IN FOCUS

FALL/WINTER 2023

A Publication for Members of the FOUNDATION FIGHTING BLINDNESS

Théa Acquires ProQR's LCA10 and USH2A Treatment Programs, Plans to Continue Clinical Development

Known as antisense oligonucleotides, the treatments performed encouragingly in ProQR's clinical trials

Laboratoires Théa, the leading European developer of eye care products with more than $1 billion in sales last year, has acquired two emerging antisense oligonucleotide (AON) treatments for inherited retinal diseases from ProQR Therapeutics. Both AON therapies — sepofarsen and ultevursen — had demonstrated vision improvements in ProQR's clinical trials. However, in August 2022, ProQR announced plans to divest its ophthalmic assets. With its acquisition, Théa plans to move both sepofarsen and ultevursen back into clinical development.

The RD Fund, the venture philanthropy arm of the Foundation Fighting Blindness, invested in the development of ultevursen and supported ProQR's effort to find a buyer for both of its ophthalmic assets.

"We are delighted with Théa's acquisition of sepofarsen and ultevursen and to see these promising treatments move forward in clinical development," says Rusty Kelley, PhD, managing director of the RD Fund. "With expertise in the research, development, and commercialization of eye care products, Théa is well positioned to continue advancement of these two programs for patients with these rare genetic retinal diseases."

Continued on page 2

WHAT'S INSIDE

HELP FIGHT BLINDING DISEASES

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

In Focus is published by:
Foundation Fighting Blindness, Inc.
6925 Oakland Mills Road, #701
Columbia, MD 21045

COVER STORY
CONTINUED FROM FRONT COVER

Sepofarsen was developed for people with Leber congenital amaurosis 10 (LCA10) caused by the IVS26 mutation in the gene CEP290. Some patients in ProQR's Phase 2/3 Illuminate clinical trial for sepofarsen had meaningful vision improvements. However, the treatment did not meet its primary trial endpoint, best-corrected visual acuity (BCVA), nor did it meet its secondary endpoint, navigation of a mobility course.

Ultevursen was developed for people with mutations in exon 13 of the USH2A gene which leads to Usher syndrome 2A or non-syndromic retinitis pigmentosa. In ProQR's Phase 1/2 Stellar clinical trial, ultevursen demonstrated benefits in BCVA, static perimetry (retinal sensitivity), and retinal structure as measured by optical coherence tomography (OCT).

Both sepofarsen and ultevursen are comprised of tiny pieces of genetic material that are injected into the vitreous, the soft gel in the middle of the eye. The genetic material masks the disease mutation in RNA, the genetic messages that cells read to make proteins which are critical for the cells' health and function. Masking the mutation enables cells to make the correct protein.

AONs can be advantageous when large retinal disease genes — such as CEP290 and USH2A — exceed the capacity of viral gene replacement delivery systems thereby making gene therapy development for these genes more challenging.

CHAPTER HIGHLIGHTS

We Are Growing!

Become a founding leader of our new Chapters! The Foundation Fighting Blindness is growing our Chapter network, and we need volunteers like you. Our family of volunteer leaders work together to build our community by planning engaging activities and fundraising events such as Speaker Series, networking opportunities, socials, and our signature event, VisionWalk. Our Chapter vision is to bring our community together to provide hope and resources while we fight to end blinding diseases. Our local Chapter leaders help to guide these activities and are an intricate part in identifying local needs.

Resource and Peer Guide Programs

Our Chapters are working to help those impacted through two new initiatives. The first of these is our new resource guides, created to help connect newly diagnosed families to resources in your community that will assist in their vision journey. Whether the need is assistive technology or mobility training, the Chapter network is there every step of the way. The local Chapters have also launched a new peer guide program, which will help connect those who are on similar journeys. This program is open to those personally impacted by low vision and their families to help guide them through lifestyle questions.

To learn more about becoming a founding leader or these Chapter initiatives, reach out at **Chapters@FightingBlindness.org**

VISIONS 2024

FOUNDATION FIGHTING BLINDNESS
VISIONS '24

June 21–22, 2024
Chicago Marriott Downtown Magnificent Mile
540 N. Michigan Avenue, Chicago, IL 60611

Save the date! VISIONS 2024, the national conference of the Foundation Fighting Blindness, will be held on June 21–22, 2024, featuring sessions with the latest research advancements, practical adapting and thriving, and an opportunity to connect with the blind and low vision community. Learn more at **www.FightingBlindness.org/VISIONS-2024**

Scan the QR code to go directly to the web page on your device.

BEACON STORY

Talented Singer Overcomes Blindness with the Power of Melodies

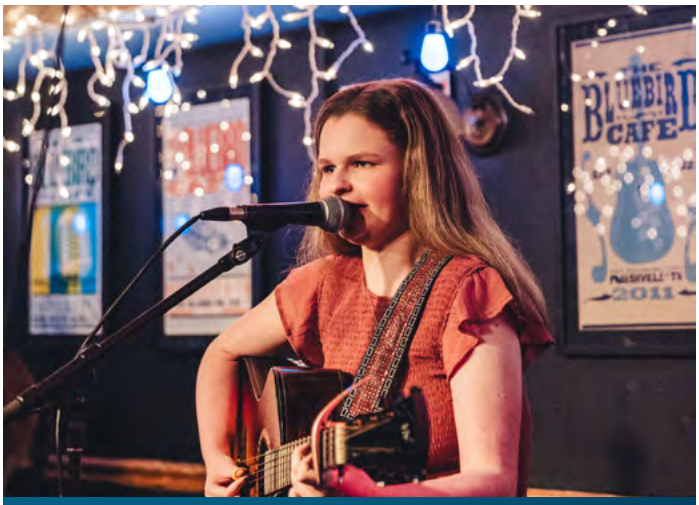
Meet the remarkable songbird Sarah Hardwig, who emerged from the sun-kissed shores of Naples, Florida. Sarah received a diagnosis of a retinal degenerative disease a few months after birth, but at the tender age of 4, music became her guiding light. The power of pop melodies and songwriting ignited her determination to push forward, becoming a beacon of light for all who lend an ear.

At just five months old, Sarah's mother noticed a troubling change in her daughter's gaze. Sarah's eyes were no longer tracking her movements. Seeking medical advice, her parents took her to the Bascom Palmer Eye Institute in Miami, where she received a formal diagnosis of Leber congenital amaurosis.

As Sarah continued to grow, her condition proved to be a significant challenge, particularly during her time in school.

"I would break down crying in the first or second grade because I couldn't see what was happening on the whiteboard in math class even though I had accommodations," recalls Sarah. "The main challenge was accepting the fact that I couldn't see, and the other challenge was figuring out how to deal with it. However, I was fortunate to have staff that helped me."

Undeterred by the initial challenges she faced during her adolescence, Sarah, now a 20-year-old living in Nashville, Tennessee, has not allowed her blindness to discourage her from accomplishing her goals. She began mobility training a few years ago to learn how to cross streets and navigate in an area.



Sarah playing a guitar at the Tennessee Songwriters Showcase Finale, after winning the showcase and becoming one of seven to sing in the finale at Bluebird Cafe.
Photo by Hunter Berry Photography

"The main thing people think when they encounter a blind person is that they cannot do much because they are blind. We may not be able to do as much as a person with vision can do, but we can certainly do a lot of things. Proving to people that I can do things despite the fact that I am blind is amazing," says Sarah.

Sarah's love for music began at an early age, nurtured by her musically inclined parents, instilling in her a deep passion for art. Since then, she has held an unwavering determination to pursue music.

"When I was 3 or 4 years old, I would stand or sit in front of the TV just listening, and that made me want to pursue music. I just loved singing and singing at my kindergarten graduation at the age of 5 made me want to become a singer even more," says Sarah.

However, the turning point in the young songstress's journey came when she attended her first CMA Fest in 2011, prompting her to start taking her singing career more seriously. Since then, Sarah has performed with renowned artists such as Charles Kelley, Steven Tyler, Lauren Alaina, and LoCash. Notably, she has amassed an impressive record of 250 national anthem performances, including the Miami Dolphins at the age of 9.

She also performed each year at Scramble Fore Sarah, a golf charity event hosted by her family. The annual event, which ended in 2020, raised approximately $125,000 for the Lighthouse of Collier, Inc., and the Foundation Fighting Blindness over the course of eight years.

Now enrolled as a songwriting major at Belmont University, she looks forward to beginning her junior year this upcoming fall.

"Belmont has been very good to me. I have had the best professors when it comes to songwriting," she says. "The greatest professors I've had so far are Drew Ramsey, James Elliot, Jodi Marr, and Mrs. Victoria Banks, who has written songs for a lot of country singers such as Mickey Guyton."

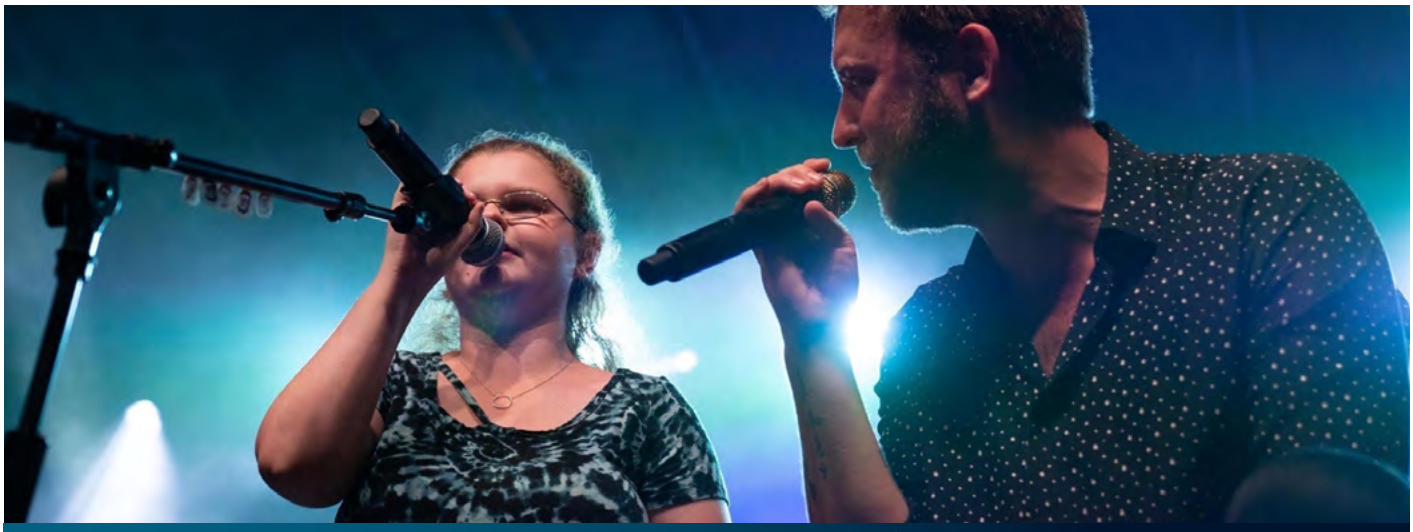
With her vision restricted to just light perception due to her condition, she has taken a unique approach in the way she crafts her music.

"A lot of songwriting tends to be detailed and image-based, but I can definitely say that my songwriting is less image-based. It's primarily focused on thoughts because incorporating feelings and thoughts helps other people relate to the song more," she says.

When envisioning the future of her music career, Sarah is determined to ensure that the label of blindness doesn't define her or her artistry.

"A lot of people will try to put you in a box, and boxes are very limiting. I am going to be the person that breaks out of the box," she says. "I want to be seen as a songwriter who just so happens to be blind, but I don't want that to define me. This is why I love artists who truly experiment with expressing themselves sonically and visually because they are not letting anything define them," she says.

With boundless potential ahead, Sarah plans to release three new songs next year, a prelude to her ultimate goal of creating an EP and releasing a full-length album.



Sarah performing with Charles Kelley of Lady A (formerly Lady Antebellum) at the pro-am party for the QBE Shootout in Naples, Florida, on Dec. 7, 2018. Photo by Michael O'Bryon Photography

CLINICAL-TRIAL PIPELINE

Retinal-Disease Therapy

Inherited Retinal Diseases and Dry AMD: 45 Trials (select) | Updated July 2023

GENE THERAPIES (GENE TARGET)	PROGRESS
Achromatopsia (CNGB3) – MeiraGTx/Janssen	Phase 1/2
Achromatopsia (CNGA3) – MeiraGTx/Janssen	Phase 1/2
Achromatopsia (CNGA3) – Tubingen Hosp	Phase 1/2
AMD-dry, GA (CD59) -- Janssen	Phase 2
AMD-dry, GA (CFI) – Novartis	Phase 2
AMD-dry, GA (CFH) – Perceive Bio	Phase 1/2
Batten disease (CLN5) – Neurogene	Phase 1/2
Choroideremia (REP1) – 4DMT	Phase 1/2
LCA (GUCY2D) – Atsena	Phase 1/2
LCA and RP (RPE65) – MeiraGTx/Janssen	Phase 1/2
RP (PDE6B) – Coave	Phase 1/2
RP (RLBP1) – Novartis	Phase 1/2
RP (NR2E3, RHO) – Ocugen	Phase 1/2
RP (PDE6A) – Tubingen Hosp	Phase 1/2
Retinoschisis (RS1) – Atsena	Phase 1/2
Retinoschisis (RS1) – NEI	Phase 1/2
X-linked RP (RPGR) – Beacon	Phase 2
X-linked RP (RPGR) – MeiraGTx/Janssen	Phase 3
X-linked RP (RPGR) – 4DMT	Phase 1/2

RNA/OTHER THERAPIES (MECHANISM)	PROGRESS
AMD-dry (CB inhibitor) – Ionis	Phase 2
LCA (CEP290, AON) – ProQR	Phase 2/3
RP (RdCVF) – SparingVision	Phase 1/2
RP, Usher, others (optogenetic) – Bionic Sight	Phase 1/2
RP, Usher, others (optogenetic) – GenSight	Phase 1/2
RP, Usher, others (optogenetic) – Nanoscope	Phase 2
Stargardt disease (optogenetic) – Nanoscope	Phase 2
Usher syndrome 2A (AON) – ProQR	Phase 2/3

CELL-BASED THERAPIES (CELL TYPE)	PROGRESS
AMD-dry, GA (RPE) – Astellas	Phase 1/2
AMD-dry, GA (RPE) – Lineage	Phase 1/2
AMD-dry, GA (RPE) – Luxa	Phase 1/2
AMD-dry, GA (RPE from iPSC) – NEI	Phase 1/2
AMD-dry, GA (RPE on scaffold) – Regen Patch	Phase 1/2
RP, Usher (retinal progenitors) – jCyte	Phase 2b
RP (CD34+ stem cells) – UC Davis	Phase 1

SMALL MOLECULES (MECHANISM)	PROGRESS
AMD-dry, GA (deuterated vit. A) -- Alkeus	Phase 3
AMD-dry, GA (RBP4 inhibitor) – Belite Bio	Phase 3
RP (NAC-anti-oxidant) – Johns Hopkins	Phase 3
RP (methotrexate) – Aldeyra	Phase 2
RP (small molecule) – Endogena	Phase 1/2
RP (small molecule, photoswitch) – Kiora	Phase 1/2
Stargardt disease (deuterated vit A) – Alkeus	Phase 2
Stargardt disease (C5 inhibitor) – Iveric bio	Phase 2
Stargardt disease (anti-RBP4) – Belite Bio	Phase 3
Stargardt disease (metformin) – NEI	Phase 1/2
Usher syndrome (NACA-anti-oxidant) – Nacuity	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.

For questions, visit **FightingBlindness.org** or call **888-394-3937**.

Note: Some trials listed may have been paused and/or the sponsors are seeking partners to continue their trials.

Microsoft Scramble for Sight Golf Tournament

The 23rd Annual Microsoft Scramble for Sight Golf Tournament presented by RE/MAX took place on July 24, 2023, at the exclusive Sanctuary Golf Course in Sedalia, Colorado. The event was a hole-in-one, raising over $355,000 for the Foundation Fighting Blindness, thanks to the amazing donors and sponsors. The golfers had the special opportunity to compete against professional long-drive entertainer Andrew Eigner, who also performed an exhibition of long drives and trick shots for the attendees. The dinner program included an interactive and heartfelt panel discussion with loved ones of the previous year's generational panel that raised awareness of the meaningful and important work of the Foundation. Thank you to the event co-chairs, Scott Burt and Sheri Kroonenberg, and the auction chair, Lindsey Blankenship.

Foundation supporters at the golf event. Left to right - Remy Martin-Fenske, Todd Fenske, Amalia Teran, Ramon Teran, and Marti Martin Waneka.

Attendees outside of the green at the 23rd Annual Microsoft Scramble for Sight Golf Tournament.

New York Night for Sight

On May 11, 2023, the Foundation's Night for Sight gala raised over $800,000 at The Lighthouse at Chelsea Piers in New York City through the efforts of event co-chairs and Foundation board directors Evan Mittman and Jason Ferreira, our dedicated committee, and many incredibly generous supporters. Through Night for Sight, the Foundation celebrated the incredible contributions of three impressive Visionary Award honorees: Pravin U. Dugel, MD of Iveric Bio, Avi Kaner of Morton Williams Supermarkets, and Doug Zarkin, formerly of Pearle Vision. Guests at Night for Sight were among the first to hear the moving story of the Lemay Pelletier family, who had just returned from a year-long visual memory world tour after three of their four children were diagnosed with retinitis pigmentosa.

The Foundation's CEO, Jason Menzo, and special guests, Edith Lemay and Sebastian Pelletier.

Night for Sight's co-chairs Evan Mittman and Jason Ferreira at the gala's podium.

RESEARCH HIGHLIGHTS

IZERVAY Approved by FDA for Treatment of Geographic Atrophy Secondary to Advanced Dry AMD

Astellas Pharma Inc. has announced that the U.S. Food and Drug Administration (FDA) approved IZERVAY™ (avacincaptad pegol) for the treatment of geographic atrophy (GA) secondary to advanced dry age-related macular degeneration (AMD) on August 4, 2023. The treatment was developed by Iveric Bio, which was acquired by Astellas in July 2023. The treatment is administered through intravitreal injections — injections made in the soft gel in the middle of the eye — in a doctor's office.

Astellas says that approximately 1.5 million people in the U.S. have GA.

IZERVAY met the primary endpoint, slowing the growth rate of GA lesions, in two global Phase 3 clinical trials. In the 448-participant GATHER1 clinical trial, IZERVAY slowed lesion growth by 27.7 percent at 12 months of treatment. In the 286-participant GATHER2 clinical trial, IZERVAY slowed lesion growth by 14.3 percent at 12 months of treatment. In both trials, patients were randomized to receive either two mgs of IZERVAY or a sham monthly.

IZERVAY is designed to work by inhibiting the C5 protein, which is part of the complement system. Researchers believe that the overactive complement system, part of the innate immune system, is a key culprit in the development of AMD. While the complement system plays an important role in fighting off viruses, bacteria, and other pathogens, it can be damaging when overactive.

2023 VisionWalk participants cutting the ribbon at the start line in Baltimore.

Children attending the DC Metro VisionWalk in 2023.

Attendees mark the beginning of the 2023 DC Metro VisionWalk.

Join a Fall VisionWalk!

VisionWalk is taking place in 13 communities across the country this fall – with 20 more planned in the spring of 2024. These fun, family-friendly events will bring together hundreds of teams and thousands of walkers as we take steps toward treatments and cures for blinding retinal diseases.

To find the nearest VisionWalk to you, visit **www.VisionWalk.org** or call **(800) 683-5555**.

Beacon Therapeutics to Advance XLRP, Cone-Rod Dystrophy, and Dry AMD Gene Therapies

Beacon Therapeutics, a company focused on the development of gene therapies for retinal diseases, has been launched with £96 million ($120 million) in investments from Syncona Limited, Oxford Sciences Enterprises (OSE), and additional partners. Initially, the new company will focus its development efforts on three emerging gene therapies:

- The X-linked retinitis pigmentosa (RPGR) gene therapy program acquired from Applied Genetics Technology Corporation (AGTC) is currently in the Phase 2 SKYLINE clinical trial. AGTC previously reported vision improvements for some patients in SKYLINE.
- A preclinical cone-rod dystrophy (CDHR1) program licensed from the laboratory of Robert MacLaren, MB ChB, PhD, professor of Ophthalmology at the University of Oxford.
- An intravitreally delivered gene therapy in preclinical development for the dry form of age-related macular degeneration (AMD).

PYC Doses First Patient in Clinical Trial of RNA Therapy for RP11 (PRPF31 Mutations)

PYC Therapeutics, an Australia-based developer of RNA therapies, has launched a Phase 1 clinical trial for its RNA therapy known as VP-001 for people with retinitis pigmentosa 11 (RP11), which is caused by mutations in the gene PRPF31. The 20-person clinical trial is taking place in the US. The first patient was dosed at the Retina Foundation of the Southwest in Dallas. Three doses of VP-001 are being evaluated. VP-001 is administered through an intravitreal injection. Investigators will be evaluating safety as well as a number of measures of retinal structure and visual function.

PYC's emerging therapies are designed to modify RNA, the genetic messages that cells read to make the proteins that are critical to the health and function of all the cells in the body. By modifying RNA, protein expression can be boosted or reduced, depending on the therapeutic need.

In people with RP11, one copy of their PRPF31 gene is normal and produces a relatively normal level of protein, while the other PRPF31 copy is mutated and not producing sufficient protein. The overall reduced level of PRPF31 protein for RP11 patients leads to retinal degeneration and vision loss.

Researchers from PYC found that by downregulating the activity of a different gene, CNOT3, they could boost PRPF31 protein expression. So, they developed VP-001, a tiny piece of synthetic genetic material designed to alter the RNA expressed by the gene CNOT3, thereby increasing PRPF31 protein expression.

Bring Raising Our Sights into this Holiday Season!

Take part in an ongoing Raising Our Sights do-it-yourself fundraising initiative like Wine for a Cure, or create your own way to bring Raising Our Sights to your local community this holiday season.

DIY CAMPAIGN SUCCESS STORY

Wine for a Cure

Lindsey Blankenship, president of the Foundation Fighting Blindness Colorado Chapter, has created a one-of-a-kind Raising Our Sights Event. Wine for a Cure aims to spread awareness and fundraise on behalf of the Foundation Fighting Blindness with two signature wines from the Oregon Winery, Stoller Family Estates. The featured wines are a Chardonnay named "Variant" and a Pinot Noir named "Pigmentosa."

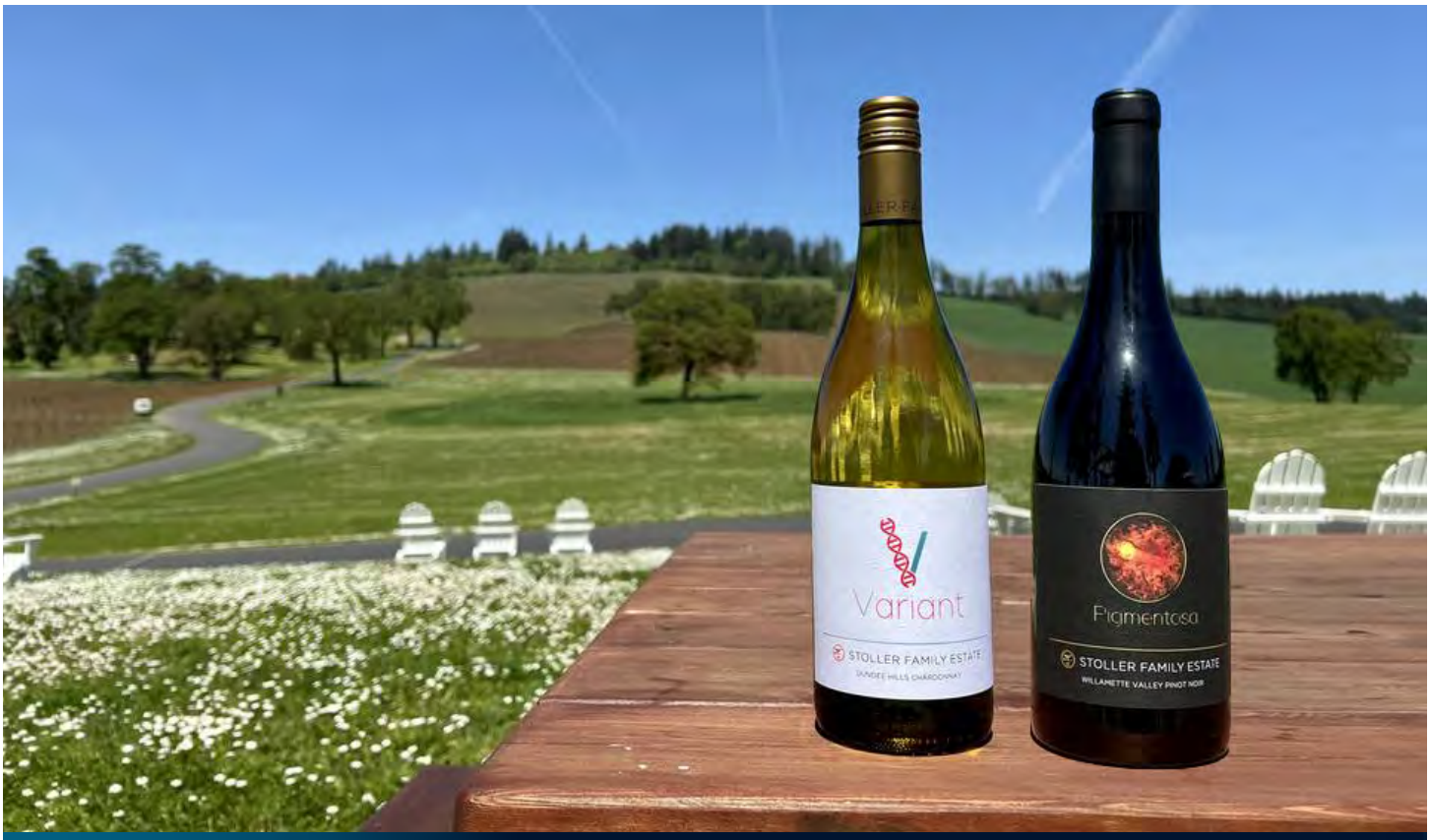
Colorado Chapter president Lindsey Blankenship has utilized the Raising Our Sights program to create a unique project. With the help of one of the best wineries in all of Oregon, Stoller Family Estates, Lindsey has created two featured labels that raise awareness for the Foundation Fighting Blindness and, specifically, retinitis pigmentosa. Lindsey and select members of her family are affected with RP themselves so this incredibly creative initiative hits close to home. Lindsey who is also the Director of her own non-profit organization, Creating SPACE, is naturally driven to make a large impact on the missions closest to her with large ideas. What pairs best with her incredible drive is her love for wine, which is how she ended up with the idea of Wine for a Cure.

The first of the featured wines, Variant, is a 2018 Chardonnay that has the aromas of ripe pear and baked apple, accompanied by balanced fruit and wonderful natural acidity on the palate.

The second featured wine, Pigmentosa, is a Pinot Noir that shows perfumed red fruits with undertones of earth and baking spice. The palate is soft, with dark cherry flavors balanced by a delicate tension from the tannins.

Both featured labels are a part of the Stoller Family Estate's "Wines For A Good Cause." Lindsey has worked with the winery to best capture the journey of those diagnosed with retinitis pigmentosa and other inherited retinal diseases through the labeling process, aptly landing on "Variant" and "Pigmentosa." This initiative aims to raise awareness and fundraise on behalf of the Foundation Fighting Blindness. 30% of proceeds from each bottle purchased will go directly towards our mission to drive the research for preventions, treatments, and cure for the entire spectrum of blinding retinal diseases.

For more information and available resources on DIY fundraising campaigns, please visit, **www.FightingBlindness.org/RaisingOurSights** or email **RaisingOurSights@FightingBlindness.org.**



Variant chardonnay and Pigmentosa pinot noir wine bottles

Leave Your Legacy

Have you ever thought about a legacy gift to the Foundation? You can impact the fight for sight with a gift that costs you nothing today.

Do you already have a legacy commitment to the Foundation? If so, we want to know! Knowing about future legacy gifts will help us plan our investments in retinal disease research. Please share your plans with us so that we can acknowledge your generosity and welcome you into our Legacy Society.

We are here to help
Contact Darcy Meadows at 443-631-0570, DMeadows@FightingBlindness.org or John Corneille at 952-314-7578, JCorneille@FightingBlindness.org

Benefits of Legacy Society

- Special invitation to the Legacy Society Dinner held in conjunction with the biennial VISIONS Conference
- Invitations to participate in virtual calls with the Foundation Science Team
- Foundation Annual Report mailed to your preferred address
- Invitations to Foundation's Chapter meetings, symposia, and special events
- Quarterly research updates via email

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is published by:

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Foundation Fighting Blindness, Inc.
PO Box 179
Annapolis Junction, MD 20701

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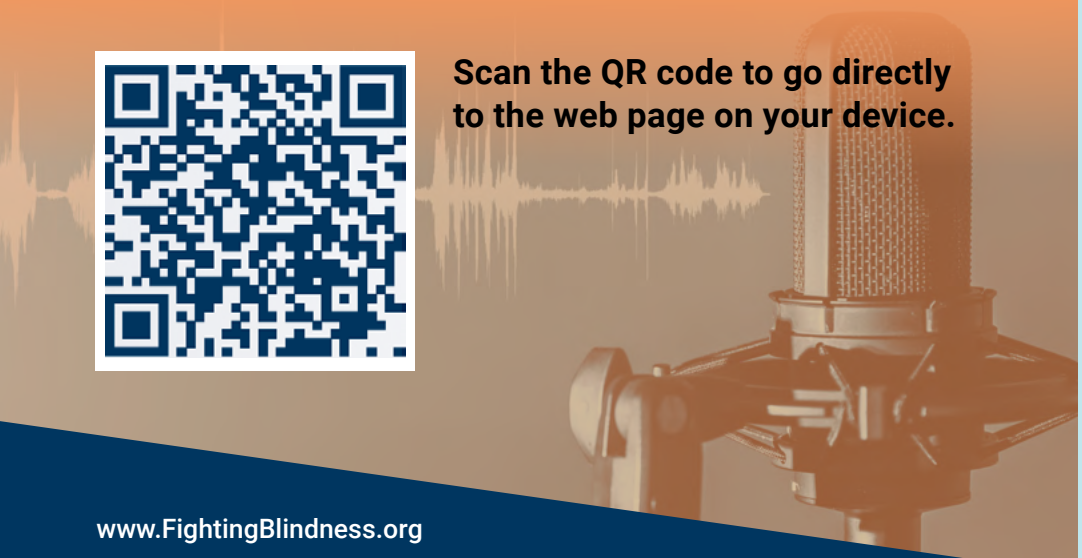
Eye on the Cure Podcast

Want to learn more about the latest from the world of vision? Check out our Eye on the Cure Podcast, hosted by Ben Shaberman, vice president, science communications. Stream the Podcast on SoundCloud, Spotify, Audible, Pandora, and more: **www.FightingBlindness.org/Podcasts**

Scan the QR code to go directly to the web page on your device.



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 **www.FightingBlindness.org/In-Focus-Newsletter**.

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