

First Patient Receives Emerging CRISPR Therapy in Clinical Trial for LCA 10

First time emerging CRISPR therapy administered inside the human body

by Ben Shaberman

Clinical researchers at Casey Eye Institute, Oregon Health & Science University (OHSU), have dosed the first patient with an experimental CRISPR/Cas9 therapy in the BRILLIANCE Phase 1/2 clinical trial for people with Leber congenital amaurosis 10 (LCA 10). The emerging treatment targets a specific mutation (c.2991+1655A>G in Intron 26) of the gene CEP290.

Sponsored by Allergan, a global pharmaceutical company, and Editas, a gene-editing therapy company, the trial is assessing safety and efficacy of their emerging gene-editing therapy in 18 patients at four sites in the US.

Known as EDIT-101, the CRISPR/Cas9 gene-editing technology is designed to locate and remove the mutation in LCA10. 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 (replacement) 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.

Continued on page 11

WHAT'S INSIDE ▼

- Pg. 2 |** A Message from Our COO
- Pg. 3 |** No Limits for Determined Paralympian Triathlete
- Pg. 5 |** 10 Things to Know Before You Fall Victim to a Retinal Stem Cell Scam
- Pg. 6 |** Clinical-Trial Pipeline
- Pg. 8 |** National Virtual VisionWalk Day
VISIONS 2020
- Pg. 9 |** Astellas' Abilities Dining in the Dark
Columbus Chapter Co-Presidents:
Jen & Kevin Walker
- Pg. 10 |** Genetic Testing for Inherited Retinal Diseases through the Foundation's Open Access Program

HELP FIGHT BLINDNESS

Use the enclosed envelope to make a life-changing gift.

In Focus is published by:
Foundation Fighting Blindness, Inc.
7168 Columbia Gateway Drive
Suite 100
Columbia, MD 21046

Foundation Board Officers

David Brint, *Chairman*

Gordon Gund, *Chairman Emeritus*

Joel Davis, *Vice Chairman,
Major Gifts*

Eddie Russnow, *Vice Chairman,
Development*

Jonathan Steinberg, MD,
Vice Chairman, Research

Warren Thaler, *Vice Chairman, Board,
Development & Communications*

Haynes Lea, *Treasurer*

Yvonne Chester, *Secretary*

Foundation National Management Staff

Benjamin Yerxa, PhD, *Chief
Executive Officer*

Jason Menzo, *Chief Operating Officer*

Patricia Dudley, *Chief Human
Resources Officer*

Brian Mansfield, PhD, *Executive Vice
President of Research/Interim Chief
Scientific Officer*

Chris Adams, *Vice President,
Marketing & Communications*

Nancy Davenport, CPA,
Vice President, Finance

Michele DiVincenzo, *Vice President,
Events*

Todd Durham, PhD, *Vice President,
Clinical & Outcomes Research*

Russell Kelley, PhD, *Vice President,
Investments & Alliances*

Amy Laster, PhD, *Vice President,
Science & Awards Programs*

Judy Taylor, *Vice President,
Development*

Foundation In Focus Newsletter Staff

Ben Shaberman, *Senior Director,
Scientific Outreach & Community
Engagement*

Lauren Reeves, *Senior Specialist,
Content Marketing*

A MESSAGE FROM OUR COO



With the ongoing spread of the coronavirus (COVID-19), there is nothing more important than the health and safety of our Foundation Fighting Blindness families and the larger community. As important as the Foundation Fighting Blindness is to you, now is the time we must prioritize around the safety of our loved ones and take care of our families – our

parents, children, sisters and brothers.

What you and I do to social distance is critically important to slow the spread of the coronavirus. With that, we have had to make tough decisions to move our upcoming events – VisionWalks, special events, chapter meetings and Vision Seminars – to virtual experiences.

While you're staying home, we're taking advantage of these virtual events to continue the momentum and energy of our mission. Even though we won't be gathering in person, our mission to fight blindness is unchanging.

As we're all reorganizing our priorities, we just want to say thank you for your commitment. Thank you for your unwavering support in the fight to end blinding retinal diseases. We know that we are stronger together. Together, we are making a difference.

Sincerely,

A handwritten signature in blue ink that reads "Jason Menzo". The signature is fluid and cursive, with a large initial "J" and "M".

Jason Menzo, *Chief Operating Officer*

Any products and/or services mentioned within In Focus are presented as a source of information and should not be misinterpreted as a recommendation of the Foundation. The Foundation has not tested or evaluated the products reported upon to determine their safety or effectiveness.

For a copy of this publication, write to In Focus at the above address, or call (800) 683-5555 (TOLL FREE); (800) 683-5551 (FOR TTD). Or visit us at FightingBlindness.org.

Physicians differ in their approach to incorporating research results into their clinical practices. You should always consult with and be guided by your physician's advice when considering treatment based on research results.

No Limits for Determined Paralympian Triathlete



Elizabeth competing in triathlon race with her guide, transitioning from swimming, to cycling to running.

by Lauren Reeves

Elizabeth Baker was diagnosed with Stargardt disease at the age of 15. At that time, Elizabeth felt like she was limitless, and nothing could bring her down. But once Elizabeth started college at the University of Georgia, her vision quickly declined and her eventual blindness became more of a reality.

"I definitely wrestled with a lot of challenges in trying to figure out how to learn when I could no longer see boards or books," says Elizabeth. "I then realized that I could not control the amount of vision I would lose, but I could control how I responded to it. It was sink or swim, and I chose to swim."

This "sink or swim" attitude has led Elizabeth to extraordinary feats. Now 45 years old, Elizabeth lives in Chattanooga, Tennessee, with her husband, two children, and competes with the USA Paratriathlon Team, which features completing 750 meters of swimming, 20 kilometers of cycling and 5 kilometers of running.

Elizabeth raced in her first triathlon in 2004, but unfortunately crashed on her bike multiple times due to her lack of central vision. After that





Elizabeth with her husband, Brian, and two children on a hike with a waterfall and trees behind them.

experience, she decided to continue racing as a visually impaired athlete, which entails competing alongside a guide, and started training for the Chattanooga IRONMAN. At age 40, Elizabeth completed her first IRONMAN and won her division.

The sport of paratriathlon made its Paralympic debut at the 2016 Rio de Janeiro Games, which motivated Elizabeth to begin her intense training to join the USA team.

Elizabeth qualified for the Rio de Janeiro Paralympic Games and has since raced in Australia, Japan, Switzerland, Spain and many other locations all over the world. But Elizabeth's favorite part about being a paratriathlete is her teammates.

"Our team is made up of amazing athletes who race in different categories such as the wheelchair class, amputee class, and visually impaired class," says Elizabeth. "All of these people are the highlight of my racing. Being a paratriathlete is more of a team sport for me, where my guide and I really have to be in sync."

As Elizabeth plans to retire after the 2021 Paralympic Games, she hopes to use her

triumphant experiences to be a resource and help advise those involved with the Foundation and blindness community.

"I would love to help others realize all the opportunities they can have regardless of their retinal disease," says Elizabeth. "I have many days in my life where I'm in a grumpy mood. But during these times, I allow myself 30 minutes to "feel sorry for myself," and then I move on and get over it. I have had these 30-minute "pity sessions" over the years, but as I have adjusted to living with Stargardt, I seem to need them less and less."

Although Elizabeth has had her share of challenges throughout life and her athletic career, she credits her Stargardt disease for making her a tougher person.

"I don't think of my vision loss or diagnosis as something that limits me," says Elizabeth. "It's a part of me and although having limited vision isn't the easiest, it's made me the strong person I am today and opened new doors to accomplish some pretty amazing things." 

10 Things to Know Before You Fall Victim to a Retinal Stem Cell Scam



by David Gamm, MD, PhD
*Foundation-funded
researcher at the
University of
Wisconsin-Madison*

1. **The hope is real.**

Stem cell technology has created exciting possibilities for treating diseases that have perpetually plagued humankind. But these remain early days in the technology and we have an obligation to be transparent.

2. **The difference between hope and hype is a single letter and a compelling website.** Private stem cell clinics touting miracle cures can cause you to lose whatever vision you have left – or your entire eye – due to infection or another catastrophic event.

3. **Confused? It's not your fault.** Stem cell technology is complicated and still new, and there are a growing number of clinics that are attempting to financially capitalize on patients. You should know that in many cases, the “stem cells” that are being transplanted in these for-profit clinics are from fat, bone marrow, or another source that has no proven ability to replace missing retinal cells.

4. **Be highly skeptical of any clinic touting a stem cell therapy that requires you to pay a fee or that claims to be a cure-all.** Almost all valid stem cell therapies are still in the clinical trial stage, or even earlier. Ethical scientists will enroll patients in these trials without asking for, or accepting, payment (often, they pay you for travel and accommodations).

5. **In order to avoid scams, it is important to understand the retina.** The retina is a complex

“layer cake,” with each layer containing specific types of cells that perform a precise job and connect to other cells to form a neural circuit. Deepest within the retina lies a layer of photoreceptors that detect light and initiate a cascade of events that ultimately lead to our perception of vision. Retinal pigmented epithelial cells, or RPE cells, do not detect light but rather help photoreceptors do their job. If you lose RPE cells, the photoreceptors they serve will eventually lose their ability to function and die.

6. **Also, it is important to understand what happens when retinal cells die.** Some of the most devastating and incurable causes of blindness are rooted in the death of retinal cells.

7. **We are born with all the retinal “parts” we are ever going to have.** The human retina has no innate ability to replace these cells once they are lost. This is one reason why stem cells have drawn so much attention.

8. **Stem cell therapies may provide an option to replace the lost cells** by introducing new cells obtained from an outside source. Pluripotent stem cells (PSCs) can theoretically make any cell in the entire body. Many highly differentiated and specialized cell types can now be produced from human PSCs.

9. **The “installation challenge” is formidable for all cell types,** and scientists are just beginning to tackle the question of developing effective methods of installing the new cells and getting them to function within the retina. For-profit stem cell clinics will often just randomly inject their product far away from the area where they would need to go.

10. **There is no magic to stem cells,** but there is a great deal of excellent and well-designed research being performed in the field. Stem cells have unique but variable properties that, if thoughtfully tested and applied, may be of considerable help in the foreseeable future. We're optimistic about this future...and you should be, too.

Retinal-Disease Therapy

Inherited Retinal Diseases and Dry AMD: 38 trials (Select trials) | Updated April 2020

GENE THERAPIES	Progress
Achromatopsia (CNGB3) – AGTC	Phase 1/2
Achromatopsia (CNGB3) – MeiraGTX	Phase 1/2
Achromatopsia (CNGA3) – AGTC	Phase 1/2
Achromatopsia (CNGA3) – Tubingen Hosp	Phase 1/2
AMD (Dry) – Gyroscope	Phase 1/2
Choroideremia (REP1) – Nightstar	Phase 3
Choroideremia (REP1) – Spark	Phase 1/2
Choroideremia (REP1) – Tubingen Hosp	Phase 2
LCA and RP (RPE65) – MeiraGTX	Phase 1/2
LCA and RP (RPE65) – Spark	FDA Approved
RP (PDE6B) – Horama	Phase 1/2
RP, Usher, others (optogenetic) – Allergan	Phase 1/2
RP, Usher, others (optogenetic) – GenSight	Phase 1/2
RP (RLBP1) – Novartis	Phase 1/2
Retinoschisis (RS1) – AGTC	Phase 1/2
Retinoschisis (RS1) – NEI	Phase 1/2
Stargardt disease (ABCA4) – Sanofi	Phase 1/2
Usher syndrome 1B (MYO7A) – Sanofi	Phase 1/2
X-linked RP (RPGR) – AGTC	Phase 1/2
X-linked RP (RPGR) – MeiraGTX	Phase 1/2
X-linked RP (RPGR) – Nightstar	Phase 2/3

CELL-BASED THERAPIES

Progress

AMD-dry (RPE) – Astellas	Phase 1/2
AMD-dry (RPE) – Cell Cure	Phase 1/2
AMD-dry (RPE from iPSC) – NEI	
AMD-dry (RPE on scaffold) – Regen Patch	Phase 1/2
RP, Usher (retinal progenitors) – jCyte	Phase 2b
RP, Usher (retinal progenitors) – ReNeuron	Phase 2
Stargardt (RPE) – Astellas	Phase 1/2

MOLECULES, PROTEINS, AONS

Progress

AMD-dry (C3 inhibitor) – Apellis	Phase 3
AMD-dry (C5 inhibitor) – Iveric bio	Phase 2
LCA (CEP290, AON) – ProQR	Phase 2/3
LCA (CEP290, CRISPR) – Editas	Phase 1/2
Retinitis pigmentosa (RHO-P23H) AON	Phase 1/2
Stargardt disease (emixustat) – Acucela	Phase 3
Stargardt disease (deuterated vit A) – Alkeus	Phase 2
Stargardt disease (C5 inhibitor) – Iveric bio	Phase 2
Stargardt disease (anti-RBP4) – Belite Bio	Phase 1
Usher syndrome 2A (AON) – ProQR	Phase 1/2

Visit **ClinicalTrials.gov** for more details and trial contact information. This document is for informational purposes only. Information is subject to change, and its accuracy cannot be guaranteed.

VIRTUAL EXPERIENCES

National Virtual VisionWalk Day

After careful consideration to keep our Fighting Blindness family safe, all of our VisionWalks that were scheduled to take place through June 2020 will be transformed into one nationwide virtual event. We invite you to join us on **Saturday, June 6, 2020** for our new **National Virtual VisionWalk Day!**

While we are sad to not be walking with you in person this year, we are focusing on what we can do together from afar to continue fighting blindness. On June 6th, take a walk around your block, on your treadmill, or in spirit and show us how you're celebrating using #VisionWalkStrong on social media.

Our VisionWalks may look different this year, but our mission to find treatments and cures is

unchanging. Now more than ever, we can stand strong together as a community and make a difference. We appreciate the continued support.

Register your virtual VisionWalk team at: **VisionWalk.org**



VISIONS 2020

Presented by Foundation Fighting Blindness

VISIONS 2020: Our Mission Is Your Vision

The Foundation has made the tough decision to pivot our approach to VISIONS 2020, the national conference of the Foundation Fighting Blindness, that was planned for June 18-20 in Minneapolis, MN.

The new approach will still allow us to meet, but not in person. We are actively developing a virtual experience that will provide a wide range of science and research presentations, practical adapting and thriving sessions and an opportunity to connect with others from across the country.

Stay tuned as we share more about our new VISIONS 2020 virtual event in the coming weeks. We look forward to bringing you this new engaging experience. Stay up to date by visiting: **FightingBlindness.org/VISIONS2020**

Thank You to Our
VISIONS 2020 Sponsors:

Gold Partner & Accessibility Underwriter



Silver Partners



Bronze Partner



COMMUNITY PARTNER

Astellas' Abilities Dining in the Dark



Grace Nash and Nancy Martin, MD, PharmD, Executive Medical Director, Astellas

In February, Astellas' Abilities Employee Impact Group, in partnership with the Foundation Fighting Blindness, hosted a "Dining in the Dark" where Astellas employees ate lunch with blindfolds on to simulate living with visual impairment. Attendees then heard from a patient and her mother, Michelle and Grace Nash, who spoke about the challenges of living

with retinal degenerative disease. Astellas values the contributions of people of all abilities and understands that different perspectives are a critical component of innovation. The company strives to foster an inclusive culture that enables people of all abilities to thrive and bring their best selves to work, every day.



Left: Grace behind a podium speaking at the Astellas event. **Right:** Michelle and Grace Nash (Mother and Daughter)

CHAPTER SPOTLIGHT

Columbus Chapter Co-Presidents: Jen & Kevin Walker



Kevin and Jen Walker

Jen Walker was diagnosed with retinitis pigmentosa (RP) at 14 years old. Jen now lives in Columbus, Ohio, with her husband, Kevin, and two daughters. Jen and Kevin attended their first Foundation

Fighting Blindness event in 2017, which was the Columbus Chapter's Dining in the Dark fundraiser.

"We were so amazed at how many people came out to support those of us with inherited retinal diseases," says Jen. "By 2018, we were chapter co-presidents."

Since becoming the Columbus Co-Presidents, the chapter's annual Dining in the Dark event has grown in the last two years, having over 320 guests and raising more than \$45,900. Jen and Kevin are also dedicated to bringing VisionWalk back to their local community and have been planning the first Columbus VisionWalk in 10 years for August 2020.

Thank you to Jen and Kevin for your commitment to raising awareness and funds for the Foundation and being beacons for those with blinding retinal diseases!



Jen and Kevin Walker at a Dining in the Dark wearing blindfolded simulator masks.

Genetic Testing for Inherited Retinal Diseases through the Foundation's My Retina Tracker Program

The Foundation Fighting Blindness, in partnership with Blueprint Genetics and InformedDNA, offers no-cost genetic testing and counseling to people affected by the entire spectrum of inherited retinal diseases (IRDs) including retinitis pigmentosa (RP), Usher syndrome, and Stargardt disease. The test is available to those clinically diagnosed with an IRD living in the US or US territories.

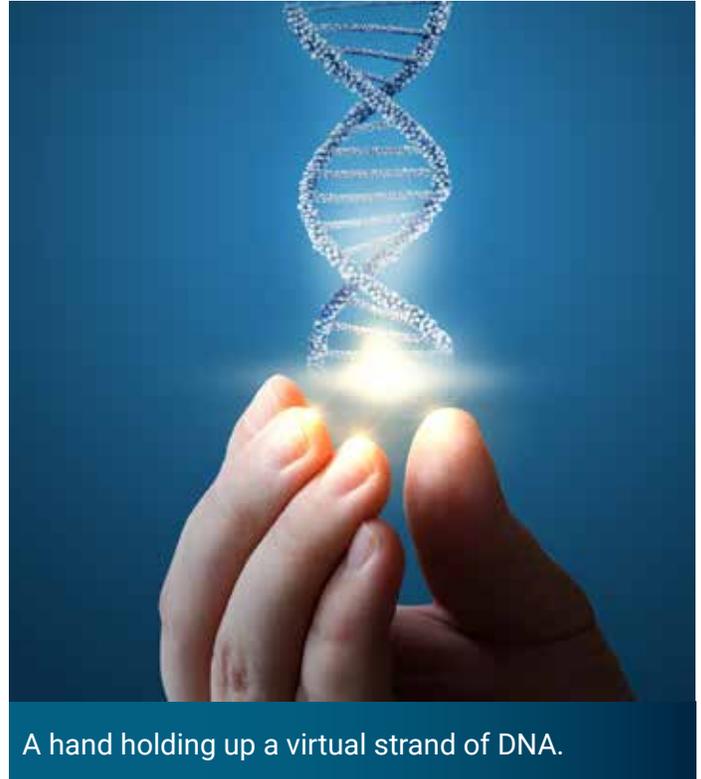
Why genetic testing for IRDs?

Eye care professionals make a clinical diagnosis of an IRD by examining a patient's retinas. While a clinical examination provides critical information about the retinal condition, identifying the IRD-causing gene mutations through genetic testing can provide more diagnostic information. In fact, studies have shown that clinical diagnoses change in about 15 percent of cases after genetic testing.

Identifying the disease-causing gene mutation(s) not only can provide more detail of a diagnosis, but it can help a patient better understand the risk for other family members (siblings, children, etc.) for inheriting the IRD. Also, knowing one's IRD gene mutation(s) can help them qualify for a clinical trial for an emerging therapy, many of which are now gene- or mutation-specific.

Why the Blueprint Genetics testing panel?

The Blueprint panel provides high-quality, broad, and deep testing for IRD genes. The panel screens 322 genes and includes the gene RPGR, a



A hand holding up a virtual strand of DNA.

relatively common IRD gene, which when mutated causes X-linked RP. (Other panels may not test for the complete RPGR gene) The Blueprint panel also can identify hard-to-find mutations, which other panels may not screen for.

Furthermore, Blueprint Genetics and its partners, the Foundation Fighting Blindness and InformedDNA, will never release a person's personal information. A person's privacy is always protected. With other IRD genetic tests, the patient's personal information may be released.

The test ordering process

Tests can only be ordered by a clinician. The testing company, Blueprint Genetics, cannot take test orders directly from patients.

Any doctor in the US who is able to clinically diagnose a patient with an IRD can order the test online from Blueprint Genetics through the company's Nucleus portal.

Patients with IRDs should contact their doctor and ask him or her to order the test. Doctors need to select the My Retina Tracker® Program Panel to order the genetic test. Patients who have questions about testing or the program should contact their doctor. The test itself is simple; the clinician only needs to collect a saliva sample from the patient. Patients should not contact Blueprint Genetics.

What to expect

Once a saliva sample is submitted to Blueprint Genetics, the test results are sent to the doctor in about four weeks. The results are conclusive in about 60-65 percent of cases. Whether the results are conclusive or not, the genetic counselor will help the patient understand what the results mean and potential next steps for the patient and family. Keep in mind that many emerging IRD therapies are designed to work independent of the mutated gene. So, while knowing one's IRD gene is helpful in disease management, there are emerging treatment options for those who haven't had their gene identified.

Why genetic counseling?

A genetic counselor helps patients and families understand what the genetic test results mean, what research (including clinical trials) may be relevant, the IRD inheritance pattern, and potential next steps. InformedDNA has extensive knowledge and experience in the IRD space and provides comprehensive, telephone-based genetic counseling to patients and families. The counseling session is typically 60-75 minutes.

My Retina Tracker® Registry

Any patient with an IRD can register in the Foundation's global, secure My Retina Tracker Registry (MyRetinaTracker.org) to share their

disease information with researchers and companies, many of which are recruiting for clinical trials for emerging therapies. Only de-identified information is shared. Personal information is never shared. A patient's privacy is always protected. The Foundation notifies the patient if he or she matches the researcher's or company's search criteria and then it is up to the patient to contact the researcher or company. While a person's genetic profile is valuable information to include in their registry record, they do not have to know their IRD gene mutation(s) to register.

CRISPR

Continued from front cover

"This is an exciting milestone for using CRISPR/Cas9 gene-editing to potentially treat inherited retinal diseases," says Brian Mansfield, PhD, executive vice president and interim chief scientific officer at the Foundation. "Gene-editing is an attractive approach for addressing large genes which exceed the cargo capacity of commonly used viral delivery systems such as adeno-associated viruses or AAVs."

The Foundation Fighting Blindness currently funds the following CRISPR/Cas9 lab research projects:

- University of Wisconsin-Madison (LCA caused by a mutation in KCNJ13)
- Mass Eye and Ear (RP caused by a mutation in RP1)
- Mass Eye and Ear (Retinal disease caused by a mutation in USH2A)
- UCLA (Usher syndrome 1B caused by a mutation in MYO7A)

IN FOCUS

is published by:



Foundation Fighting Blindness, Inc.
7168 Columbia Gateway Drive
Suite 100
Columbia, Maryland 21046



Foundation Fighting Blindness meets all of the standards of the BBB Wise Giving Alliance.

Stay in touch and receive updates by signing up for our emails at [FightingBlindness.org/sign-up](https://www.fightingblindness.org/sign-up). You can now edit your communications preferences. Our subscription options include:

- **Breaking News:** News related to science or the Foundation
- **Calls to Action:** Urgent communications to elicit grassroots support
- **Communications from Partners:** Messages from our partner organizations
- **Education:** Announcements related to national, regional, or virtual educational seminars
- **Information:** Includes the latest in research funded by the Foundation, clinical trials, or human-interest stories
- **Support:** Opportunities to support the Foundation's mission
- **Special Events:** Registration information for special events
- **Surveys:** Asks to participate in surveys to inform the Foundation
- **VisionWalks:** Information for our VisionWalk events

IN FOCUS

This and previous issues of **In Focus** are available online, where you can get the latest retinal-research information, as well as updates on the Foundation's activities, on your PC and mobile devices.

For an online and accessible version of **In Focus**, visit [FightingBlindness.org/In-Focus-Newsletter](https://www.fightingblindness.org/In-Focus-Newsletter).

CONNECT WITH US

- [FoundationFightingBlindness](https://www.facebook.com/FoundationFightingBlindness)
- [FightBlindness](https://twitter.com/FightBlindness)
- [FNDFightingBlindness](https://www.youtube.com/FNDFightingBlindness)
- [FightBlindness](https://www.instagram.com/FightBlindness)