SOFIA SEES HOPE

Supporting the LCA and rare retinal disease community.
We see a cure for blindness.

SEEING HOPE | Newsletter

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October 2017 | Issue 1

From the Founder

Sofia & Laura Manfre

In January 2014, Laura Manfre founded Sofia Sees Hope. The nonprofit funds the development of cures not just for her daughter Sofia's LCA gene, but also supports diagnosis, treatment and cures for all children and adults suffering from blindness caused by any of the 27 genes related to LCA.

So, Where Were You?

I remember exactly where I was when we received Sofia's clinical diagnosis of LCA. And I remember exactly where I was when the lightning bolt struck and I realized—really realized—she was considered legally blind and would at some point in the future lose her sight completely.

These two events were months apart—the real "sinking" in happened in a room full of teachers discussing Sofia's Braille studies and staring sideways at me. Suddenly I was the mom who knew her daughter was blind, had pushed for this meeting, and yet was freaking out and wondering why her daughter needed Braille instruction. Clearly, one of my finer moments.

Of course I listened to the professionals, asked questions and Googled LCA a thousand different ways looking for that one article or post that I could understand, relate to and that might even offer some clear answers for what the future would hold. Despite it all, like many other families in the LCA community, we didn't know anyone else who had a rare retinal disease, or even any other blind children.

Even eight years later, I still have those struck-by-lightning moments.

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Living With LCA: Juliet's Story

By Rosanne Smyle

Scott and Heather Soady and big sister Gillian welcomed baby Juliet two years ago, and life progressed in an understandably hectic way for the San Diego parents who also are practicing lawyers. But life soon became more complicated as the couple's new baby was diagnosed with Leber congenital amaurosis.

Juliet was born with strabismus, also known as crossed eyes, a condition that often disappears with time. At the age of 4 months, Juliet's pediatrician noticed she had involuntary eye movement, a condition called nystagmus. The doctor said Juliet presented the worst case she'd ever seen in a child.

Doctors placed Juliet under general anesthesia to scan her optic nerve and eliminate causes of her condition. It was a difficult time, Scott said, for Heather, especially, because she was breastfeeding and Juliet was only 4 months old.

When doctors told Scott, "It's probably not brain cancer," he said, "I didn't realize that was an option."

Two months later, with Juliet again under anesthesia, a specialist measured her retina's light perception by placing contact lenses with electrodes in her eyes. This procedure is called an Electroretinography (ERG) and is used to clinically diagnose LCA and other inherited retinal disorders such as Retinis Pigmentosa (RP), cone dystrophies, X-linked juvenile retinoschisis, achromatopsia and others.

Twenty minutes later, the family received a confirmed clinical diagnosis of Leber congenital amaurosis.

"What you're told is, there's this condition you've never heard of, that's extremely rare, that has no cure, that she's going to be blind and there is nothing you can do about it," Scott said.

"... You go through this grieving process of the life that you envisioned for your child. I would constantly think about these things, going to the beach, seeing a sunset, watching a movie, doing all of these things with her and sharing the world with her,

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Many Genes, One Community

Leber congenital amaurosis is a rare inherited retinal disease characterized by severe vision loss at birth. 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 period of time, and then eventually complete vision loss as the retina deteriorates into total blindness.

We often hear of only a handful of gene mutations caused by LCA. There are currently an estimated 27 validated LCA genes according to the Retinal Information Network.

AIPL1
CABP4
CEP290
CCT2
CTNNA1
CYP4V2
CLUAP1
CRB1
CRX
DTHD1
GDF6
GUCY2D
IFT140
IQCB1
KCNJ13
LCA5
LRAT
NMNAT1
PRPH2
RD3
RDH12
RPE65
RPGRIP1
SPATA7
TULP1
IMPDH1
OTX2

Ben Shaberman
Director, Science Communications
Foundation Fighting Blindness

Encouraging Research Progress for Multiple Forms of LCA

FOUNDATION FIGHTING BLINDNESS

By Ben Shaberman
Foundation Fighting Blindness

Finding treatments for the 27+ genetic forms of LCA is no doubt a challenging pursuit, but promising advances are being made on several fronts, especially in gene-therapy development.

Spark Therapeutics' **RPE65 (LCA2)** gene therapy (marketing name LUXTURNA™) is poised to become the first gene therapy for any inherited or ocular condition to receive FDA approval, thanks to its safety and the impressive vision restoration it delivered to children and young adults with severe vision loss in clinical trials.

Spark has filed its biologic license application (BLA) for LUXTURNA™ with the projected date for an approval decision of January 12, 2018. Spark is also seeking regulatory approval for the treatment in Europe.

FDA approval for LUXTURNA™ would provide strong affirmation for the biotech industry that gene therapy is a viable approach to treating LCA, a broad spectrum of inherited retinal diseases, and other genetic conditions.

Several other LCA therapies are advancing through the development pipeline. Here are overviews of some of those projects:

Clinical Trial Authorized in the U.S. for LCA10 (CEP290) Treatment

ProQR, a biotechnology company in the Netherlands, has received authorization from the FDA to start a Phase I/II clinical trial for its therapy known as QR-110, which is being developed for LCA10. QR-110 targets the specific mutation p.Cys998X in the CEP290 gene, also known as c.2991+1655A>G mutation. Known as an antisense oligonucleotide (AON), QR-110 is a drug that works like "genetic tape" to repair the mutation. The mutation affects about 2,000 people in the Western world.

Emerging Gene Therapy for LCA6 (RPGRIP1)*

Eric Pierce, M.D., Ph.D., Massachusetts Eye and Ear Infirmary (MEEI), in collaboration with Luk Vandenberghe, Ph.D., also at MEEI, is developing a gene therapy for LCA6, which is caused by mutations in RPGRIP1. He is currently evaluating the latest version of the treatment in an RPGRIP1 mouse model. Plans include generating a clinical-grade gene-therapy vector for toxicology studies, and ultimately, a clinical trial. Dr. Pierce's clinic has also identified seven families with RPGRIP1 mutations—families who could potentially participate in a natural history study or clinical trial.

University of Florida, Genzyme Collaborating on LCA1 (GUCY2D)*

With support from the biotechnology company Genentech, Shannon Boye, Ph.D., University of Florida, is developing a gene therapy for LCA1, which is caused by mutations in GUCY2D and affects cone photoreceptors. Previously, she and her colleagues fully restored vision in a cone-rich mouse model with a retinal disease similar to LCA1. Dr. Boye and her team are now working toward moving a gene therapy for LCA1 into a clinical trial.

Researchers in the Netherlands Developing LCA8 (CRB1) Gene Therapy*

Jan Wijnholds, Ph.D., Leiden University Medical Center, is developing a gene therapy for people with LCA8, which is caused by mutations in CRB1. Dr. Wijnholds is making good progress in overcoming two challenges with a CRB1 gene therapy. Those challenges are: 1) the CRB1 is too large for the viral gene delivery systems frequently used in retinal gene therapies, and 2) mice with LCA8 express CRB2 protein (not CRB1) in their photoreceptors. (The CRB2 gene is similar in function to CRB1 and smaller.) Dr. Wijnholds is determining if a CRB2 gene therapy is a good candidate for people with LCA8. Or, he may "shrink" the CRB1 gene so it can fit into a viral delivery system for a human gene therapy.

Researchers Pursue Gene Therapy for LCA Caused by IQCB1 Mutations*

A team of University of Pennsylvania researchers has identified a canine model of LCA caused by mutations in the gene IQCB1, which encodes the protein NPHP5. In humans, the condition causes early and severe vision loss from LCA, and in some cases, kidney dysfunction. The investigators found that in canines, the retinal degeneration is remarkably similar to that in humans with NPHP5 mutations, though dogs don't have the renal dysfunction. Using the model, the researchers are now testing potential gene therapy approaches to eventually slow or halt vision loss, or possibly improve vision, in humans. They've already had some success with gene therapy in canines.

**Projects supported by the Foundation Fighting Blindness*

Juliet's Story

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and all of a sudden, that's never going to happen with her."

Gradually, his perspective changed: "You're still going to do all these things, but you're going to do it in a different way. ...There is nothing in the world that tells you what that's going to be like for her. ...You have to adapt everything so that it will happen."

At the age of 2, Juliet is legally blind. With glasses, her vision is 20/470. In other words, Scott said, the same object and details you can see at 470 feet away, she will only be able to see at 20 feet. Doctors say her vision may deteriorate over time.

Looking for more information and answers, Scott attended the national VISIONS conference hosted by the Foundation Fighting Blindness last summer in Baltimore.

"That's where I met Laura (Manfre, Sofia Sees Hope co-founder) and a bunch of other families that have kids with the same condition. That was truly amazing," Scott said. "You feel so alone, the condition is so rare, there's not going to be someone you just run into."

He said he was touched that for the first time, people asked how *he* was doing.

Meeting parents who are dealing with LCA and seeing young people with LCA functioning as normal teen-agers gave Scott comfort and hope that everything's going to be OK.

Through Laura, Scott and Heather connected with Spark Therapeutics' "ID your IRD" initiative for Juliet's genetic testing. Scott said he still held hope that maybe Juliet really did not have LCA, but the genetic findings confirmed otherwise.

The testing also revealed that Juliet has what is called a de

novo mutation of the CRX gene, which caused it to be autosomal dominant rather than autosomal recessive. This means Juliet's condition is a result of a gene mutation, rather than inheriting it from her parents. It also means that Juliet could pass it on to her children.

"It's not quite the normal LCA," Scott said. Of those who have LCA, 1 percent to 5 percent have this gene mutation.

Genetic therapy also is more complicated. Rather than inserting a good gene and having the bad one go away or bypassed, the CRX dominant gene first needs to be turned off before a good gene can be inserted.

The Soadys connected with a doctor who was conducting this research but had to stop for lack of funding.

"The light at the end of the tunnel got much dimmer," Scott said of the end of the research. "It would be nice to see if there's a potential cure."

For now, the family is in the intense process of preparing Juliet for a new time in her life, from a home environment to a school environment, as she begins preschool. Gillian, who turned 5 in September, will be in kindergarten.

So, Where Were You?

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While I still don't have many answers, and I don't know if my daughter will ever be able to see the stars at night like she hopes to, there are some things I have learned over the last few years:

Sofia isn't the only kid dealing with vision loss or blindness. I'm certainly not the first or last parent to feel helpless, frustrated, and let's face it, just plain frightened by the knowledge that I can't just kiss this and make it better.

On the flip side, I know that:

Cures and treatments for blindness are not as far off as they used to be.

The more of us who participate in genetic testing, patient registries, and opportunities for our voices to be heard, the better we can support the research to cure blindness.

Connecting with other families to share stories helps us all be a little less isolated, better informed, and perhaps even comforted knowing others have gone this way already.

With the fantastic team we've assembled at Sofia Sees Hope, I am learning what it means to be a patient advocacy organization and how outreach and education can speed up the research we all hope for and make us a stronger community.

We owe many thanks to the families and individuals who have shared their stories with us in this first newsletter and online. We're just getting started on this journey, and still have so much to learn! We hope you will join us as we move forward and I'm looking forward to where this path takes us all. Share your stories, share your events and news, share your questions. You can always contact us at info@sofiaseeshope.org and visit us online at sofiaseeshope.org.

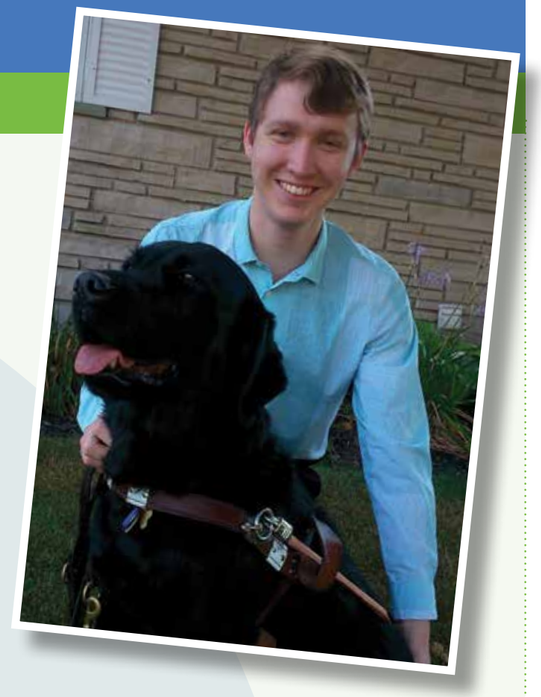
All the best,

Laura

Laura

College Connection

Diagnosing My Passion



When I was diagnosed with Leber congenital amaurosis, I experienced an overwhelming number of emotions. I felt unsure of the future, upset, and relieved. Why these emotions? Well, for me it was a long and complicated process to get to my diagnosis.

The story starts about a year after my birth in 1996. My parents could tell that I was not like other babies and concluded that I couldn't see properly because my eyes tended to focus on lights rather than on faces. The ophthalmologist said I could see fine, and, believing I had an intellectual disability, referred us to a neurologist.

The neurologist agreed with my parents that I had visual impairment. Eventually my ophthalmologist provided my parents with a clinical diagnosis, Cone Rod Dystrophy, and told them I would never see well but my vision would be stable.

For the most part, growing up with a vision impairment resulted in a normal childhood. I played sports, went to school and made memories with my family.

However, vision loss also creates many of its own challenges. I was a C or B student until seventh grade when my teachers finally realized how to make classes accessible for me (I am now in University with a 3.88 GPA). I also was bullied a lot—vision loss means difficulty in picking up social cues, and children target those who are different.

Fast forward to 2012, I was sitting in my second-period classroom in high school when I noticed a light that I couldn't stop seeing, no matter how many times I blinked. My mind began to race: What if the doctors were wrong? What if my vision wasn't stable?

It took well over a year, countless procedures and eventually genetic testing to find out that the doctors were wrong. I had LCA and was gradually losing my vision. At first, I was terrified, wondering how would this diagnosis affect my life? This soon changed. My diagnosis helped me find my passion.

I have always known that people treat me differently because of my visual impairment, but I have become increasingly more aware of this with the deterioration of my vision. It is no secret that people with disabilities are seriously underemployed, experience discrimination and are required to overcome accessibility barriers every day.

Because of this, I have become passionate about accessibility and inclusion. I bring these passions everywhere I go. I am an active accessibility advocate and I am co-founder of a student club called Eye to Eye, with a mission to eliminate stigma associated with visual impairments.

I am excited to bring these passions to this newsletter. I hope that in sharing my experiences and what I have learned from them that I can help others living with LCA overcome the barriers in their lives.

"It took well over a year, countless procedures and eventually genetic testing to find out that the doctors were wrong."

Jack McCormick is a business student at Canada's Wilfrid Laurier University, and a guide dog user who lives with Leber congenital amaurosis, an inherited retinal disease. He is an active accessibility advocate who dreams of a future where society no longer defines people by single characteristics. Upon graduation, Jack hopes to start work in the field of Human Resources and continue to volunteer as an accessibility advocate.

You can read his blog here: ***jackdamccormick.wordpress.com****.*

Dear Diary:

I wish I could see more stars

August 22, 2017

Dear Diary,

I like the stars, even though I can't see them. I was excited for the eclipse. Everyone was talking about it, and since it's summer and mom works from home we were all there to watch it together. Dad got a brownie box and a cereal box and made some sort of contraption for us to safely watch the eclipse. I joked that it was funny that the sun was in the box. Also that I might damage my eyes more, since I'm going to be totally blind someday anyway.

Once the eclipse started, we all hung out on the porch and looked into our boxes. I could see the dot inside the box. I couldn't tell that sun was being covered though. Only that the light was getting dimmer. Mom and Dad kept asking me what I could see, and I kept telling them I could see it. I think that made them happy.

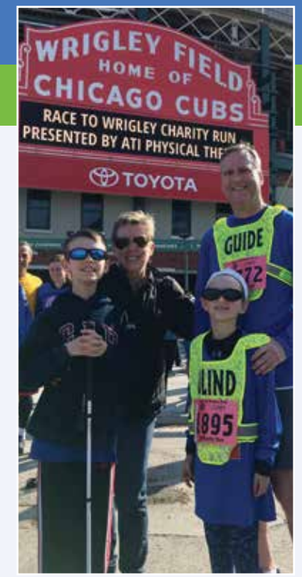
When I look up in the night sky I just see darkness. Sometimes I can see the moon. Sometimes I can see some really bright stars. Once, I was excited to see the moon huge and bright but Mom told me that it was just a street lamp and I was looking in the wrong direction. But the other times I know that I saw moon. I wish I could see more stars. Someday I hope to see all the stars, but I guess I probably won't. I hope I'm wrong.

Sincerely,
A Stargazer with LCA
Age 14

We'll be sharing a DEAR DIARY story as part of every LCA "Seeing Hope" newsletter. We'd love to hear your child's DEAR DIARY story! Send it along, with your name or anonymously. You can email it to rosanne@sofiaseeshope.org

LCA Connections

Ditka Dash



Lee St. Arnaud and his daughter Mirielle are training for the 5K Ditka Dash this October, named for the retired Chicago Bears football coach Mike Ditka, ("Da Coach") who is adored by all of Chicago. The event is a fundraiser for Special Olympics of Chicago and as participants, Lee and Mireille will receive a proper mustache, aviator sunglasses and a race shirt reminiscent of Coach Ditka's fine wool sweater vest. We can't wait to see the photos! Here is a photo of the family outside Wrigley stadium this summer. Mireille and her brother Patrick have the IQCB1 gene.

Bank For The Buck At This Backyard Bash

Jenny and Kevin Cohane began raising funds for Leber congenital amaurosis in 2012, about the time their daughter, Annie, was being mainstreamed into the local school. In 2009, doctors diagnosed Annie at 3 months old with LCA-CEP290. After being inspired at the Foundation for Retinal Research conferences, the Cohanes decided to get involved. Their objectives were: to help fund LCA research; to raise awareness for Annie in her community, as well as others who are blind; to bring people together and to have fun. They decided on a simple idea of a "backyard tailgate" with open bar, snacks, sweets and a rollicking live band and a suggested donation at the door. Since 2012, they have raised over $130,000 and their most recent party had over 350 attendees under the stars. This year, they hope to continue their success with their "Back to Basics" party in Norwell, Mass., on Saturday, Sept. 23. In the past, the Cohanes gave the funds to the Foundation for Retinal Research. Now the funds will go to the Foundation Fighting Blindness since the two organizations merged. Congratulations to the Cohanes for hosting such fun and fruitful parties!

Have an update, event or a shout-out to share? We want to hear from you! Send us your news at rosanne@sofiaseeshope.org

The Role of the Patient Voice in Research

By Rosanne Smyle

Extraordinary and exciting developments are happening in LCA research, as Spark Therapeutics' gene therapy for an LCA gene mutation is under review by the Food and Drug Administration, in the hopes of becoming the first gene therapy for a genetic disease in the United States.

The therapy under FDA review would be for patients with vision loss due to confirmed biallelic RPE65 mutation-associated retinal dystrophy, according to the FDA's Department of Health and Human Services notice.

In September, the FDA announced the public meeting of the Cellular, Tissue, and Gene Therapies Advisory Committee (CTGTAC) on Oct. 12 in Silver Spring, MD. The committee will discuss and make recommendations on the safety and effectiveness of an application for voretigene neparvovec, which has the proposed trade name of LUXTURNA™, submitted by Spark Therapeutics, headquartered in Philadelphia, according to the notice.

The role of the patient community is important long before a potential treatment gets to the FDA, and patients and advocacy groups play a pivotal role in moving research to fruition.

The FDA has included the patient perspective in Advisory Committee meetings since 1991. As stated on the FDA website, they have a "difficult task when it comes to evaluating and approving new and innovative medical products. Individual patients may experience the effects of diseases and therapies differently and each individual patient has a unique perspective about treatments or diagnostic procedures that differ from those perspectives of other patients or of their healthcare provider."

However, the role of the patient community is important long before a potential treatment gets to the FDA, and patients and advocacy groups play a pivotal role in moving research to fruition.

Patient input is especially important in what can be a long and arduous process, hampered by research setbacks and by the business of research when companies are bought and sold or when personnel move from one company to another. Connecting researchers' work to patients' needs helps inform the research and also motivates teams as they continue their studies.

Researchers work at sustaining two-way conversations between patients and companies by building and growing relationships. This happens through advocacy organizations and through formal patient advisory boards to glean answers to researchers' anticipated issues.

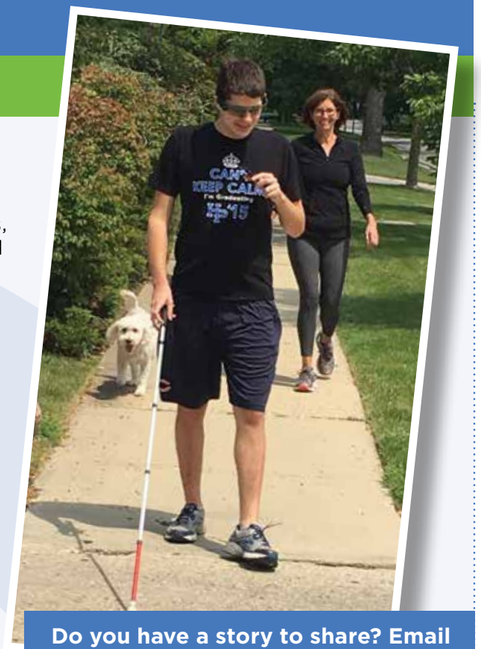
Increased awareness of rare inherited retinal diseases and recent FDA approval of the first gene therapy in the U.S. for a form of non-genetic leukemia send a positive signal to the rest of the biotech industry, encouraging more gene therapy research.

The rare inherited retinal disease community should be encouraged and ready to participate in patient registries, advocacy organizations, patient advisory panels and other awareness opportunities where their voices will continue to support and inform research to cure blindness.

Tell Us Your Story

Independence Day

By Sally Higginson



Do you have a story to share? Email rosanne@sofiaseeshope.org

Trust me when I tell you to grab a tissue. Or roll down your sleeves and get ready to wipe. Me? My eyes are welling up even as I type. Recently, I witnessed a miracle.

I'll give you a little background while you look for a Kleenex. Twenty years ago, at the age of 8 weeks, my nephew Alan was diagnosed with Leber congenital amaurosis (LCA), a rare disease that limits retinal development. Holding her infant son, my sister Betsy and her husband David listened in disbelief as the retinal specialist explained that Alan would be visually impaired at best, and fully blind at worst. The doctor informed them there was no cure, no treatment, and no adaptive device to correct their son's condition.

Like his sighted peers, Alan attended public school. His mobility instructor taught him to navigate familiar parts of his world with his white cane. By sixth grade, he could walk to school by himself. Now a junior at Beloit College, he's doing just fine. That's not the miracle.

Not to dismiss Alan's role in his accomplishments, but his successes have been in some part reliant on a team of people. Still, there are limits to his independence. Spoiler alert: here comes the miracle.

Last week, Betsy called me. "Get outside now. Alan is walking to the train station. By himself. He's near the library. Run."

I ran. Turning the corner, I saw my nephew, cane in hand, walking a route new to him. Betsy trailed silently, about 10 feet behind.

"Hey Aunt Sally. Is that you?" Cue the tears. Remember, Alan is blind. He has never seen me coming his way. For 20 years, we've all come up to him and touched him, or spoken to him, or hugged him, letting him know we were there. For the first time, he 'saw' me coming.

Alan was wearing an adaptive technology, and it was changing his life in front of my tearing eyes.

The technology is called Aira (eye-rah). According to their website, "Aira's platform works on a wearable device similar to Google glass, that can be paired with a smart phone. The tiny camera mounted on the device [cool sunglasses] provides instant feedback to a trained Aira agent who can safely guide [a wearer] in any activity."

"For 20 years, we've all come up to him and touched him, or spoken to him, or hugged him, letting him know we were there. For the first time, he 'saw' me coming."

Alan's Aira glasses had arrived the day before. The device is free, and the glasses are free. Like a cell phone contract, users pay a monthly service fee based on the minutes they use. When it's on, an agent sees a split screen. On one side is a GPS view, to map out the exact location of the route guidance. On the other screen, the agent sees the lens view from the user's camera. Simple, yet genius.

I fell in step with Betsy, following Alan's lead for the first time. He made it easily to the train station, then home via a different route. Since then, he's walked to a local bagel shop and "read" menus. I asked Alan, "What do you like best about this?"

"I like walking somewhere that I've never walked to before, by myself, without learning the route. I like reading menus. I like finding people. I found you!"

I turned to my sister. "Well? What are you thinking?"

"It's totally selfish. I want to be his eyes."

"Don't you think you've been his eyes?"

"Yeah, I guess. And now I'm turning it over to somebody else."

There wasn't a dry eye between us.

Events

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

Sofia Sees Hope

Dinner in the Dark

October 14 • 6:00 PM–11:00 PM
Mystic, CT
sofiasees.org/getinvolved/dinner-in-the-dark

Sofia Sees Hope's primary fundraiser for the year, this event 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!

National Organization for Rare Disorders (NORD)

Breakthrough Summit

October 16 8:00 AM – October 17 @ 5:00 PM
Washington, D.C.
rarediseases.org/summit-overview

National Organization for Rare Disorders (NORD) annual Breakthrough Summit—information about advocacy, meetings for members, potential collaborators.

Foundation Fighting Blindness

Vision Seminar Series

Nashville: Fall 2017
Los Angeles: Winter 2018
San Antonio-Austin: Jan. 27, 2018
Tampa, FL: Winter 2018
blindness.org/conferences

The Foundation Fighting Blindness is proud to enter the ninth year of our successful Vision Seminar Series! With so many advances in retinal disease research, you should not miss this opportunity to learn more about the latest research advancements, treatment options and clinical trials.

Foundation Fighting Blindness

VISIONS 2018 National Conference

June 21–23, 2018 • San Diego, CA
blindness.org/conferences

Wonderful weather and a myriad of family friendly activities! Hear the latest research and treatment advances. Attend sessions on thriving despite vision loss, and enjoy social and community-building opportunities. Conference registration will open January 2018.

What do you want to learn at the VISIONS conference? Send your input and ideas to info@sofiaseeshope.org

The *Seeing Hope* newsletter is published quarterly by Sofia Sees Hope, 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 Sofia Sees Hope visit our website at www.sofiaseeshope.org.

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