



USHER 1F
COLLABORATIVE

NEWSLETTER Summer 2024

Seeing Forward ... The Case for Restoring Vision

Dear Usher 1F Families and Friends,

As friends and fellow advocates, we are so pleased to announce that Usher 1F Collaborative is launching **Seeing Forward...the case for restoring vision for those with Usher syndrome 1F**. This initiative seeks to raise \$3 million in the next two years to accelerate unprecedented advances in research, now close to clinical trials.

Seeing Forward will be launched on June 20th, Summer Solstice Day. This day is particularly symbolic as it is the longest summer day with the longest period of light.

Light and vision are gifts, and something most people take for granted.

We live with Usher syndrome 1F. We cherish each day of vision and light because we are gradually losing both due to this unfortunate genetic disease.

The good news, though, is that we have three critical initiatives underway right now that provide each of us with tremendous hope. They include:

PRIORITY AREA	DOLLARS	WHAT THIS WILL DO
MINI-GENE VISION RESCUE COREY LABORATORY HARVARD MEDICAL SCHOOL	1,500,000	Allow us to take the mini-gene to clinical trial in several years. The mini-gene replaces the defective gene in order to halt further retinal degeneration and restore some vision already lost.
TARGETED DRUG SCREEN WESTERFIELD LAB UNIVERSITY OF OREGON INSTITUTE OF NEUROSCIENCE	600,000	Targeted drug screening allows us to repurpose existing FDA-approved drugs and to test them for efficacy for their ability to slow or even halt retinal degeneration. This is the fastest path to the clinic since these drugs have an already known safety profile.
REVOLUTIONARY GENE THERAPY APPROACH PFAFF LAB THE SALK INSTITUTE LA JOLLA, CALIFORNIA	915,000	Gene Therapy involves replacing the defective gene with a corrected copy delivered via a viral vector. Viral vectors are created from modified viruses to deliver the gene to cells.
TOTAL	3,015,000	

So many of you have helped us to build this incredible organization, now on the cusp of a cure for Usher syndrome 1F. In 2013, when the Collaborative was founded, no treatment was in sight, and no other organization (including academic institutions and biopharmaceutical companies) was focused on this disease. Today, because of hard work, dedication of world-renowned scientists and your own commitments, there are multiple labs and strong therapies in our pipeline. We are laser focused on the initiatives offering us the fastest path to a cure.

We are proud to be part of this effort, not only to take control of our own future, but to be a part of the research that will change the lives of everyone who lives with Usher 1F and potentially other inherited retinal diseases.

As we roll out this critical campaign, it is important for everyone to know that no gift is too small and no gift is too large. Everyone matters in the fight to save our vision. We'll be inviting you and others to participate in ways that align with your interests and abilities.

We sincerely thank you. We are so grateful for those who are helping us to See Forward.

Very Sincerely,

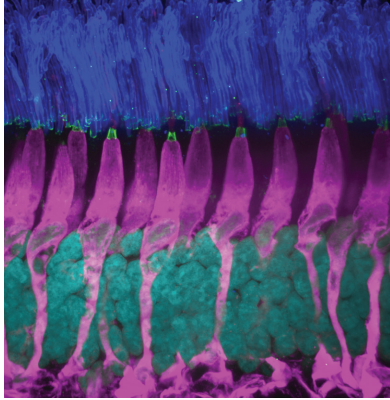


Dorie Shapiro, Board Member,
Usher 1F Collaborative



Jessica Chaikof

Exciting Research Updates



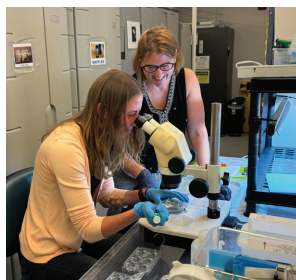
Expression of PDCH15 (Usher 1F gene) protein (green) in a Nonhuman Primate retina resulting from the insertion of the Usher 1F mini-gene

Photo courtesy of Maryna Ivanchenko; Lab of David Corey; Harvard Medical School

The Usher 1F gene is too large to fit on the standard delivery vehicle used in retinal gene therapy, a viral vector. The mini-gene contains only those portions of the gene necessary for vision, and it fits on one viral vector. Testing over the past year demonstrated that the mini-gene not only restores hearing in our Usher 1F mouse model but also rescues vision in our Usher 1F zebrafish. Dr. Corey's team is now conducting preclinical testing of the mini-gene, and Dr. Corey has described results thus far as "stunning." He has published two papers describing the success of the mini-gene. In addition, Foundation Fighting Blindness, the most prominent funder of vision research, recognized his Usher 1F work this year, both with an invitation to speak at their annual research conference and with a three-year \$1.2 million grant to help support preclinical testing of the mini-gene over the next three years.

In addition, our University of Oregon Institute of Neuroscience team, Monte Westerfield Lab, completed testing on

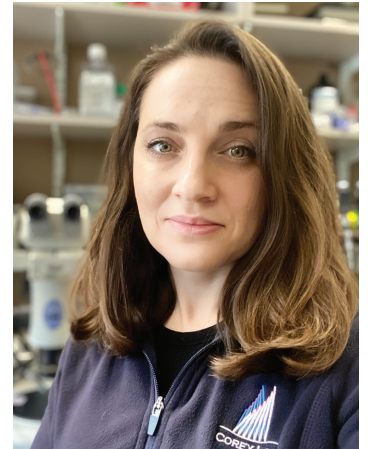
our zebrafish model of a compound, hexafluoro, which is made from the sap of the magnolia tree. At the end of 2023, they published a paper, *Hexafluoro slows retinal degeneration and improves visual function in zebrafish models of Usher syndrome 1F*, in which they state, "We find that



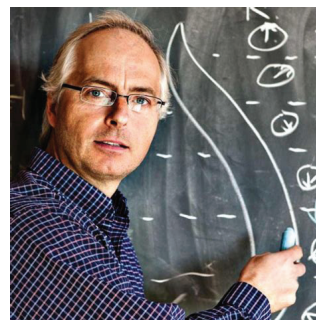
Jennifer Phillips, PhD, and honors thesis student Sara Swinson, University of Oregon Institute of Neuroscience, testing an existing drug for Usher 1F

During the past year, the Collaborative has made exciting progress, and we received recognition for significantly accelerating research. The most advanced treatment is our Usher 1F mini-gene from Harvard Medical School, David Corey Lab.

hexafluoro improves visual function, reduces photoreceptor degeneration, and protects the retina against exposure to bright light in this USH1F model." Our Oregon team received an outside grant to test hexafluoro on all of their additional Usher syndrome zebrafish models. Proof of efficacy for multiple types of Usher syndrome will increase attractiveness of hexafluoro with biopharma companies. In addition, Dr. Westerfield's team is now testing additional compounds for efficacy in slowing retinal degeneration for those with Usher 1F. The majority of these are already FDA-approved for other uses so would represent the fastest path to the clinic, buying us much needed time to bring a cure in the form of a gene therapy to fruition.



Maryna Ivanchenko, MD, PhD, Harvard Medical School, who has spearheaded our Usher 1F research in the Corey Lab



Samuel Pfaff, PhD, The Salk Institute for Biological Studies. Photo courtesy of The Salk Institute

Finally, our newest exciting research is at the Samuel Pfaff Lab at The Salk Institute. Dr. Pfaff's team has developed a cutting-edge means of delivering large genes, RNA End Joining (REJ). While splitting large genes into two parts and having them recombine once in the eye is not new, REJ is a new approach that is demonstrating significantly higher efficacy and rescue of a wider visual field. A biopharma company, Insmad, has purchased the license to REJ and is investing significantly to develop it for clinical use for inherited retinal diseases. Dr. Pfaff is developing REJ for Usher 1F, with the vectors nearing completion. Once ready for testing, he and Dr. Corey will collaborate, with Dr. Corey testing Dr. Pfaff's vectors in his Usher 1F mouse model. ♦

Changes to Our Board as We Say a Sad Goodbye to Longtime Board Member Laurie Shapiro

Sadly, in December 2023, Usher 1F Collaborative lost one of our own, board member Laurie Shapiro, mother of Dorie Shapiro, our Usher 1F Ambassador. The Shapiros were one of the first Usher 1F families that founders Melissa and Elliot Chaikof met, and Laurie and her husband Gary joined the Chaikofs in their work for a cure. Following Gary's death in 2014, Laurie joined the board and worked tirelessly to raise funds for research. Gary, a local Arizonian optometrist, had told her he believed there would be a cure, and she was determined to honor him and make this a reality. We greatly miss Laurie's smile and laugh that were always a bright spot at our board meetings.

Laurie lived her life to the fullest, honoring Gary by taking over his optical practice, Optical Expressions, following his death. She was also an incredible cook and baker, as well as a wine aficionado, and loved to travel. In addition to Dorie, she is survived by her son David, his wife Elizabeth, and three grandsons.

In recognition of Dorie's work not only to fund research but also to help others understand life with Usher 1F, as well as to honor Laurie, the Usher 1F Board of Trustees voted unanimously to give Dorie Laurie's board position. In addition to her work for Usher 1F Collaborative, Dorie's dedication to the Usher 1F community is paralleled by her vibrant life in Phoenix, where she infuses her passion for hospitality into her daily work at a local hotel. This role not only aligns with her enthusiastic nature but also her desire to create memorable experiences for visitors.

Beyond her professional commitments, Dorie is a culinary enthusiast, often found experimenting with new recipes and treating her loved ones to delicious homemade dishes. Her love for animals shines through her care for her dog, with whom she enjoys regular walks, making the most of the Arizona sunshine. Fitness also plays a significant role in her life, maintaining her well-being with workouts at her neighborhood gym. Additionally, Dorie's part-time role at Optical Expressions is not just a job but a heartfelt effort to sustain her family's legacy,



Laurie and Dorie Shapiro

enhancing patient care with her inherent warmth and dedication. This multifaceted involvement in both her professional and personal life underscores Dorie's dynamic approach to balancing various aspects of her life while making a significant impact in her community.



Margi Levitt

In addition, one of Laurie and Gary's closest friends, Margi Levitt, has also joined the board to honor her friends and to ensure that their dream of a cure for Dorie becomes a reality. Margi works for The Aspen Press, a marketing communications company she founded in 1996 in Aspen, CO.

She has served on the board of the Aspen International Mountain Foundation (AIMF) since 2002, coordinating AIMF's effort to host the 2022 Sixth Global Meeting of the UN Mountain Partnership. The meeting produced United Nations DG Action 49806, a Five Year Plan for Mountains, which was approved by the United Nations General Assembly as part of the resolution A/RES/77/172 in 2023.

Margi is originally from Washington, DC, and holds a B.A. in Biology from the University of Virginia. She and her husband now live in the Phoenix area and have three children. They are deeply committed to helping those afflicted with Usher syndrome type 1F because of their close relationship with Dorie and her parents. ♦



Students display their finished artwork



Left to right: Brianna Pares, student filmmaker, Jody Lazarski, teacher, and Brendan Pares

Teacher and Student Filmmaker Raise Awareness and Funding for Research

In October 2023, Usher 1F Collaborative hosted our Seeing Forward film event in Morristown, New Jersey. Among our special guests that evening was Jody Lazarski, a friend of the Root family, and one of her high school students, Brianna Pares. Jody and Brianna were inspired by Zachary Root and others with Usher 1F and set a plan into action to raise additional money and awareness.

A talented videographer, Brianna filmed the event and compiled footage to create a documentary. Her documentary was featured in the Garden State Film Festival earlier this year, bringing awareness to a wide audience.

Jody reached out to her colleagues and students at Passaic County Technical-Vocational Schools (PCTVS) and planned an event in coordination with the ASL & Video Clubs. Students each reached out to their families and friends via an online platform, requesting donations for Usher 1F Collaborative for a “Pledge to Paint” event. They created glasses that simulate peripheral vision loss, then gathered in the cafeteria, donned the glasses, and painted artwork on canvas. The event was an enormous success, bringing students together for a common cause, and raising \$2,500 for Usher 1F Collaborative.

This event shows what can happen when a small number of people reach out to their networks. Thirty-four students and staff set up fundraising pages, resulting in 75 new donors to Usher 1F Collaborative, and \$2,500 in donations. We are grateful to Jody, Brianna and the PCTVS community for their support.

If you have a peer-to-peer fundraising idea, or would like to replicate this event, please reach out to our Development Director, Sarah Gauch (sarah.gauch@usher1f.org), and she will provide support in setting up an online platform and your event. ♦



Students at Passaic County Technical-Vocational Schools attempting to paint while wearing glasses simulating the tunnel vision of Usher 1F



www.usher1f.org

321 Walnut Street, #228

Newtonville, MA 02460

info@usher1f.org

P. 339.221.2743