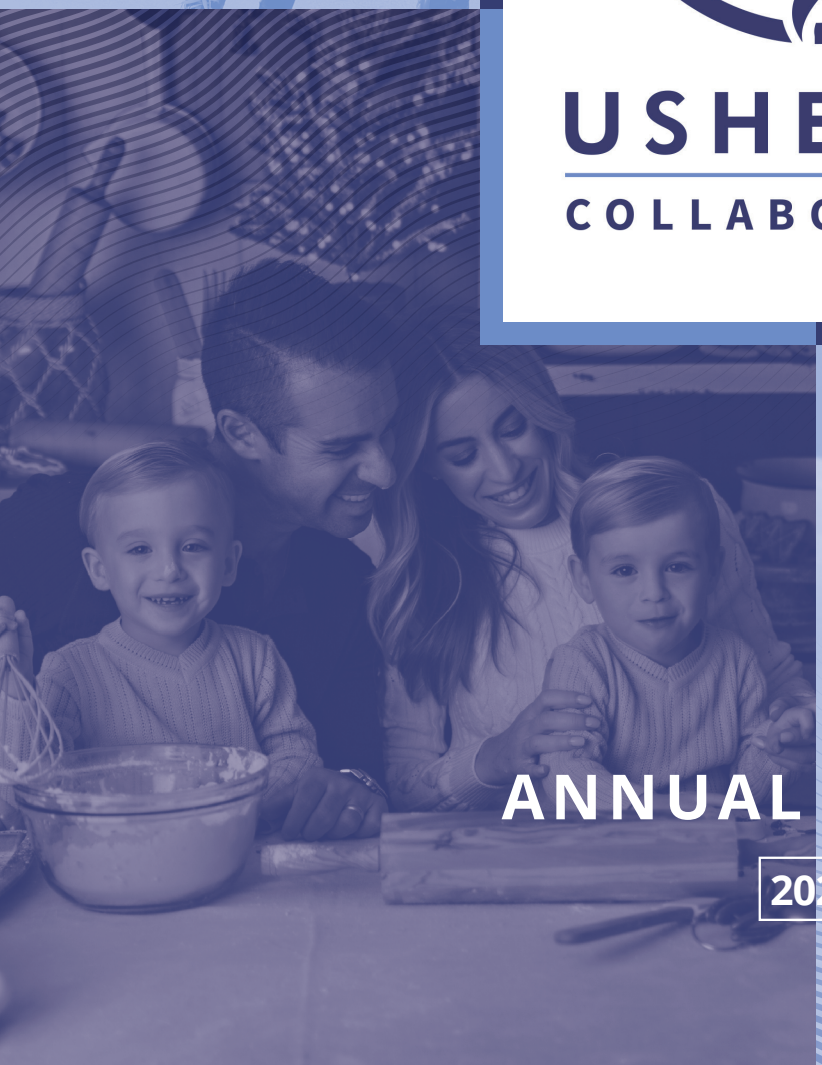
USHER 1F COLLABORATIVE



ANNUAL REPORT

2022

Sight.Sound.Sweat teammates and supporters.

2022

The Year in Review

2022 was a productive and exciting year. In terms of fundraising, we saw new initiatives and re-energized events that had taken a break during the pandemic. Friends and families of Usher 1F Collaborative hosted workout events, bake sales, shopping nights, holiday events, and even ran the Boston marathon (completed by an individual who lives with Usher 1F!) to support the organization. **Overall, we raised $907,000 that will be invested in research for a cure.**

In 2022, **we granted a record $659,100 to research**, which led to significant lab updates and new collaborations by our scientists. We are excited to share highlights of 2022.

2022 Spring

We kicked off the year with our Sight.Sound.Cycle@Home and Sight.Sound.Sweat events. Sight.Sound.Cycle@Home was a virtual take on an event previously held in gyms. Participants from across the country hopped on their at-home exercise equipment at the same time and completed a workout "together." A few weeks later we held our Sight.Sound.Sweat event in San Francisco. **These fun, uplifting workout events raised more than $83,000 together.**

2022 Summer

Moving outdoors to enjoy the warm weather, Usher 1F friends held an at-home cultivation event in Westchester, NY, and coordinated a walk/run in London, **the latter raising $11,000**. These events brought together many individuals who were interested in learning more and supporting those who live with Usher 1F.

2022 Fall

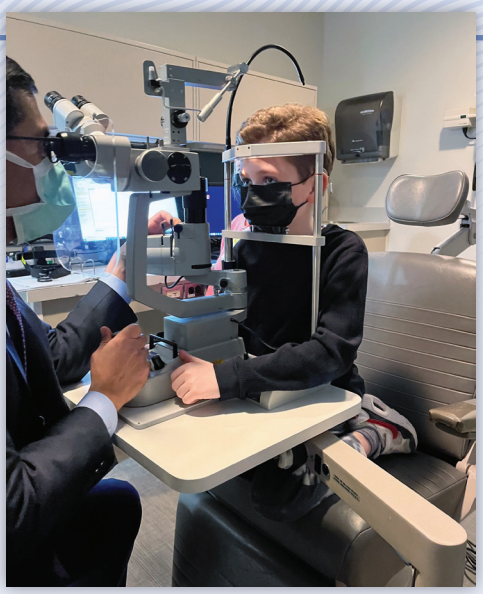
Opportunities for partnerships and collaborations expanded in the fall. We partnered with the Usher Syndrome Coalition and the Usher Syndrome Society in the creation of a RARE-X patient registry. RARE-X is a collaborative platform for global data sharing and analysis to accelerate treatments for rare disease. In October, we brought our researchers together from around the globe for a virtual scientific research conference. Timing was challenging with time zones ranging from eastern Australia, to Europe, to the west coast of the United States for a total of an 18-hour span. One of our Australian researchers was kind enough to give his talk after 11:00 p.m., while our researcher in California was up bright and early at 5:00 a.m. Making these conferences an annual event benefits not only our network of researchers, enabling them to share and learn from each other, but also our families, giving them hope as they learn of our progress toward a cure.

RUSH1F

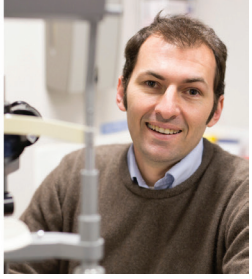
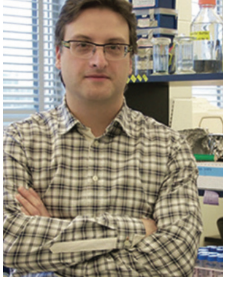
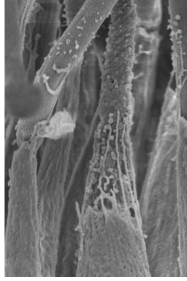
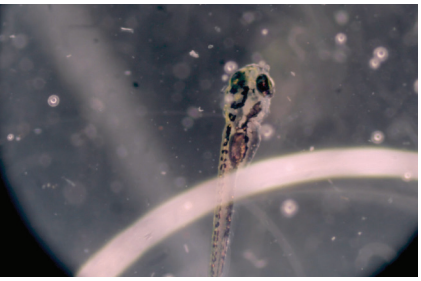
Our Natural History Study

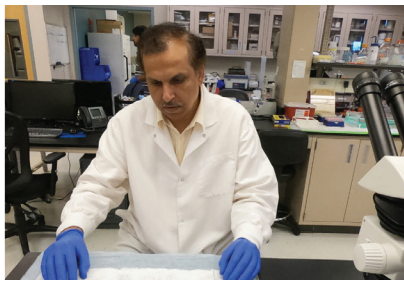
Our natural history study, RUSH1F, in partnership with Foundation Fighting Blindness, is up and running at all ten locations across the U.S., Canada, Europe, and Israel. Year two appointments of the four planned years have already begun at some locations. This study will provide data critical for a future clinical trial, documenting the progression of vision loss in those with Usher 1F in the absence of treatment. Essentially, it provides a control group for a clinical trial so that all patients will be able to get the actual treatment and not a placebo.

In 2022, the Usher 1F Collaborative Board voted to allocate an additional $100,000 to RUSH1F, enabling the study to enroll 45 patients instead of the originally planned 40, providing more robust data. We currently have 39 patients enrolled. If you have Usher 1F, are at least eight-years-old, and have usable vision, please enroll in RUSH1F. You will be helping all with Usher 1F ensure that a future clinical trial will proceed, including yourself. Travel expenses are reimbursed up to $3500. We send a huge thank you to those of our families who have already enrolled!





2022 Winter

We gathered research updates from our scientists and proudly distributed them to our friends and families of Usher 1F Collaborative. The updates included:

- **Harvard Medical School**
  (led by David Corey, PhD): This laboratory continues to test three therapeutic strategies: dual-AAV delivery of a split PCDH15 gene, a mini PCDH15 gene, and gene editing of the common R245X mutation. All three rescue hearing in mice, with dual-AAV and mini-gene being more effective. Some also rescue balance in mice. In zebrafish retina, the mini-gene approach prevents photoreceptor degeneration and restores photoreceptor electrical function. Dr. Corey presented his team's Usher 1F work at two conferences this year, and project head Maryna Ivanchenko, MD, PhD, presented their research at four conferences, most significantly at the annual meeting of the Association for Research in Vision and Ophthalmology, the largest international vision research conference.

- **The Salk Institute**
  (led by Samuel Pfaff, PhD): Dr. Pfaff has developed a revolutionary approach to delivering large genes and believes that Usher 1F would be an excellent application of this approach. Dr. Pfaff met our other Usher 1F researchers when he presented at our conference in October. He was excited to learn of our animal and retinal organoid models and is collaborating with our other researchers.

- **University of Oregon**
  (led by Monte Westerfield, PhD): Dr. Westerfield is conducting preclinical testing for efficacy of a potent antioxidant. Oxidative stress is a factor in vision loss in those with Usher 1F, and this compound is a potent antioxidant that holds the potential to protect the retinal photoreceptor cells from oxidative stress. Testing on our Usher 1F zebrafish shows that it is safe and that it partially rescues visual function.

- **University of Maryland**
  (led by Zubair Ahmed, PhD): Dr. Ahmed is testing the split gene dual vector systems obtained from our University of Western Australia and University of Pittsburgh research teams. Testing on their Usher 1F mouse model is demonstrating rescue of vision. His team also continues to test a promising compound, which is showing encouraging results in rescuing vision.

The Impact of Our Transformative Chan Zuckerberg Initiative Rare As One Project Grant

When we began 2020, the first year of our Chan Zuckerberg Initiative (CZI) Rare As One (RAO) Project grant, we were very excited to be part of a group with 29 other rare disease organizations, learning from each other and from the experts and training CZI would provide us. The grant provided Usher 1F Collaborative with $600,000 over three years. Similar to the proverb, "Give a man a fish and he will eat for a day. Teach a man how to fish and you feed him for a lifetime," the purpose of the grant was not to directly fund research but, instead, to fund capacity building with a goal of growing our organization and ensuring its sustainability. Over the course of the three-year grant period, we have done just that, growing our organization to ensure that we can continue to fund the research. Highlights realized from the grant include:

Hiring of staff and consultants to grow our organization, enabling us to identify and pursue new and more opportunities

- Hiring a full-time Development Manager, Sarah Gauch, who has become an invaluable, integral part of our team, helping us identify new opportunities and obtain grants and donations.
- Working with Laurie Kirkegaard, CFRE, NPL Impact Agency, who has helped us grow our board and define board responsibilities and success. In particular, this included the formation of our Development Committee, which is doing a great job increasing our fundraising outreach and dollars raised. Laurie is also guiding us on obtaining major gifts.
- Working with Josh Wolf of Cooperative Impact Lab, ensuring our accounting and finances are not only in order but adhering to proper accrual accounting practices.

Hosting conferences to bring researchers together to share work and form collaborations

- In May 2021, we held a virtual scientific research conference, Therapeutic Strategies for Large Protein Coding Genes in Usher Syndrome. Hosting a conference was part of the requirement of our CZI grant. CZI introduced us to and helped us fund hiring a professional conference coordinator. We felt that Usher 1F alone was too small for such a large conference and that we could not only share the gift of our grant with others but also benefit all with Usher syndrome caused, as is Usher 1F, by large genes, which pose a unique challenge for gene therapy. Bringing together researchers from all over the world working to tackle this problem served to benefit so many with Usher syndrome as the researchers learned from each other and formed connections. It also gave us the opportunity to showcase our own Usher 1F researchers and their accomplishments.
- In October 2022, we held a one-day Usher 1F researchers conference. All of our researchers were present. Not only was it great to learn the latest updates about their work, but also we were thrilled to see new research collaborations formed as a result of the conference.

Natural History Study and Registry

- We learned of the importance of both and partnered with Foundation Fighting Blindness for RUSH1F, our natural history study.
- We partnered with the Usher Syndrome Coalition, which took the lead in establishing an Usher patient registry using RARE-X's platform.

Funding for a professionally made documentary film on Usher 1F Collaborative that we will be using at house party fundraisers and possibly at film festivals

Drug repurposing

- We had the opportunity to hear from organizations who have successfully identified existing drugs that benefit their rare disease and are working to identify the optimal way to pursue this approach for Usher 1F.

Trainings and guidance to become a true professional organization

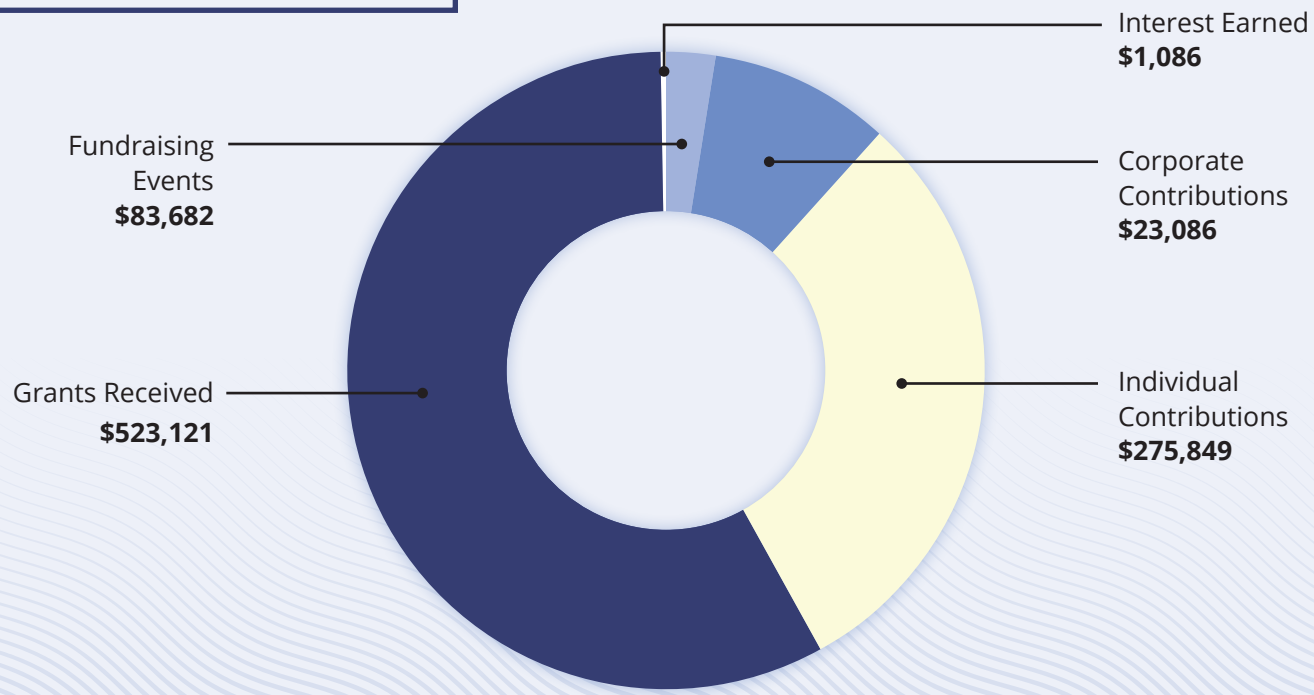
- Strategic planning
- Board structure
- Major gifts
- Grant writing
- Finance and operations
- State registration compliance
- Storytelling
- Website enhancement for greatest impact

Another benefit that cannot be understated was the opportunity to engage with leaders from the other patient-led rare disease organizations, a group that grew to 50 total with the addition of cycle two grantees at the beginning of 2022. Fortunately, we will be able to continue benefitting from this network as a continued part of the grantee discussion forum and future convenings.

With the conclusion of our grant period, we send a huge thank you to the wonderful team at CZI for the invaluable support and guidance in advancing our pursuit of a cure!

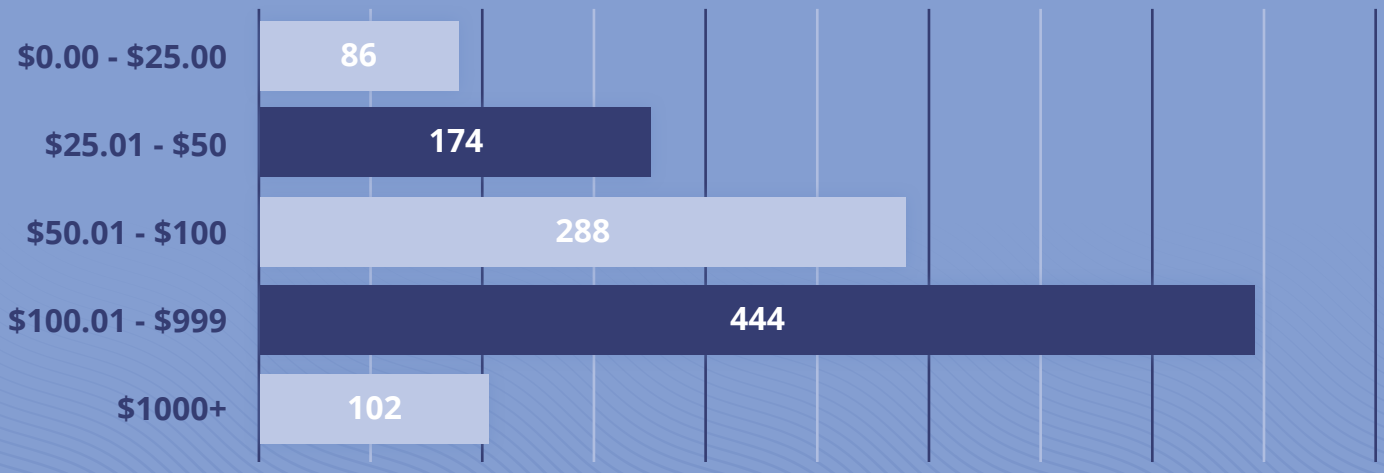
FUNDING RAISED

Total: $906,824



GIVING BREAKDOWN

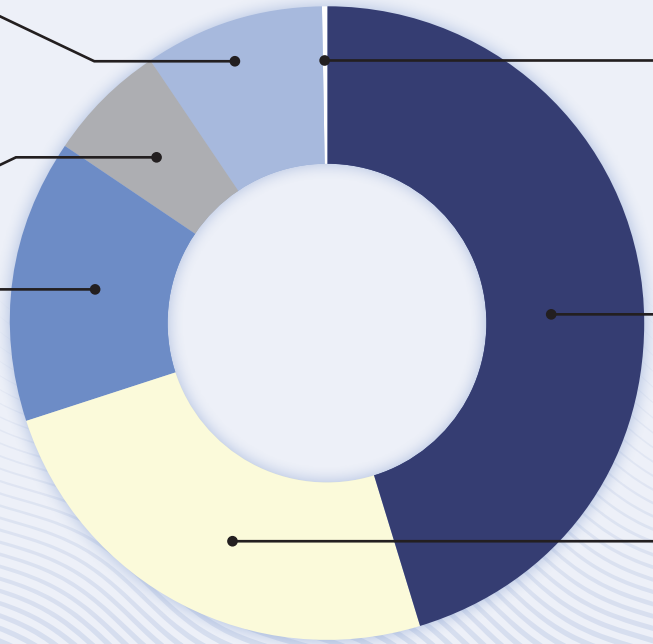
Total Number of Gifts: 1094



TOTAL GRANT DISTRIBUTION

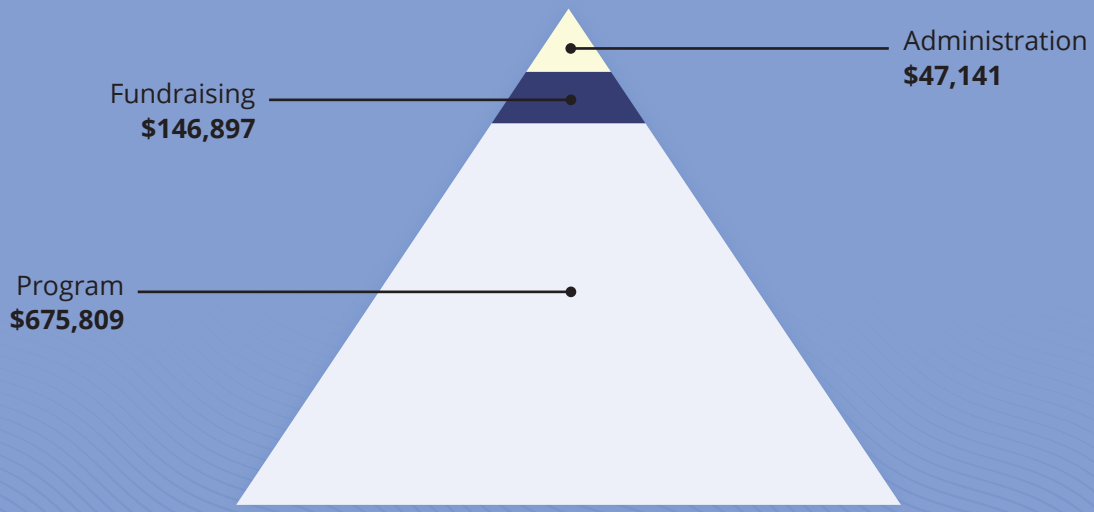
Total Grants Given: $659,100

**$200,000 from funds previously set aside for natural history study*



EXPENDITURES BY FUNCTIONAL AREA

Total: $869,847



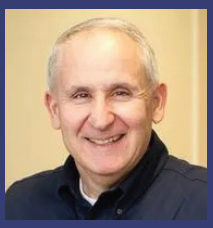
Total assets as of 12/31/22

$1,180,040

Board of Trustees

Melissa Chaikof
Chair and Trustee

Elliot Chaikof, MD, PhD
Vice Chair & Trustee
Scientific Oversight Team



Frank Gentile, PhD
Treasurer & Trustee
Scientific Oversight Team

Jared Root
Secretary & Trustee
Chair, Development Committee

Joshua Cohen
Trustee

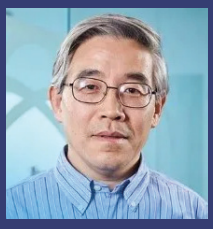
Rachel Root
Trustee

Heather Rosenstein
Trustee

Julian Seewald
Trustee

Laurie Shapiro
Trustee

Sari L. Springer
Trustee



Lijun Sun, PhD
Trustee, Scientific Oversight Team

Scientific Advisory Board

Aravinda Chakravarti, PhD

Richard Cummings, PhD

David Liu, PhD

Peter J. McDonnell, MD

Edward Scolnick, MD

USHER 1F COLLABORATIVE

Usher 1F Collaborative | #228 | 321 Walnut Street, Newtonville, MA 02460-1927 | usher1f.org