a pair of molecular scissors to cut out the mutation. The treatment is delivered to photoreceptors by a subretinal injection.

Gene editing is different from gene (augmentation) therapy. In gene therapy, copies of an entirely new gene are delivered to the retina to replace the defective copies. In CRISPR/Cas9 gene editing, only the mutated region of the gene is corrected.

Gene-editing is an attractive approach for addressing large genes (e.g., CEP290) which exceed the cargo capacity of commonly used viral delivery systems such as adeno-associated viruses or AAVs.

*Visit **FightBlindness.org** to stay informed about the latest research advances for LCA and other IRDs.*

Events

DO YOU HAVE AN EVENT YOU WANT TO SHARE? LET US KNOW!
Email rosanne@hopeinfocus.org with the information and a link.

Hope in Focus Let's Chat About…" webinar
Jan 18, 2022 @ 1pm EST
hopeinfocus.org/for-families/lets-chat-about
Hope in Focus is proud to bring our web series "Let's Chat About …" to the rare inherited retinal disease communities. January's episode features Daniel de Boer, Founder and Chief Executive Officer, ProQR Therapeutics. We developed the series with those living with LCA and IRDs in mind, but we invite all members of our community, including those in research, industry, and the regulatory communities to join the sessions, as we look ahead to a common goal of advancing treatments for rare retinal disease.

Global Genes • Rare in the Square
Jan 10–13, 2022 • San Francisco's Union Square
globalgenes.org/event/rare-in-the-square
RARE in the Square brings together rare disease innovators to provide a unique opportunity to network with industry thought leaders and to promote the role of patients as partners and drivers in rare disease drug development that lay the foundation for positive change in the rare disease space.

National Organization for Rare Disorders (NORD) Rare Disease Day
Feb 28, 2022 • rarediseaseday.org
Events of the day raise awareness globally for patients, families, and caregivers affected by rare diseases. Annually, Rare Disease Day is the last day of February. NORD is the official Sponsor of Rare Disease Day in the United States.

Foundation Fighting Blindness • VisionWalk
Mar 27, 2022 • Orlando • Fightingblindness.org/events
Since its inception in the Spring of 2006, VisionWalk has raised more than $58 million to fund sight-saving research.

International Conference on Orphan Drugs and Rare Disease • Orphan Drugs: Ray of Hope for Rare Disease
Apr 21–23, 2022 • Las Vegas, NV • Onsite and Virtual Versions • orphan-drugs.magnusconferences.com
This global congress on orphan drugs and rare disease provides an interdisciplinary stage for experts to introduce their most recent research findings and portray developing advances. The conference presents novel research results in all aspects of Orphan Drugs and Rare Diseases and addresses the hardships faced by the scientific community, from development to marketing.

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The *Seeing Hope* Newsletter
is published quarterly by Hope in Focus, a 501(c)3 patient advocacy organization dedicated to generating awareness, raising funds for research, and providing education and outreach to the LCA and rare inherited retinal disease community.

To learn more about Hope in Focus, visit www.hopeinfocus.org.

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