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

SEEING HOPE | Newsletter

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LCA Mix & Mingle

By Rosanne Smyle

Three people who received diagnoses of Leber congenital amaurosis (LCA) in recent years — but lived most of their lives thinking they had retinitis pigmentosa (RP) — shared their stories during a special session of the VISIONS 2022 conference this summer.

An RP diagnosis is currently given to patients with photoreceptor degeneration but with good central vision within the first decade of life; an LCA diagnosis is given to patients who are born blind or who lose vision within a few months after birth.

At the two-day conference hosted by the Foundation Fighting Blindness, several of us from Hope in Focus in an LCA Mix & Mingle session heard about the sometimes-rocky road to a getting a genetic diagnosis of a rare inherited retinal disease (IRD), especially in the years before access to genetic testing.

Ultimately, that difficulty did not hold these people back from creating happy and productive lives because they did not allow their blindness to define them.

Linda Joy Wirth

Linda Joy Wirth

Blind since birth, Linda Joy Wirth, now 75 and living in Lakewood, Colo., was diagnosed with RP in the 1960s. Because she was told from an early age that nothing could be done for her blindness, she stopped thinking about her diagnosis and focused on her education, marriage, and children.

By the 1990s, she sought out a highly recommended doctor who treated her with a strong dose of cruel words.

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From the Founder:

Laura Manfre

While we are way into September already, we've got a lot to fill you in on from a busy summer here at Hope in Focus.

Several members of our team attended the Foundation Fighting Blindness VISIONS 2022 national conference in June in Orlando, Fla., where we met many wonderful people living with Leber congenital amaurosis and other rare inherited retinal diseases.

In this edition of our newsletter, we're excited to share the stories of three people we met at a special session of the VISIONS conference. Until undergoing recent genetic testing, for years they lived with a misdiagnosis of their retinal degeneration.

We're happy to let you know that the governor of our home state of Connecticut signed legislation in July to help people with rare diseases, and we'll help you learn whether your state has such an advisory group or how you can help work toward creating a similar proposal.

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LCA Mix & Mingle

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" 'You're blind. What do you want me to tell you?' " she recalled the doctor saying. "I was so distraught by the visit; I did not go back to the doctor for years and years and years."

About 10 years ago, though, she went to a Foundation conference, where she received a referral to Dr. Alan Kimura, a Denver retinal specialist who changed her life.

"When I finally saw Dr. Kimura, I said I don't even know why I'm here. I walked out two hours later, and I was walking on cloud nine. It's so important to have the right retinal doctor."

Dr. Kimura told her she had LCA. Genetic testing gave her a confirmed diagnosis of LCA10, caused by mutations in the *CEP290* gene.

People had told Linda she shouldn't marry or have children or follow her passion for acting because of her blindness. And, she'd heard those stinging words from that earlier doctor.

Linda is a retired clinical social worker in geriatric long-term care, an actor in a theater company, a Foundation volunteer, a mother of four, a grandmother of seven, a motivational speaker, and the author of "Just Because I Am Blind Does Not Mean I Can't See!"

Russ Davis

Russ Davis, 60, of Jacksonville, Fla., still gets conflicting information about the cause of his rare inherited retinal disease.

"One minute I hear it's probably LCA, or no, that it's classic RP. I got that at the conference."

Some retinal experts do consider LCA to be a severe form of RP.

In 2019, Russ received a genetic diagnosis of LCA2, caused by a mutation in the *RPE65* gene. Dr. Stephen Russell at the University of Iowa told Russ he could have RP or LCA.

Russ Davis

" 'It could be either one,' " he recalled the doctor saying. " 'But at your age with so few retinal cells, we're not going to know.' "

Russ is a little frustrated with the lack of a certain label for the disease, but it's not going to change his life.

"The blindness part, that's fine. I am who I am. It doesn't control my life. But I'd like to have answers."

These days, Russ is going with LCA.

His vision loss occurred at birth. Growing up he could read a book with a bright light, ride a bike, and he enjoyed long-distance running.

"I could see most everything, except at night when everything disappeared. When the sun went down, I was toast," he said. "There was nothing there. There was darkness and light bulbs."

His vision worsened early in his mid-20s while working for the State of Florida, looking for people who owed child support and wanted to stay missing. About 10 years ago, with his vision getting worse and work getting harder, he retired.

Russ's partner, Denise Valkema — who lives with optic nerve hypoplasia, an underdevelopment of the optic nerve — also attended the session. They met through the National Federation of the Blind, where Denise served as NFB's Florida Affiliate President.

They serve on the organization's board, working on legislation to bring about better accessibility to medical care, technology, banking, voting, and more.

"The blind community is still not able to participate fully in society because we don't have access to all the aspects of living that the sighted community community has," he said. "Try finding a talking blood pressure cuff."

Russ also advocates for people with diminishing eyesight, reassuring them that life will go on.

"It's all about your attitude. I try to tell them, no, that it's not going to be easy. Lots of times, it's going to be difficult. There are a lot of things to adjust to. You simply find new ways to do the things you were doing before.

"You can't let your loss of eyesight define who you are or control you. You have to own it."

And he lives his words.

"There's so many times in life, you have the option to laugh or to cry, and I'm going to pick laughter. It would be very easy to pick the other one."

Emily Townsend Cobb

With a 2½-year-old daughter, another one on the way, and a pediatric physical therapy career, we were lucky we had the chance to talk with Emily Townsend Cobb.

Emily Townsend Cobb, husband, Ryan, and daughter, Elora

Doctors diagnosed Emily with RP at age 3. Now, 33, she received a genetic diagnosis in 2019 of LCA13, caused by a mutation in the *RDH12* gene.

Emily is in that age group of people misdiagnosed for years before the advent of genetic testing.

"Thirty and over, that's how it went," she said.

Getting the diagnosis didn't really change her life, especially because LCA13 research is in preliminary stages.

"Now I sit and wait for my number to be called," she said, referring to the possibility of a treatment or cure for LCA13. "While we wait for all these things to happen, we have to live life."

Emily's husband, and her mom and dad accompanied her at the conference. Her father, Clay, introduced himself, saying, "Oh, I'm the proud father of two girls with *RDH12* and I'd do anything to help them."

As he broke into tears, his wife, Sue, leaned into him, saying, "He's a crier."

Without saying much more, it became clear why Emily credits her family for their loving support and positive approach toward life.

She said she receives 150 percent support from her family.

"That support is so important for anybody, but especially if you have a disability."

Doctors also diagnosed her 31-year-old sister, Ashley, with RP, and later learned she had LCA13 (*RDH12*).

As a pre-teen, Emily read newsprint and played soccer, but her vision profoundly worsened as a teen-ager, a tough time for any kid, but especially for her as she was losing her sight.

Around then, she learned she had LCA but didn't undergo genetic testing because genetic data was still being mapped out.

We talked with Emily when she returned home to Jacksonville, Fla., where, she said, early on her mom set her up with a therapist who had RP, which helped build her confidence as a teen-ager.

She put off using a cane until college and in her sophomore year got her guide dog, a black lab named Fergie, now retired to pet life after 11 years of service.

"She's currently snuggled up to me on the couch while I fold laundry," Emily said as her little girl, Elora, napped.

Her second daughter is due in October. And, oh, did we mention she runs half-marathons and is a triathlete? Emily takes part in triathlons with her husband, Ryan; they are tethered during the running and swimming races and ride a tandem bike for the cycling portion.

"If you ever want to test the strength of a marriage, blindfold one of you and tether to the other," Emily quipped.

They talked about the chances of their children being born with LCA. She recalled her husband saying, " 'Emily, if they're going to end up as awesome as you, I want to.' "

Emily and Ryan knew their children could be born with LCA, but they also knew the rarity of the disease. She said the chances of having a child with LCA are about one in 400.

"I'll take those odds," Emily said. "I'm pretty happy that I'm here."

From the Founder:

Continued from page 1

You'll read about three approaches to gene therapy, as well as the most-used system of delivering therapeutic genes to cells in the retina.

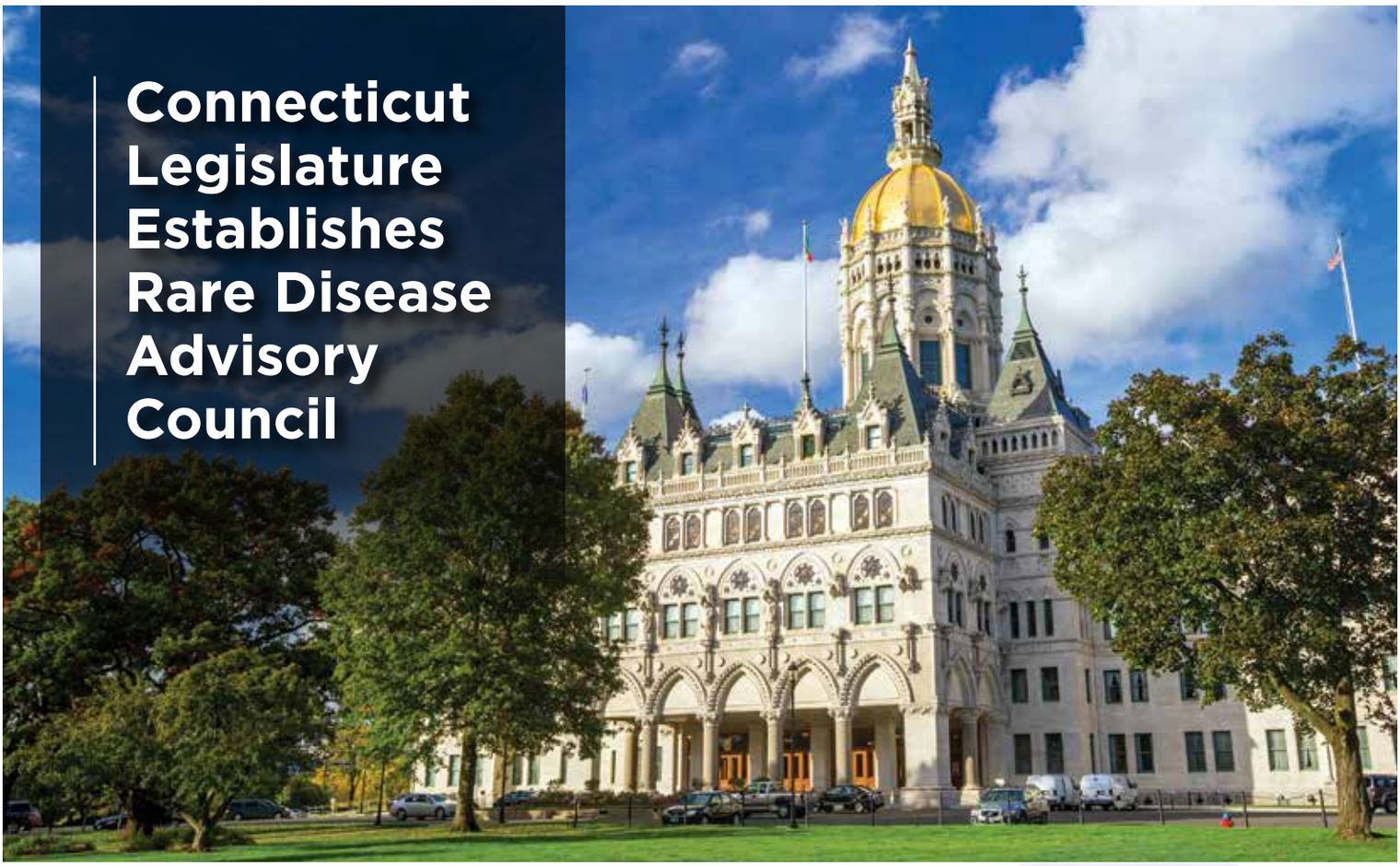
We'll also share with you extraordinarily exciting news from our columnist.

And, we are so looking forward to bringing back on October 22nd our annual gala event — Dinner in the Dark. The simple truth is without this event we would not have been able to raise funds for research to treat blindness.

We hope that you will consider joining us in October as a sponsor, a patron, or a guest, to ensure that we can once again meet our fundraising goals and keep the research moving forward!

With gratitude and focus,

Laura



Connecticut Legislature Establishes Rare Disease Advisory Council

By Rosanne Smyle

Connecticut's Governor Ned Lamont signed into law years-in-the-making legislation establishing a permanent Rare Disease Advisory Council (RDAC), effective July 1, 2022.

Lesley Bennett, Volunteer Ambassador for the Connecticut Rare Action Network of the National Organization for Rare Disorders (NORD), praised the General Assembly's Public Health Committee's bi-partisan team, Committee Chair Rep. Jonathan Steinberg and Committee Ranking Member Rep. William Petit, for bringing the legislation to fruition.

"This RDAC will give patients, families, caregivers, health care providers, advocates, researchers, and other stakeholders an opportunity to make formal recommendations to state agencies and our legislation on ways to develop public policy and health care legislation that will improve the lives of those impacted by a rare disease in Connecticut," Bennett said.

Connecticut-based Hope in Focus advocated over the years with with NORD's Rare Action Network for the establishment of the council. The state created a temporary rare disease task force in 2017 that never got off the ground.

This year, in a short legislative session — with lots of input from advocacy organizations, patients, caregivers, doctors, researchers, and advisory council members from other states — Connecticut's governor signed into law House Bill 5500, now known as Public Act 22-58, establishing a permanent RDAC.

Laura Manfre, Hope in Focus Co-Founder and Board Chair, commended the action, saying it will bring much-needed awareness to rare diseases.

"Helping people living with rare disease all begins with awareness and Connecticut's Rare Disease Advisory Council will help with that, and more, for the 7,000 known rare diseases affecting 25–30 million people, about 10 percent of the country's population," she said.

"Rare disease by definition needs all the attention it can get and establishing a Rare Disease Advisory Council here can only bring more awareness to those living with rare conditions and bring needed support to help improve people's lives.

"Rare diseases, such as Leber congenital amaurosis (LCA) and other inherited retinal diseases (IRDs) know no geographical boundaries, so it is a terrific step for Connecticut to join other 22 states that already have established such councils."

Hope in Focus representatives testified in the last several years at the capitol in Hartford in support of establishing a permanent council by educating legislators about our organization and LCA to demonstrate in human terms the necessity for such a council.

We told them that LCA is characterized by severe vision loss at birth, and that while some children are born with little or no vision, others may have significant vision loss in the first few years of life, stable vision for a time, and, as the retina deteriorates, eventually blindness.

We let them know that LCA patients treated with the gene therapy LUXTURNA® experienced dramatic changes in their lives with improved or restored vision. Five, 6, 7-year-old children treated with LUXTURNA® view life in a new light in big and little ways, and they now can see rainbows arcing in the sky and stars shining at night.

The legislators also needed to know that the optimal window for reversing vision loss is during the early phase of the disease. Current clinical trials and preclinical research give hope to those with one of the 26 other gene mutations identified to cause LCA, as those scientific studies are critical to advancing treatments for LCA and other IRDs.

After the U.S. Food and Drug Administration (FDA) approved LUXTURNA® in 2017, several states attempted to pass laws denying access to treatment to individuals, saying a certain degree of blindness must be met before they could access treatment. Such restrictions are unacceptable and go against federal health recommendations, which state the earlier the intervention, the better the expected outcome.

Hope in Focus made the point that no one who qualifies according to FDA guidelines should ever have to wait to be "blind enough" to receive access to treatment. We, along with other organizations, were quick to call these states out and urged the Connecticut General Assembly to support patient access to FDA-approved treatments.

Rare Disease Advisory Council Specifics

The new law establishes a 13-member Connecticut RDAC to advise and make recommendations to the Department of Public Health and other state agencies about the needs of people in the state living with a rare disease and their caregivers. Advisory councils may differ from state to state in some ways. Go to **rarediseases.org/projectrdac/rdacs-by-state** to check whether your state has an RDAC, is working to establish one, and how you can help.

Council members will include insurance, public health, and social services commissioners, or their designees, and 10 members appointed by the governor and the Public Health Committee leadership.

The 10 members are:

- a representative of an association of hospitals or a hospital administrator, and a physician with expertise in medical genetics.
- a representative of a patient advocacy group in the state representing all rare diseases, and a family member or caregiver of a pediatric patient living with a rare disease.
- a representative of the biopharmaceutical industry involved in rare disease research and therapy development, and an adult living with a rare disease.
- a member of the scientific community engaged in rare disease research, and a caregiver of a child or adult living with a rare disease.
- a physician who treats people living with a rare disease, and a representative, family member, or caregiver of a person living with a rare disease.

Initial appointments are required to be made by October 31, 2022. Members are not compensated for their services but may be reimbursed for necessary expenses.

The advisory council is required to meet in-person or remotely at least six times between November 30, 2022, and October 31, 2023, and quarterly thereafter. The council also must provide opportunities for the public to make comments, hear council updates, and give input on council activities.

The group also can hold public hearings to solicit comments from the public to assist with a study or a survey about people living with rare disease, their caregivers, and their health care providers.

The RDAC can consult with experts to develop policy recommendations and conduct research to make recommendations covering treatment, care, safeguards against discrimination, health insurance coverage, drug formularies, and more.

The law also requires the council, starting by November 30, 2023, to annually report to the governor and the Public Health Committee on its findings and recommendations, including council activities, research findings, and legislative recommendations; and potential funding sources for its activities, including grants, donations, sponsorships, or in-kind donations.

The first meeting of the council will be by November 30, 2022.

Can Gene Therapy Address Your Inherited Retinal Disease?

By Ben Shaberman
Senior Director, Scientific Outreach & Community Engagement

FOUNDATION FIGHTING BLINDNESS

When it comes to saving or restoring vision for people with inherited retinal disease (IRD), such as Leber congenital amaurosis (LCA), no treatment approach has received more attention than gene therapy. And rightfully so.

The U.S. Food and Drug Administration (FDA) in late 2017 approved LUXTURNA® — the first gene therapy for the eye or any inherited disease — for people with *RPE65* mutations causing LCA or retinitis pigmentosa (RP). LUXTURNA® is bringing dramatic vision improvements to most who receive it, and many gene therapies in clinical trials are showing encouraging results. Currently, about two dozen gene-therapy clinical trials are underway for IRDs.

One advantage of gene therapy is that it can be designed to address IRDs in different ways. Whom the gene therapy can help depends on which therapeutic gene is delivered to retinal cells. And the good news is that researchers are developing a range of gene therapies to address IRDs, even for those who don't know the genetic profile of their disease. Gene therapies even exist for those who have lost all their photoreceptors, the retinal cells that make vision possible.

THREE GENE THERAPY APPROACHES

Here are summaries of three approaches that, together, can potentially address the needs of a majority of IRD patients:

• **Gene replacement or augmentation:** This approach involves delivering new gene copies to replace or augment the mutated copies. LUXTURNA® is a gene-augmentation therapy. In some cases, the mutated copies may also need to be turned off. Gene replacement may be a good option if you know what mutated gene is causing your disease, whether a gene therapy targeting your gene is in development, and you have some photoreceptors remaining. One of the many benefits of genetic testing is to identify your gene to see if a gene-replacement therapy is emerging for it.

• **Neuroprotective gene therapy:** This approach is for slowing or halting disease progression, regardless of the mutated gene causing your vision loss. Neuroprotection is applicable to you if you would be satisfied with saving your remaining vision (i.e., you have photoreceptors left to preserve).

The gene delivered in neuroprotection leads to the production of growth factors that keep your retinal cells healthy. The company SparingVision is planning to launch a clinical trial soon for its neuroprotective gene therapy for preserving cone photoreceptors.

• **Optogenetics:** If you have lost all your photoreceptors, neither gene replacement nor neuroprotection will be helpful. However, optogenetics is a form of gene therapy for people who have lost all or most of their photoreceptors and vision.

It involves bestowing light sensitivity — delivering a gene that expresses a light-sensitive protein — to retinal ganglion or bipolar cells that survive in many cases after photoreceptors are lost. In other words, optogenetics is designed to enable your ganglion or bipolar cells to work something like photoreceptors.

GenSight Biologics, Bionic Sight, and Nanoscope Technologies currently have early-stage clinical trials underway for optogenetic therapies that have shown some encouraging results (restoration of rudimentary vision). We will learn more about the potential for optogenetics to restore vision as these trials and other emerging approaches move forward.

DELIVERING GENE THERAPIES

In today's world of retinal gene-therapy development, adeno-associated viruses (AAVs) are most often used to deliver therapeutic genes to cells in the retina. That's because AAVs are safe and able to penetrate cells with their genetic cargo. They naturally occur in humans and don't cause any known illness. For regulators like the FDA, that excellent safety profile is highly desirable.

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

You can think of an AAV as a large container delivery system. The containers, which scientists call capsids, hold copies of the therapeutic gene. A retinal dose of AAV could contain 300–500 billion capsids. Not all capsids will make it into the nucleus of the retinal cell — where they need to be to work — and some capsids don't have cargo. That's why so many capsids need to be in the bleb for enough of the therapeutic gene to get into the retinal cells.

But once the genes are delivered, they work — i.e., express the proteins necessary for retinal health and function — for many years, perhaps the lifetime of the patient.

• Save the Date •

LCA Family Conference

June 23–24, 2023
Omni Severin Hotel
Indianapolis

Hope in Focus is happy to present our third LCA Family Conference, bringing together families, researchers, and experts for a day of learning and connecting. You'll meet an amazing group of people and hear the latest in LCA and IRD research. You won't want to miss it!

More info will be posted soon at hopeinfocus.org

Jack McCormick column

Relief, Gratitude, and Hope After Retinal Surgery

Jack and his guide dog, Baloo

My vision with Leber congenital amaurosis had been getting worse. There was some hope that treatments for LCA would become available before it was too late. Key word "some."

I watched my vision with LCA2 (*RPE65*) worsen as researchers published trial results for LUXTURNA® and the U.S. and other countries gave it regulatory approval to treat LCA with the *RPE65* gene mutation.

Eventually Canada followed suit. But gene therapy is expensive, and funding was not easy to obtain. I continued to watch my vision get worse and began losing hope.

And then, everything changed! It became possible for me to have this breakthrough procedure.

It was mind-blowing to wake up during the weeks following the surgeries. It was so exciting to explore what new things I was able to see — my dog's eyes looking up at me as I pet him, the spray bottle I set down on the other side of the room while I clean my home, the things I drop on the floor (LUXTURNA® didn't fix my clumsiness), seeing color for the first time in years, and the best of all — being able to see in dim light.

I remain severely visually impaired after treatment. My disease was advanced and only limited cells existed in my eyes for the medication to fix, but these changes have really made a difference.

Most of all, I feel relieved. I am no longer watching my vision get worse. The improvements have stopped but should remain.

I am beyond thankful to have received this treatment and am hopeful that with continued support for sight-saving research more treatments will continue to become available.

Jack McCormick graduated in 2018 from Canada's Wilfrid Laurier University in Waterloo, Ontario. He was diagnosed in high school with LCA2 (RPE65). Jack is a Hope in Focus ambassador, helping people living with LCA and IRDs. You can read his blog at ***jackdamccormick.wordpress.com***

Events

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

Dinner in the Dark • Hope in Focus
Oct. 22, 2022 • Mystic Marriott • Groton, CT
hopeinfocus.org/dinner
Our primary fundraiser for the year, Dinner in the Dark helps fund research to cure blindness caused by LCA, provide support for genetic testing, and drive awareness, education, and connections for LCA and IRD families. Be prepared for a unique menu, fine wines, and a lively sensory adventure. In person!

Breakthrough Summit 2022
National Organization for Rare Diseases
Oct. 17–18, 2022 • Washington, D.C.
nordsummit.org
NORD is thrilled to welcome the rare family and all community stakeholders back together in-person for the 2022 Rare Diseases and Orphan Products Breakthrough Summit. Join rare disease leaders from patient advocacy groups, government, industry, and academia for exclusive access to fresh insights, compelling connections, and expert resources.

A new "Let's Chat About..." webinar episode is coming soon. Please check www.hopeinfocus.org for our upcoming sessions this fall!

VisionWalks • Foundation Fighting Blindness
Oct. 1, 2022: Philadelphia, St. Louis & Seattle
Oct. 8, 2022: Denver
Oct. 15, 2022: Columbus
Oct. 22, 2022: Charlotte
Oct. 23, 2022: San Diego
Oct. 29, 2022: Pittsburgh & Los Angeles
www.fightingblindness.org/events
Since its inception in the spring of 2006, VisionWalk has raised more than $60 million to fund sight-saving research. Join your VisionWalk community. Together, we step closer to fighting blinding diseases.

2022 RARE Health Equity Summit Partners in Action
Nov. 9–11, 2022 • Atlanta, GA (and virtually)
globalgenes.org/event/rare-health-equity-summit
Presented in partnership with the Rare Disease Diversity Coalition, the RARE Health Equity Summit connects stakeholders from the rare disease community to find ways to collaborate on addressing inequities in the care of patients with rare diseases. Sessions will focus on shortening the diagnostic odyssey, reducing racial disparities in care, and building more inclusive research programs.

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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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