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

SEEING HOPE | Newsletter

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From the Founder:

Laura Manfre

What an amazing 2022! Back to a semblance of normalcy and grateful for the generosity of our contributors, we forged ahead with our Hope in Focus mission this year, including a return to in-person events!

At the end of October, about 260 guests, including speakers, sponsors, and volunteers, came together for our first Hope in Focus Dinner in the Dark since 2019. We are so grateful for this opportunity to celebrate advances in retinal research and to raise funds for treatments for blindness caused by Leber congenital amaurosis (LCA).

Dinner in the Dark 2022 was, hmm, let's call it "extra special" for our team. Everything was harder. We were out of practice throwing events, and many of us volunteering are simply in different life and career stages than we were three years ago. And yet, as the big night approached, the response from everyone — those who attended and those of you who contributed from afar — was incredible.

Your energy, enthusiasm, and generosity of spirit lifted our

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Boy's Vision Improves After UK Compassionate Use Gene Therapy for LCA4 (*AIPL1*)

By Rosanne Smyle

Jace Broadbin

DJ and Brendan Broadbin came to our Hope in Focus LCA Family Conference with a lot of questions about their little boy's blindness, and they left with amazing answers leading to innovative treatment for his type of Leber congenital amaurosis (LCA).

The couple traveled from their southwestern Connecticut home to the July 2019 Philadelphia conference knowing their son Jace had LCA, but not knowing the specific form of the rare disease because the 11-month-old had yet to be tested genetically.

Jace's parents introduced themselves to retinal specialist Prof. Michel Michaelides, one of Britain's top ophthalmologists and a panelist at the conference. Dr. Michaelides is a founding member of MeiraGTx, where he is Head of Clinical Ophthalmology.

"At that time," DJ said, "we hadn't even met with a geneticist yet, but Michel gave us his contact information 'just to have.' We then got to hear the panel discussion at the conference regarding the clinical trials taking place across several of the gene variants.

"A few days before we went to Boston to hear Jace's genetic results (in October 2019, three months after the conference), we received the Sofia Sees Hope (now Hope in Focus) newsletter in the mail, outlining the treatments discussed at the conference.

"We brought the newsletter with us to our appointment and almost fell out of our seats when we learned that Jace had the *AIPL1* variant, and that MeiraGTx was currently working

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Journey to Improved Vision Through LCA4 (*AIPL1*) Gene Therapy

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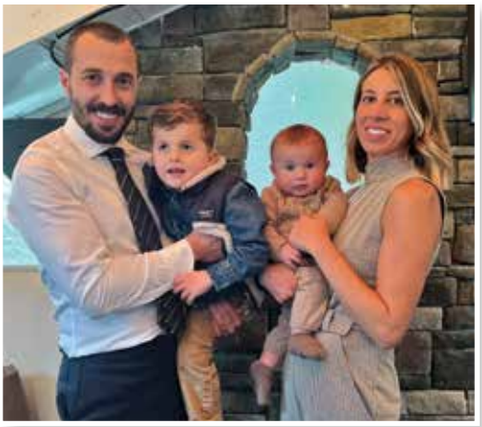
on a treatment through the compassionate use case program in the UK — we emailed Michel that same day."

Compassionate use treatment

Dr. Michaelides is a Professor of Ophthalmology at University College London Institute of Ophthalmology in the Department of Genetics. He also serves as a Consultant Ophthalmologist at Moorfields Eye Hospital in the departments of Inherited Eye Disease, Medical Retina, and Pediatric Ophthalmology.



Broadbin Family

The professor has discussed the UK's compassionate use program in a Hope in Focus webinar series episode called "**L**et's **C**hat **A**bout… Gene Therapy for LCA," describing LCA4 as an exceedingly rare and severe form of the disease in which children have profoundly reduced vision from birth.

"There is a narrow window of opportunity (for treatment) because the retina degenerates and thins out by the age of 4 years," Dr. Michaelides said. "Treatment needs to be before 4 years of age. MeiraGTx has manufactured a gene therapy that they are making available under a specials license in the UK."

A special unlicensed medicine is one manufactured without marketing authorization from the Medicines and Healthcare products Regulatory Agency. The agency only grants a product license once a medicinal product has been proven to be safe and effective. Prescribed products not holding a marketing authorization include those prepared on an individual basis by "special order" manufacturers, according to the National Institutes of Health.

After months of conversations, sharing test results and talking with hospital board members and surgeons, Jace received approval for the compassionate use treatment in one eye on March 17, 2020.

The family traveled to London, Jace underwent pre-op testing, and the surgery was canceled: The world had just begun shutting down because of the COVID-19 epidemic.

DJ and Brendan thought the surgery would be canceled indefinitely, but to their wonderment, they returned in September, quarantined for two weeks, and Jace received the gene therapy in his left eye, which is stronger, on Sept. 30, 2020. He had just turned 2 that August.

Before LCA4 (*AIPL1*) surgery

The couple first began to realize when Jace was about 8 weeks old that he was not looking at them or trying to track toys.

"He was smiling from touch, but never in response to one of our smiles. He wasn't blinking when lights were shown in his eyes and wasn't shutting his eyes or even squinting in the brightest of sunlight. His eyes never seemed to move out of that 'newborn' stage of being all over the place," DJ said.

"When we brought him to the pediatrician, hoping we were just being paranoid and this was something he'd grow out of, they confirmed that something wasn't right, and within an hour we were meeting with a pediatric ophthalmologist — kicking off a year-long journey for answers."

Before his surgery, Jace had minimal light perception and not much functional vision.

"Lights had to be very bright for him to react to, and his reaction was at least two seconds delayed. Phone screens and TV screens were not bright enough to elicit a reaction from him, and outside he had to always be in sunglasses because the sun was never too strong for him to look away from.

"With his left eye, we felt like he could have some shadow perception or make out very high contrast shapes and objects," DJ said. "He had some words at the time, and labeled toys by feel and sound, but never by sight."

Post surgery

About a year after Jace's surgery, his parents — now both 33, with mom working in market research and dad as a sourcing manager for a major retailer's store design team — welcomed another son. Jace's little brother, Gio, just turned 1 in August.

Gio is sighted and in awe of his big brother — so much so, DJ and Brendan said he always felt like a toddler to them, missing the newborn stage, because he's always trying to keep up with Jace.

"He learned how to crawl so he could be closer to his brother

Jace with his guitar

Jace and his brother, Gio

and now runs out of bed to meet Jace every morning," DJ said. "Jace assumed the patient-older-brother role incredibly well. He's even learned to share his most favorite toys, and it's music to our ears when the boys are both belly laughing as they rough-house with one another and try out their wrestling moves."

Since the surgery, Jace can identify most of his toys by sight when they're held three feet or closer to him.

"He is especially good at identifying the ones that are brightly colored and his favorite cars and dinosaurs, of course," she said.

The couple believe Jace gained valuable functional vision from his surgery.

"Our hope was always that the surgery could protect some of the light perception he did have for a bit longer, never imagining that it could lead to anything more."

Jace's mom talked about LUXTURNA®, the only federally approved treatment for LCA2 caused by a mutation in the *RPE65* gene, which has demonstrated improved vision in people who underwent surgery for the gene therapy.

"Someone who received LUXTURNA® described vision improvement as regaining 'pockets' of vision in the area where the retina remained intact, and this is exactly how we believe Jace has also regained some vision in his left eye. He will turn his head in certain directions to get a better look at what is in front of him.

"In terms of being able to better navigate, Jace now bends down to pick up small objects that might be in his way, noticing them solely based on sight, not feel."

Jace's teachers have commented he'll squat down to look under things when he wants a specific toy in the classroom and stand on tippy-toes to find things placed on countertops.

"This makes us laugh to hear."

Jace, now 4 years old, smiles when he catches a glimpse of his favorite people and things.

"It is heart melting. But he also still flashes that same perfect smile when he feels the sand at beach, hears his favorite country songs, or tastes an ice cream cone — so, yes, his vision has changed and it's amazing to experience, but to us he's always been amazing to experience."

Hope in Focus featured Jace and his family in a video shown in October at our gala fundraising event, Dinner in the Dark. Please visit www.hopeinfocus.org to view the video.

From the Founder:

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spirits, and, yes, made Dinner in the Dark a highly successful fundraising event.

As you read through the stories and research updates in this edition of *Seeing Hope*, please know that what we do is possible only because of your financial support, your time, and your constant cheering us on. Thank you!

With joy, gratitude, and best wishes for 2023,

Laura

P.S. If you're a Dinner in the Dark volunteer, an "extra special" thanks to you!

Now go get some sleep, and I'll see you next month to begin planning for Dinner in the Dark on October 14, 2023! :)

We're Back — DINNER IN THE DARK 2022!

By Rosanne Smyle

Our 7th Annual Dinner in the Dark came off as an exciting evening of hope and joy, and a spirited event to foster and connect with the mission of Hope in Focus.

About 260 people gathered at the Mystic Marriott in Groton, Connecticut, on the evening of Oct. 22 to celebrate research advances into Leber congenital amaurosis (LCA) and other rare inherited retinal diseases (IRDs).

The extraordinary evening included a gourmet, multi-course dinner, paired with wine or beer — extraordinary because the night represented the return of our annual gala fundraiser since the pre-pandemic days of 2019, and because our guests tried to figure out the contents of their courses while wearing blindfolds. Only guests with visual impairment and the ability to read Braille knew exactly what they were eating because of the Braille-printed menu.

The experience gave people a taste of the isolation and social challenges that accompany visual impairment. It's not easy.

Who's talking to whom became confusing when listening to conversation without seeing the speakers. Unable to see among a ballroom full of people felt isolating at times, and the world easily reduced to one only within earshot.

I can tell you a lot of finger-sliding around plates went on after trying to get that piece of protein on the fork, despite handy tips from Sofia Priebe, the daughter of Hope in Focus Founders Laura Manfre and Charles Priebe. Sofia, the catalyst for the organization, received her LCA genetic diagnosis as a pre-teen, and, before dinner, delivered successful-dining advice for the visually impaired via video, as the 19-year-old is away at college.

An enlightening and humbling experience

A first-time Dinner in the Dark attendee from the biotech industry said the experience made a lasting impression, adding, "We think about the research aspect of LCA daily, but to experience a mere hour of life without sight was enlightening and humbling, and it gives us many new things to think about as we continue our research plans."

Susette Tibus, who with her husband, Chuck Sneddon, own and operate Simply Majestic of Mystic and helped launch Hope in Focus, told the gathering about her good friend Elisse Rosen, who asked in 2013 if she could introduce her to a woman named Laura who needed help fundraising. Susette, heavily involved in the community, told her what she tells everyone: "Yes, but tell her she's only got five minutes."

"Today," she said, "Hope in Focus is the leading global advocacy organization for those living with the rare blinding disease Leber congenital amaurosis."

Hope in Focus beginnings

Laura Manfre, Hope in Focus Board Chair and Member of the Board of Directors for Foundation Fighting Blindness, explained her role to the guests.

"I didn't get into rare disease advocacy because I like science, or want to learn more about gene therapy, or am fascinated with the retina. I know many of you here tonight are, and I'm so glad you are. I am in it because I had a child born with something I couldn't fix.

"I was a liberal arts major in college so I know how to bring people together to problem solve — in four languages and iambic pentameter — and I can throw a party.

"But when you want to advance cutting-edge, life-changing treatments — when I want to make it possible for Sofia to retain the vision she has — I want the Foundation Fighting Blindness to lead the way. The partnership Hope in Focus has with the Foundation is critical to ensuring the funds we raise for treatments for LCA are put to the best use possible."

The evening's featured speaker, Foundation Chief Scientific Officer Claire M. Gelfman, PhD, said the Foundation funds grants worldwide and manages My Retina Tracker®, a patient registry vital to advancing research.

"Once your mutation has been identified, or information about your diagnosis has been given to you by your physician, our registry allows for enrollment not only in clinical trials, but also for research studies so that companies and researchers can learn more about the patient experience and incorporate that information into future clinical trials."

Bidding, winning, and dancing

After dinner, guests bid on auction items ranging from a collection of spa services, jewelry, wines, and art to vacations in the United States and in Italy, Chile, and Mexico.

Guests, who previously bought Simply Majestic boxes, opened their packages, all containing pink mother-of-pearl pendants, except one. The person opening the box with the only blue pendant won the grand prize of a stunning diamond-and-sapphire ring.

Then we danced the night away to The Dillon and Cooper Band.

"What an extraordinary evening," Laura said. "We were so happy to bring together, live and in-person, our first Dinner in the Dark since before the pandemic. And we are so thankful for the sponsors and donors who made this a successful event."

RESEARCH MOVED IMPRESSIVELY IN 2022

By Ben Shaberman
Vice President,
Science Communications

FOUNDATION FIGHTING BLINDNESS

The news coming from the retinal disease research frontlines overall has been promising in the past year, as emerging treatments move into and through clinical trials. While research progress isn't always linear, the field moved forward impressively.

Here is a roundup of some of the 2022 research stories involving Leber congenital amaurosis (LCA) and other rare inherited retinal diseases (IRDs).

Atsena Therapeutics Reports Impressive Results from Phase 1/2 Clinical Trial for its LCA1 (*GUCY2D* mutations) Gene Therapy

Atsena Therapeutics, a gene therapy development company focused on preventing and reversing blindness, announced positive results from its Phase 1/2 gene therapy clinical trial for people with LCA1, caused by mutations in the gene *GUCY2D*.

The company reported results for 15 trial participants. Overall, the gene therapy, ATSN-101, was well tolerated. The nine patients receiving the highest dose of ATSN-101 had clinically meaningful vision improvements as measured by a full-field stimulus test (FST), which measures the patient's ability to respond to different levels of light and to navigate a multi-luminance mobility course.

Excitingly, the company is planning to move the emerging gene therapy into a pivotal trial, which will hopefully position it for regulatory approval.

The *GUCY2D* gene therapy was created in the laboratory of Atsena Founder and Chief Scientific Officer Shannon Boye, PhD, and Founder and Chief Technology Officer Sanford Boye, MSc, at the University of Florida.

Atsena is funded by an investment from the Foundation Fighting Blindness' Retinal Degeneration (RD) Fund, a venture philanthropy fund for emerging treatments in, or moving toward, early-stage clinical trials.

Opus Genetics Plans to Seek Authorization to Launch Phase 1/2 Clinical Trial for LCA5 Gene Therapy

Opus Genetics, a gene therapy company launched by the Foundation, reported plans to submit an investigational new drug (IND) application to the Food and Drug Administration by the end of this year for its LCA5 (lebercillin) gene therapy. The IND, if authorized, would enable Opus to launch its planned Phase 1/2 for the emerging treatment.

The company is also in preclinical development for gene therapies for LCA13 (*RDH12*) and LCA9 (*NMNAT1*), and hopes to launch a new clinical trial every year.

Opus is funded through the Foundation's RD Fund.

Phase 2/3 Clinical Trial for Sepofarsen Does Not Meet Endpoints — ProQR Therapeutics Seeks Partner for the LCA10 and USH2A RNA Therapies

ProQR Therapeutics, a developer of RNA therapies, announced it will wind down the clinical development of its ocular programs: Sepofarsen for LCA10 caused by the mutation p.Cys998X in the gene *CEP290*, and ultevursen for Usher syndrome type 2A (USH2A) caused by mutations in exon 13.

Earlier in the year, ProQR reported that sepofarsen did not meet its endpoints for efficacy in a Phase 2/3 clinical trial. The European Medicines Agency subsequently recommended that ProQR conduct another clinical trial for sepofarsen before seeking marketing approval in Europe.

The company is looking for a partner to take on its programs for sepofarsen, ultevursen, and an additional program for retinitis pigmentosa (RP). ProQR will continue to provide access to sepofarsen and ultevursen for patients in the Phase 2/3 clinical trials.

ProQR had previously reported vision improvements in Phase 1/2 clinical trials for its LCA10 and USH2A RNA therapies.

Kiora Pharmaceuticals Gains Authorization to Launch Clinical Trial for its Photoswitch

Kiora Pharmaceuticals received authorization to launch a clinical trial for KIO-301, its emerging small-molecule therapy to restore vision in people with advanced RP and potentially other retinal conditions, independent of the mutated gene

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

causing the disease. Known as the ABACUS study, the Phase 1B clinical trial will take place at The Royal Adelaide Hospital in Adelaide, South Australia.

KIO-301 is known as a "photoswitch," a light-sensitive small molecule designed to bestow light sensitivity to ganglion cells that are downstream from degenerated rods and cones.

KIO-301 will be delivered through monthly intravitreal injections.

The Foundation provided $1.3 million through its Translational Research Acceleration Program and a Gund Harrington Scholar Award to Richard Kramer, PhD, University of California, Berkeley, for the development of related photoswitches for restoring vision.

A Thank You to Hope in Focus

The Foundation greatly appreciates the strong partnership with Hope in Focus, and its sustained and generous support for our My Retina Tracker® Patient Registry, Open Access No-Cost Genetic Testing Program, and research for treatments and cures being developed through the RD Fund.

Jack McCormick column

LOOKING BACK AT A YEAR OF SETTING GOALS AND ACCOMPLISHING THEM

Jack and his guide dog, Baloo

My 2022 has been a year of focus and intentionality where I've seen a lot of my challenging work pay off.

My advocacy resulted in my receiving LUXTURNA® gene therapy; my drive to make an impact resulted in a promotion at work and being named the 2022 Rising Star by the *Canadian HR Reporter*; and my desire to improve my health resulted in my finding a love for running and achieving my goal to run a 10K in less than an hour.

These accomplishments have not come without their challenges. In many ways, 2022 has also been the hardest year of my life. It has been like most years. Many highs and lows.

This year has been different though. I've gotten better at setting goals and following through with them. I've also gotten better at looking for, and working toward, the light during the lows.

I've written a lot in the past about feeling unable to do something because of my visual impairment, thinking no one would want to hire me, that I would not be given opportunities to advance my career, and, most recently, thinking that I would not be able to get fit due to a belief that most physical activity isn't very accessible for someone with a visual impairment.

Again, I was proven wrong. I found a community of visually impaired and fully sighted people who work together to create accessible physical activities. This means I no longer have an excuse. It means I've been able to achieve new goals.

Having a visual impairment isn't easy. However, I am reminded all the time that the hard work that comes with it is worth it. When you encounter barriers and challenges in your life, whether they be related to your visual impairment or not, remember to start looking for, and working toward, the light.

Set small, obtainable goals that lead you closer to where you want to be. It takes practice. I'm learning that it is a muscle that requires on-going effort, and that the stronger it gets, the more fulfilling life is.

The year 2022 has been eventful, one with many peaks and valleys. But thanks to this muscle, it might just be the most fulfilling year yet.

I hope that you learn from my experience, and that you have a fulfilling 2023.

Events

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

A new "Let's Chat About…" webinar episode is coming soon. Please check www.hopeinfocus.org

RARE in the Square • Global Genes
Jan. 8–11, 2023 • San Francisco's Union Square
https://globalgenes.org
RARE in the Square brings together rare disease innovators each year for a unique opportunity to network with industry thought-leaders and 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. #RareInTheSquare

Rare Disease Day
National Organization for Rare Disorders
Feb. 28, 2023
rarediseaseday.org
Join NORD in raising awareness and generating change for the 300 million people worldwide living with a rare disease, their families, and caregivers. Check online to take part in any of the more than 600 events happening throughout more than 100 countries.

VisionWalks • Foundation Fighting Blindness
Feb. 25, 2023 — Arizona VisionWalk
March 4, 2023 — Austin-San Antonio VisionWalk
March 19, 2023 — Orlando VisionWalk
www.fightingblindness.org/events
Since its inception in the spring of 2006, VisionWalk has raised more than $62 million to fund sight-saving research. Join your VisionWalk community! Together, we step closer to fighting blinding diseases.

SAVE THE DATES

Visions Ball • Foundation Fighting Blindness
April 1, 2023 • Chicago
Join the Foundation in honoring David Brint & Ira Schulman at the Ritz-Carlton.

LCA Family Conference • Hope in Focus
June 23–24, 2023 • Indianapolis
Join Hope in Focus at the Omni Severin Hotel for its third LCA Family Conference. We're bringing together families, advocates, researchers, and experts to connect and learn about the latest research advances toward cures for blindness.

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

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