PITT HOPKINS RESEARCH FOUNDATION

Don't just hope for MIRACLES, FIGHT for THEM!

PITT HOPKINS NEWSLETTER - May 2025

ANNOUNCING THE INAUGURAL Be Better Award in honor of Victor Pauca

Corey Lab at UT Southwestern

We are so very honored to announce The Pitt Hopkins Research Foundation's inaugural **BE BETTER award in honor of Victor Pauca.** Victor Pauca was the son of Paul Pauca and our foundation's VP, Theresa Pauca. He was one of the first children in the world diagnosed with Pitt Hopkins and tragically, he passed away in December at the age of 19, after a long and debilitating battle with respiratory illness complicated by Pitt Hopkins Syndrome.

Through it all, his family lived by the motto - "Be Better, not Bitter." They exemplify this motto in a way that most people never could. In fact, Theresa remains on our board, continuing to fight for Victor's legacy.

We are honored to grant this award to the **Corey Lab at UT Southwestern**, led by renowned RNA scientist **Dr. David Corey**, to explore a novel RNA-based therapy aimed at increasing TCF4 protein expression in Pitt Hopkins syndrome (PTHS).

Small RNA Activation Therapy for Pitt Hopkins

The root cause of Pitt Hopkins syndrome is insufficient production of a critical protein called **TCF4**. Correcting this deficit at the genetic level remains one of the most promising paths toward a meaningful treatment.

Dr. Corey's lab is pioneering the use of **small activating RNAs (saRNAs)**—short RNA molecules designed to precisely target and "turn on" genes that aren't making enough protein. In this case, the therapy will focus on increasing expression of **TCF4** by binding to regulatory regions of the gene, effectively boosting its activity.

The Corey Lab has spent years refining this approach and will now test its potential in Pitt Hopkins. Their immediate goal is to determine whether sbRNA can reliably elevate TCF4 protein levels—a critical proof-of-concept milestone expected within six months.

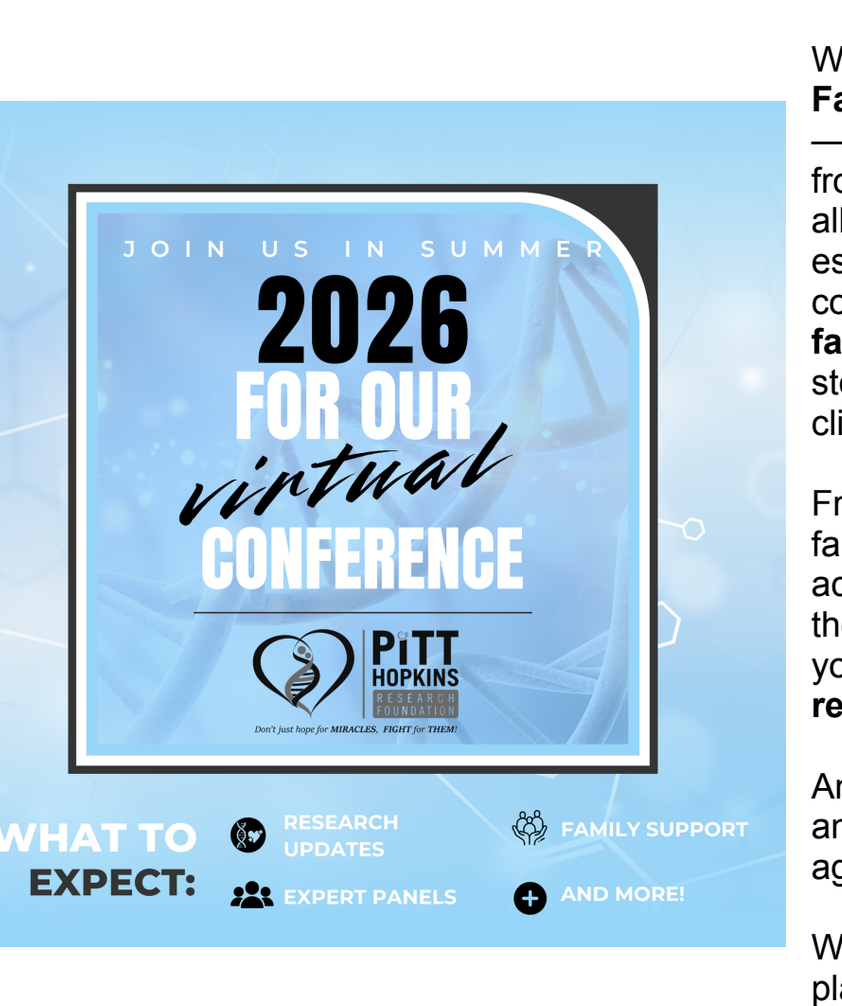
This work is part of the Foundation's larger strategy to invest in multiple, complementary approaches to increase TCF4 and drive progress toward a cure.

We are honored to support this cutting-edge work and grateful to Dr. Corey and his team for their dedication to our children.

Read more about the Corey Lab's work at coreyutswlab.com

In our talks with David Corey and his collaborator Bethany Jankowski, it's clear they are most concerned with discovering a viable treatment for our children as soon as possible. And to us, that is the epitome of Being Better. Thank you Victor, for giving us the inspiration and fuel to continue fighting.

Mark Your Calendars: Our 2026 Family Conference is Going Virtual!



We're thrilled to announce that the **Pitt Hopkins Family Conference will be held virtually in 2026**—bringing our entire global community together from the comfort of home! This virtual format will allow **more families than ever before** to attend—especially those for whom travel is difficult or costly. It also opens the door for our **international families** to join the conversation, share their stories, and connect in real time with researchers, clinicians, and each other.

From expert panels and scientific updates to family support sessions and community-building activities, the 2026 conference will be packed with the same heart, hope, and helpful information you've come to expect—just with **no airfare required**.

And don't worry—we'll be back **in person in 2027**, and we can't wait to see many of you face-to-face again then.

Whether you'll be logging in from a laptop or planning to join us in person the following year, we can't wait to connect, grow, and move this mission forward—together.

Clinical Trials Update: Progress Today, Hope for Tomorrow

Gene Therapy on the Horizon

Mahzi Therapeutics | Licensed from PHRF funded work at UCSD's Muotri Lab

Gene therapy is no longer a dream—it's becoming a reality. Building on foundational research from the Muotri Lab at UC San Diego, Mahzi Therapeutics is preparing to launch the first-ever gene therapy trial for Pitt Hopkins Syndrome. Recruitment is anticipated to begin in late 2025 or early 2026. The trial will include two age cohorts—ages 2–11, and 12–25—with the oldest group enrolling first. Trial site selection is underway, with both U.S. and international locations under consideration. This is a historic moment for our community, and we'll be sharing more details as they unfold.

Microbiota Transfer Trial Nears Completion

Arizona State University | Dr. James Adams

Following the success of our first Microbiota Transfer Therapy (MTT) Trial, the next Phase 2 study of the MTT is nearing completion. This next phase uses a liquid formulation rather than capsules, and early feedback from participating families is encouraging—many report reduced pain and additional positive changes. The research team at ASU has since launched a company, Gut Brain Axis, with the goal of bringing this biologic treatment to market. Pending results, the team hopes to seek FDA approval for Pitt Hopkins Syndrome, marking a major step forward for our community.

Fast Track Designation for Pitt Hopkins

Neuren Pharmaceuticals

Neuren Pharmaceuticals announced in February 2025 that the US Food and Drug Administration (FDA) has granted Fast Track designation for NNZ-2591 for the treatment of Pitt Hopkins syndrome (PTHS). Fast Track is designed to facilitate the development and expedite the review of drugs to treat serious conditions. Currently there are no treatments approved to treat PTHS. In Neuren's Phase 2 clinical trial of NNZ-2591 in children with PTHS, 82% of participants showed improvement, including communication, social interaction, cognition and motor abilities. We hope to have more information on the next steps soon.

Progress Reports from Our Labs: Pushing the Boundaries in Genetic Therapy

Milestone Achieved: U7 snRNA Therapy Boosts TCF4 in Mouse Model

The Research Institute at Nationwide Children's Hospital

We're excited to share a major research milestone in our efforts to develop gene therapies for Pitt Hopkins syndrome. Initiated by Dr. Kathrin Meyer's lab at Nationwide Children's Hospital and now being advanced by Dr. Afrooz Rashnonejad at the same institution, this project focused on using a novel approach—repurposing U7 small nuclear RNA (snRNA)—to modulate TCF4 transcript expression.

In the first phase of this study, the team successfully demonstrated increased TCF4 protein expression in a mouse model of PTHS, marking an encouraging step forward. This innovative strategy holds strong potential for addressing the underlying genetic cause of the syndrome. As we move into the next phase, our researchers will continue to refine the approach in the hopes of bringing it to clinical trials.

CRISPR Progress: Restoring TCF4 with a Smaller, Smarter Tool

Fink Lab at UC David

We're proud to share exciting progress from Dr. Kyle Fink's lab at UC Davis, where a cutting-edge gene activation strategy is showing real promise for Pitt Hopkins syndrome (PTHS). PTHS is caused by changes in a gene called TCF4, which plays a key role in brain development and function. Right now, there are no treatments that address the root cause of PTHS—but that's what this research aims to change.

With previous funding from the Pitt Hopkins Research Foundation, Dr. Fink's team showed they could successfully boost TCF4 levels in cells using a tool called CRISPR activation. This system was effective, but the version they used was too large to fit into the delivery system (AAV) typically used in gene therapy.

Now, with continued support, the Fink lab is taking the next big step: testing a new, much smaller CRISPR system called casMINI. This compact version can fit into a single AAV, making it far more practical for future therapies. The team is currently screening the best guide combinations to help restore TCF4 expression—and we're hopeful this could pave the way for a powerful, precise treatment for PTHS.

Repurposing: Discovering New Hope in Established Therapies

AI-Driven Drug Repurposing: RVL-001 Advances Toward Clinical Trials

Unravel Biosciences, an AI-enabled therapeutics company, is preparing to initiate a proof-of-concept clinical trial for RVL-001, a potential treatment for Pitt Hopkins Syndrome (PTHS), in Colombia. RVL-001 is a repurposed formulation of vorinostat, a histone deacetylase inhibitor previously identified by Drs. Andrew Kennedy and Dr. David Sweatt, PHRF-funded researchers. Unravel's proprietary BioNAV™ platform identified RVL-001 as a promising candidate for PTHS as well as Rett Syndrome.

Histone deacetylases are a type of enzyme that helps to control how tightly DNA is wrapped around histones. By blocking these enzymes, histone deacetylase inhibitors can act to modulate the activity of genes within cells.

The trial is expected to enroll 6 people with Pitt Hopkins syndrome and will test the experimental therapy against a placebo and will be conducted in collaboration with PECET, the clinical research unit at the University of Antioquia in Medellín, Colombia. PECET is certified in Good Clinical Practices by Colombia's health regulatory agency, INVIMA. The study has been submitted under INVIMA's pilot program, which allows for priority review and fast-track approval for orphan diseases and conditions with high unmet medical needs.

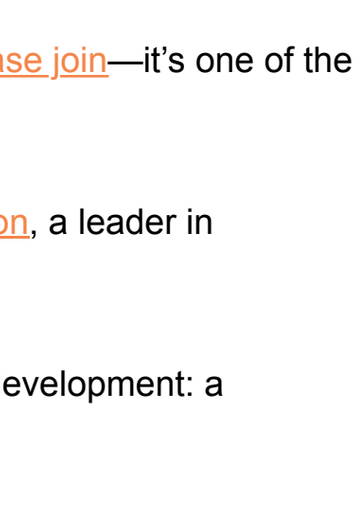
This initiative builds upon Unravel's prior efforts in Colombia, where infrastructure was established for a Rett Syndrome trial. **The Pitt Hopkins Research Foundation is funding the PTHS trial and patient enrollment for the RVL-001 trial is anticipated to begin by August 2025.** This collaborative effort exemplifies the potential of repurposing existing drugs to address rare diseases.

The Research Rundown: 10 Key Updates You Need to Know

1. Three Clinical Trials and Counting
Since 2023, we've launched *three* clinical trials: one with Neuren Pharmaceuticals targeting BDNF enhancement, and two at Arizona State University exploring Microbiota Transfer Therapy.

2. Gene Therapy is Coming
Mahzi Therapeutics has licensed our UCSD gene therapy work and is on track to file an IND this summer, with a first-in-human trial planned for late 2025 or early 2026.

3. Repurposing Old Drugs for New Hope
Unravel Therapeutics is preparing a clinical study in Medellín, Colombia using a repurposed drug for Pitt Hopkins syndrome, supported by Colombia's fast-track orphan disease program.



Click here to see our full therapeutic pipeline.

4. Expanding Our Clinical Network
We are growing a powerful network of clinical partners. The Neuren trial included five sites—Colorado Children's, UAB, Chicago Rush, and more—while Mahzi has already begun identifying its own trial sites.

5. Building Smarter with Data
To prepare for Mahzi's trial (as well as other future trials), we've partnered with Citizen Health to collect and analyze medical records. So far, ~60 families have contributed to this crucial data initiative.

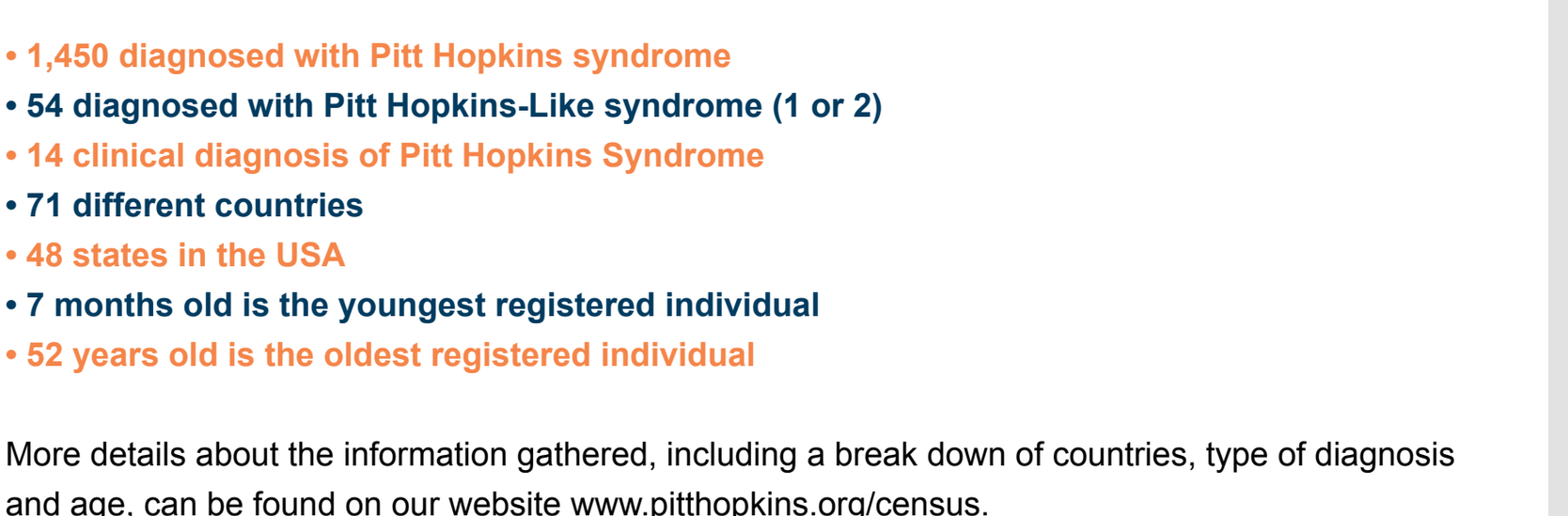
6. Join Our Registry
Our patient registry with Sanford is growing steadily. If you haven't already, please join—it's one of the most important ways to accelerate research and access future trials.

7. Biomarker Discovery is Underway
We recently collected over 30 blood and stool samples for analysis by Metabolon, a leader in metabolomics. The study is complete and now under review.

8. New Mouse Models in Development
Beyond our original heterozygous knockout mice, two new models are now in development: a humanized model at Jackson Labs and a second from the Philpot Lab.

9. Exploring ASO Therapy
We've been funding early ASO (antisense oligonucleotide) development at La Jolla Labs. Initial data is promising, and we'll soon begin testing in organoids at the Muotri Lab.

10. Every Step Brings Us Closer
Each of these efforts—clinical trials, gene therapy, patient data, biomarkers, and new models—moves us closer to effective treatments and, ultimately, a cure.



Pitt Hopkins Census

Please join!

A question that comes up often is, *how many individuals in the world live with Pitt Hopkins syndrome*? It is a difficult question to answer, but **gathering this information is vital for research**. Pharmaceutical companies are highly motivated to know this number and have asked us to help ascertain it.

As of March 30, 2025, we have **1,518 individuals in the world** registered! Some quick and interesting facts:

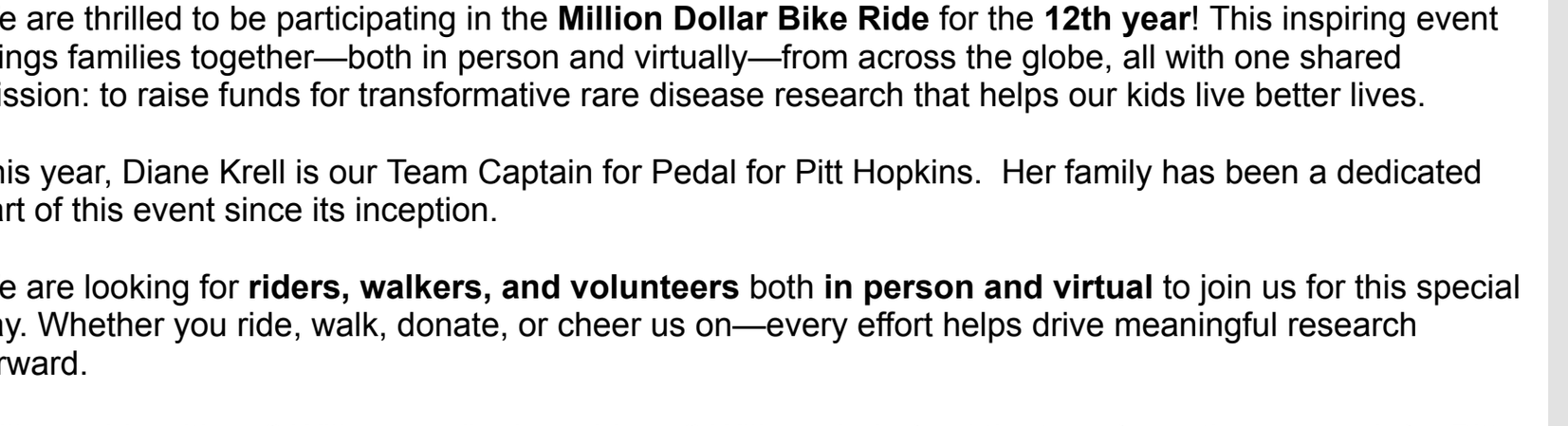
- **1,450 diagnosed with Pitt Hopkins syndrome**
- **54 diagnosed with Pitt Hopkins-Like syndrome (1 or 2)**
- **14 clinical diagnosis of Pitt Hopkins Syndrome**
- **71 different countries**
- **48 states in the USA**
- **7 months old is the youngest registered individual**
- **52 years old is the oldest registered individual**

More details about the information gathered, including a break down of countries, type of diagnosis and age, can be found on our website www.pitthopkins.org/census.

Parents and/or Legal Guardians, We are asking you to please take a couple of minutes and fill out this quick, easy and very important survey to help us get a more accurate census of diagnosed Pitt Hopkins patients worldwide.

And to make this easier, we have added the survey in multiple languages:

- **English**: https://forms.gle/ESrUNeGNabby8bbK6
- **French**: https://forms.gle/AeEFbdQsSSBUpoJ57
- **Portuguese**: https://forms.gle/yvC5VnfSsAhbnLic7
- **Spanish**: https://forms.gle/3ysjo6GAm9LoR7V4A



Million Dollar Bike Ride

Philadelphia, PA

2025

Join Us for the 12th Annual Million Dollar Bike Ride

We are thrilled to be participating in the **Million Dollar Bike Ride** for the **12th year**! This inspiring event brings families together—both in person and virtually—from across the globe, all with one shared mission: to raise funds for transformative rare disease research that helps our kids live better lives.

This year, Diane Krell is our Team Captain for Pedal for Pitt Hopkins. Her family has been a dedicated part of this event since its inception.

We are looking for **riders, walkers, and volunteers** both **in person and virtual** to join us for this special day. Whether you ride, walk, donate, or cheer us on—every effort helps drive meaningful research forward.

Will you ride with us? Will you walk alongside us? Will you help fund the transformative research for Pitt Hopkins?

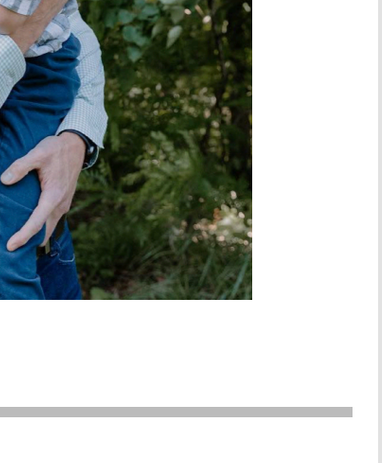
Need help registering or setting up your fundraising page? Let us know—we're here to assist! You can sign up at https://www.milliondollarbikeride.org.

Please consider being a part of Pedal for Pitt Hopkins or donating to PHRF - every contribution makes an impact! https://charity.pledgeit.org/MillionDollarBikeRide/teams/@PHRF.

Together, we can make a difference—let's ride for a brighter future!

2024

Award Recipient Announced



The Million Dollar Bike Ride 2024 grant awardee was Dr. Simone Mesman at the University of Amsterdam. A grant of $58,602 was awarded to Dr. Mesman for investigating underlying causes of gastro-intestinal problems in patients with Pitt Hopkins syndrome.

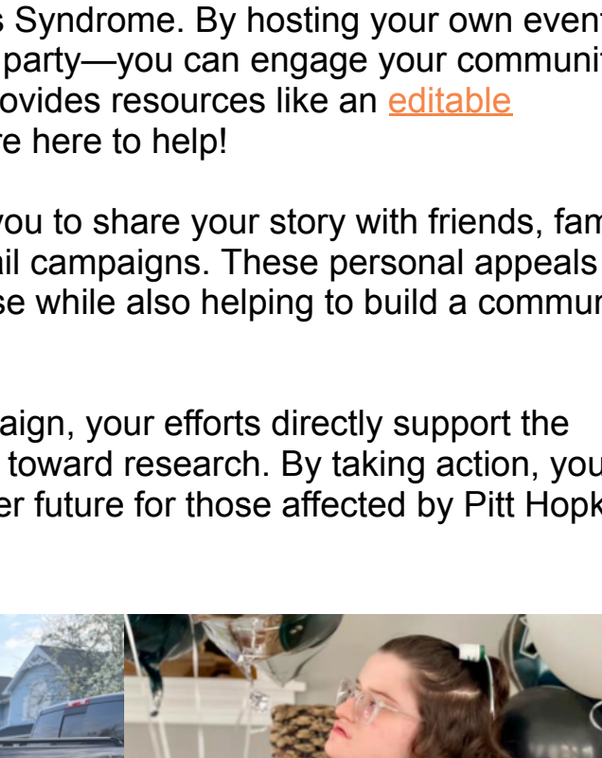
Thank you to all who participated in and donated to our MDBR 2024 fundraising efforts, you made this possible!

Details of the grant can be found here.

Got4titude: Empowering Fathers, Transforming Futures

Kirby is a devoted father to Harley, who has been diagnosed with Pitt-Hopkins Syndrome and is on the autism spectrum. Through the highs and lows of their journey, Kirby discovered the power of presence, vulnerability, and community. This realization led to the creation of Got4titude—a growing platform dedicated to supporting fathers raising children with disabilities. Got4titude offers content, resources coaching, and connection to help dads find clarity and confidence while reminding them they are not alone.

Check it out now!

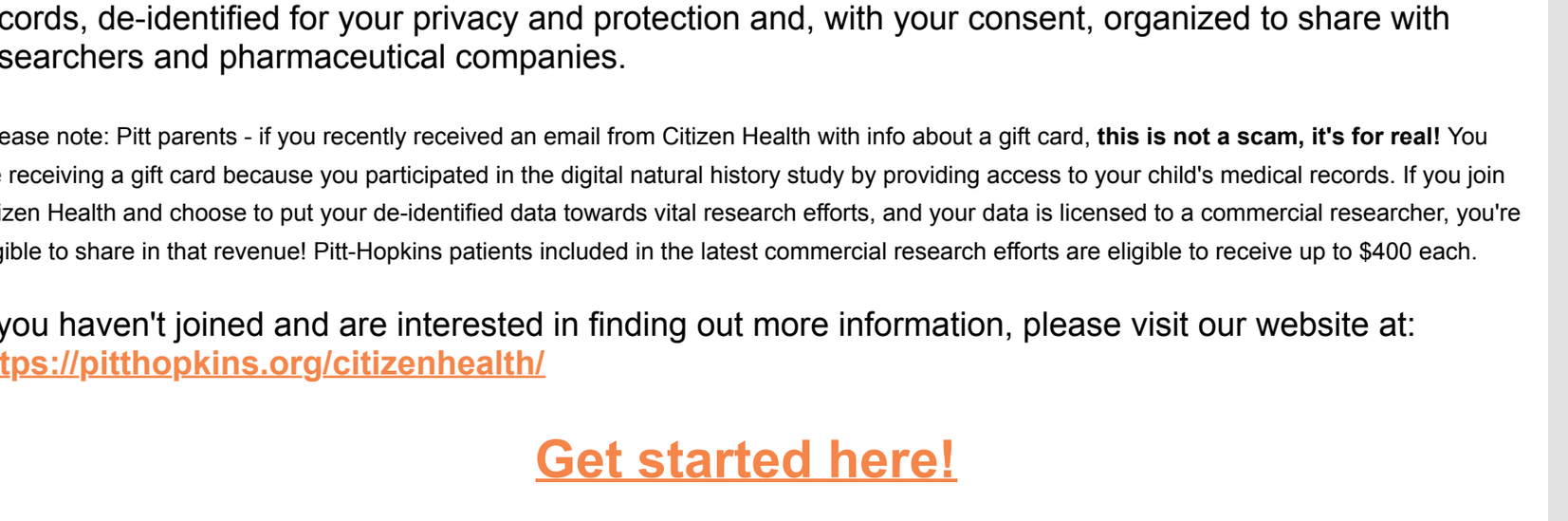


Fundraising For a Brighter Future

Raising funds for the Pitt Hopkins Research Foundation is a powerful way for families to make a lasting impact on the search for treatments and a cure for Pitt Hopkins Syndrome. By hosting your own event—such as a 5K run, golf tournament, trivia night, or even a pizza party—you can engage your community and raise both awareness and critical funds. The foundation provides resources like an editable sponsorship kit and support to help you plan your event. We are here to help!

Alternatively, starting a personal fundraising campaign allows you to share your story with friends, family, and coworkers through online giving pages, direct mail, or email campaigns. These personal appeals often resonate deeply, inspiring others to contribute to the cause while also helping to build a community around your loved one at the same time.

Whether you choose to host an event or start a personal campaign, your efforts directly support the foundation's mission, with over 94% of all funds donated going toward research. By taking action, you become a vital part of the community working towards a brighter future for those affected by Pitt Hopkins Syndrome.



Join Citizen Health

Get involved today

We have joined many other rare disease groups that have been using Citizen Health to build high-quality natural history data in a fraction of the time. Researchers and pharmaceutical companies have already used the data to submit Investigational New Drug (IND) filings with the FDA and this will help us work toward this for Pitt Hopkins as well. **Registering takes only a few minutes,** and the Rare Patient Network team will collect all your or your loved one's medical records. You will receive full access to the records through your personal portal and can share them with whomever you choose. This natural history study doesn't require any clinical visits. The data will be extracted from your existing medical records, de-identified for your privacy and protection and, with your consent, organized to share with researchers and pharmaceutical companies.

*Please note: Pitt parents - if you recently received an email from Citizen Health with info about a gift card, **this is not a scam, it's for real!** You are receiving a gift card because you participated in the digital natural history study by providing access to your child's medical records. If you join Citizen Health and choose to put your de-identified data towards vital research efforts, and your data is licensed to a commercial researcher, you're eligible to share in that revenue! Pitt-Hopkins patients included in the latest commercial research efforts are eligible to receive up to $400 each.

If you haven't joined and are interested in finding out more information, please visit our website at: **https://pitthopkins.org/citizenhealth/**

Get started here!

Pitt Parents, We Need You!

• Join the Pitt Hopkins Registry
We are proud to have partnered with CoRDS of Stanford to create this thorough and very important research initiative. The Pitt Hopkins registry is very important for many reasons, including helping us gather information for research, creating a central resource for researchers for more rapid recruitment of research participants, helping us to get an overall better picture of Pitt Hopkins syndrome and helping us connect with families. As we head toward clinical trials, this registry will also be an important tool to help with recruiting patients.
Find out more ››

• Join the Census
Help us get an accurate count of individuals with Pitt Hopkins Syndrome worldwide!
Find out more ››

• Join Citizen Health
Join our community on the Citizen Rare Patient Network today. It only takes a few minutes to sign up and you will get access to all your medical records in one place at no cost. US Patients only.
Find out more ››

• Donate Cells to Coriell
The NIGMS Repository is a research biobank. They collect samples from individuals with genetic diseases and make cell lines and DNA for scientists to use in their studies. These cells are being used to create iPSC lines and mini-brains (organoids) for our funded scientists to test medications on. More information on donating and how it can help PTHS research can be found here.
Find out more ››

Donate Today