



IMPACT REPORT

2023



Celebrating 29 years of Outstanding Research



RESEARCH UPDATE

Michael Tranfaglia, MD
Medical Director, Co-Founder

We directly fund research grants and fellowships at top universities around the world. We partner with biomedical and pharmaceutical companies, large and small, to bridge the gap between research discoveries and actual treatments. Treatments for Fragile X are likely to help people affected by autism, Alzheimer's, and other brain disorders.

Things are moving fast in Fragile X research, and it's back to business on all fronts following the pandemic. The recent unparalleled success of the Tetra PDE4D clinical trial has led to much larger, pivotal clinical trials with this drug. If this current round of trials is as successful as the initial Tetra study, this drug will be the first officially approved treatment for Fragile X.

The success of this trial, which emerged from extensive FRAXA funding over many years, has also sparked a great deal of interest at big pharma corporations. Not surprisingly, any company developing a PDE4 inhibitor is suddenly interested in Fragile X! This extends to other drug classes as well.

Getting new drugs to the market is important, but it always takes longer than we would like. This is the rationale for repurposing available drugs, which has already led to two ongoing clinical trials in Fragile X, with more coming soon!

There have also been major advances in efforts to reactivate the Fragile X gene, thanks to FRAXA-funded research. We expect one or two companies to form around these discoveries in the coming year. Additionally, several companies are developing gene therapy approaches based on previous Fragile X research, and we are now studying the potential use of mRNA vaccine technology to replace the protein which is lacking in Fragile X syndrome.

We are energized about the research possibilities of this coming year, and the excitement and hope they will ignite in Fragile X families. ***Thank you for your support and for helping us move closer to achieving our mission.***

OUR MISSION

To find effective treatments and ultimately a cure for Fragile X syndrome.

Fragile X syndrome (FXS) is the most common inherited cause of autism and intellectual disabilities worldwide.

Fragile X is key to solving autism. Treatments for Fragile X are also likely to help people who have Alzheimer's or other brain disorders.



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**\$33.6
million**

direct investment
in Fragile X
research

FRAXA'S IMPACT TO DATE 1991-2023

42

teams actively
researching
Fragile X

31

pharmaceutical
and biomedical
partners

629

research grants
awarded

19

countries home
to research teams

Learn more about how
FRAXA accelerates
progress toward a cure.
Visit fraxa.org/about



World
FRAGILE X
Day

The world shone bright on July 22, 2022 for World Fragile X Day, with an impressive 383 locations on 5 continents illuminated. While it is difficult to pick a favorite lighting, Chicago's Blue Cross Blue Shield building sparked the most excitement by displaying "Fragile X" in big bright letters.

World Fragile X Day (WFXD) celebrates families impacted by Fragile X and highlights advancements of research to find effective treatments and ultimately a cure. Launched in 2021 by FRAXA Research Foundation with communities around the globe, WFXD brings greater visibility to our field and energizes families everywhere.

Many new countries joined our efforts this year. First-time illuminations were seen in Austria, Denmark, Indonesia, Italy, Portugal, Uruguay, and the United Kingdom! There were illuminations in 18 countries!

Online, we broadcast *"Fragile X Syndrome: Innovative Approaches to Finding a Cure"* which showcased 30+ scientists, each presenting a unique approach to finding a cure.

Visit worldfragilexday.com to get involved!

Celebrating 29 years of Outstanding Research

1991

Fragile X Gene mutation is discovered and named "FRAXA". This mutation prevents the gene from producing its normal protein, causing Fragile X syndrome.

1992

Fragile X protein is identified and cloned by the gene's discoverers, Drs. Stephen Warren, David Nelson, and Ben Oostra.

1994

FRAXA Research Foundation founded by 3 parents, Katie Clapp, Michael Tranfaglia, and Kathy May.

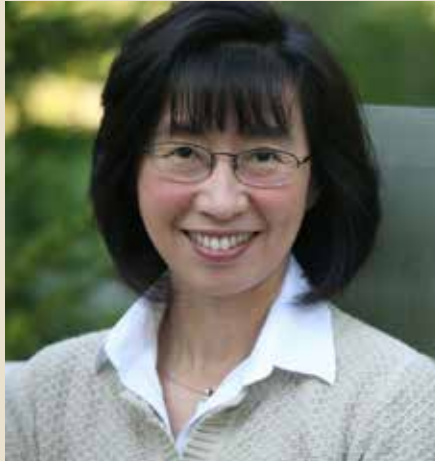
1994

FRAXA funds first research project led by Ted Brown, MD, PhD, New York State Institute for Basic Research, to develop a yeast model of Fragile X. **1**

RESEARCH Spotlights

Jeannie Lee,
MD, PhD

Harvard University/
Massachusetts
General Hospital



Reactivating the FMR1 Gene to Reverse Fragile X Syndrome

2016-2023 Grant Funding: \$320,000

Dr. Jeannie Lee, Professor of Genetics at Harvard Medical School, is addressing the root cause of Fragile X syndrome. Fragile X occurs when a single gene, FMR1, fails to produce its normal protein product - a protein essential for brain function. Dr. Lee and her team are devising a method to **reactivate the gene** using combinations of drugs. These "drug cocktails" are able to reactivate FMR1 in cells in their lab!

If the drugs work in patients, this could be a potential cure for Fragile X syndrome. FRAXA has funded Dr. Lee's work since 2016 for a total of \$320,000.



mRNA Therapy for Fragile X Syndrome Kathryn Whitehead, PhD, Carnegie Mellon University

2022-2023 Grant Funding: \$100,000



In a 2021 **TED Talk** entitled "*The tiny balls of fat that could revolutionize medicine*" Dr. Kathryn Whitehead answers the question: *what if you were holding life-saving medicine, but had no way to administer it?*

Her work on COVID-19 vaccines is forging a path to **mRNA-based therapies** for rare diseases, starting with Fragile X syndrome.

The COVID-19 pandemic has launched a new class of medicine based on messenger RNA (mRNA). Advances in mRNA technology, including modifications to mRNA itself and new delivery vehicles, mean that mRNA can be used to restore or replace different types of therapeutic proteins.

Lack of a single protein, FMRP, causes Fragile X syndrome and is also linked with other autism spectrum disorders. With funding from FRAXA, Dr. Whitehead and colleagues will take first steps toward a gene therapy solution to treat (or even cure) Fragile X. They are developing a drug delivery system using lipid nanoparticles (tiny balls of fat) to deliver the Fragile X mRNA to brain cells. If the mRNA can produce its normal protein, then Fragile X symptoms should subside.

With luck and continued funding, this work could open a new avenue of mRNA therapy for brain disorders, beginning with Fragile X.

Celebrating 29 years of Outstanding Research

1995

FRAXA funds first gene therapy study (Jude Samulski, PhD, University of North Carolina).

1995

FRAXA begins first ever **Fragile X advocacy in Washington, DC**; Congress recognizes critical need for Fragile X research for first time.

1995

FRAXA launches first ever online Fragile X community "the listserv" providing a global lifeline prior to social media.

1996

Fragile X knockout mice shared with the worldwide research community. Study with these mice leads to first understanding of the cause of Fragile X.

A Drug Screening Platform for Fragile X Syndrome

Frank Kooy, PhD
Principal Investigator

Mathijs van der Lei
FRAXA Fellow

University of Antwerp
Antwerpen, Belgium

2022-2023 Grant Funding: \$100,000

Many experts believe that combinations of drugs may be needed to treat Fragile X syndrome.

With thousands of alternatives available, how can we find the best combinations in the ideal doses? A top university research team and an innovative AI startup, both based in Belgium, tackle the challenge.

Dr. Frank Kooy's team has established an innovative and efficient **drug screening platform for Fragile X syndrome**. They are using a combination of a multi-electrode array (MEA) and live mouse tracker (LMT) to test novel compounds and repurposed drugs.

MEA: On this platform, cultured mouse neurons will be used for electrophysiological recordings of neuronal networks. Drugs can be added on a daily basis, and changes in the measures can assess the drugs.



LMT: Standard behavioral test batteries will be replaced by a single live mouse tracker recording. This tracker can assess 35 different behaviors of four mice from a single 24-hour recording, providing a powerful first look at a drug's effectiveness.

This team is collaborating with Kantify, which will use their **high-tech AI-based algorithms** to screen for drugs targeting pathways involved in Fragile X and the most efficient drug combinations. They will use their platform to prioritize combination therapies and novel drug screenings.

1998

FRAXA launches first **Fragile X website** on the internet.

1998

Randi Hagerman, MD, receives **FRAXA grant for clinical trial of melatonin** to help Fragile X syndrome patients sleep.

1998

First of three Nobel Laureates joins FRAXA's **Scientific Advisory Board** (James Watson, MD).

1999

Flora Tassone, PhD, and Paul Hagerman, PhD, discover cause of **FXTAS** (increased FMR1 mRNA) while working on a **FRAXA grant**.

Fundraising Highlights

Patrick's PALS, Cambridge, MA

Patrick's PALS is the longest-running FRAXA fundraiser, having raised around \$2 million for Fragile X research in their 26 years!

Patrick's parents, James & Pamela Vershbow, and their amazing team of volunteers tempt new and returning participants to the courts.

The Patrick's PALS 3-on-3 basketball competition began in 1997 as a twelve-team tournament and has expanded greatly since then, including sons and daughters of the original participants.

This full-day event is jam-packed with activities for both participants and spectators, all while earning funds for Fragile X research. Breakfast, lunch, a silent auction, raffles, and contests such as a three-point shootout and a half-court shot challenge are all part of the day.

It's not only the winning team who is recognized. Every year, awards and recognition are given to the hardworking volunteers who are essential to the success of this remarkable event.



Contact Jim Vershbow
(patrick.pals@comcast.net) to join the fun at Patrick's PALS or for tips on how you can run a similar event!

JT's Ice Cream Lancaster, PA

The Sardina family reminds us that fundraising can be delicious with their JT's Ice Cream for FRAXA fundraiser. In its first two years, they have raised over \$25,000 for Fragile X research!



Erin Sardina and her husband, Tom, learned about FRAXA shortly after their son was diagnosed with Fragile X syndrome at 13 months old. As an occupational therapist, Erin knew early on that JT had developmental differences. After receiving the Fragile X diagnosis, Erin and Tom delved into research and discovered FRAXA. Raising money for FRAXA gives them satisfaction, knowing they are doing everything they can to help pave the way for their son's future.

The annual event is attended by members of the local community, the Sardina children's teachers, coworkers, and out-of-state family and friends to raise money for FRAXA in JT's honor. Tom and Erin's daughters approve of this yearly fundraiser, letting everyone know that getting to eat ice cream for lunch and dinner is a pretty awesome treat, especially when your dad is a dentist!



Contact Erin Sardina
(metze49@gmail.com) for information on how you can run a similar event!

Celebrating 29 years of Outstanding Research

1999

Eric Kandel, MD, becomes the first Nobel Laureate to conduct Fragile X research, with a **FRAXA grant**.

1999

FRAXA organizes and hosts the first annual Fragile X Banbury Research meeting. These meetings, held every year through 2011, spawn many discoveries and trials.

2000

Children's Health Act of 2000 creates and funds 3 research Centers of Excellence.

2000

First Fragile X Awareness Day established by US Senate.



Callum Cup Millburn, NJ

Andrew Murphy and his friends have raised over \$94,000 for Fragile X research since their first Callum Cup in 2016!

The Callum Cup, an annual intra-club charity soccer tournament, is the highlight of the Millburn Football Club calendar. The game honors Callum Murphy, son of goalkeeper Andrew Murphy, who has Fragile X syndrome.

The Callum Cup was first conceived in St. James's Gate Publick House, often known as "The Gate," where festivities after games are still held every year. The Callum Cup is kept at The Gate, always on display behind the bar.

Andrew Murphy and his wife Amanda have kept up with every discovery since becoming a part of the Fragile X community in 2007. Believing that research is the key to success, they have done everything in their power to support FRAXA's work.

For more information on how you can run an event, contact Andrew Murphy at glasfurd31@gmail.com.



Swirl Wine Tasting Naples, FL

Dinner, wine, and friends with a silent auction on the side are the ingredients for a successful Swirl Fundraiser. Debra and Kevin Fennessey along with their good friends, Ginna and Pidge Goodrich and Jill and Jeffrey Kelley have hosted two remarkable Swirl events, raising over \$130,000 for Fragile X research in just two years!

The Fennesseys' son, Edward, spoke frankly to guests about how Fragile X impacts his son, Jackson. He shared the challenges he and his wife, Avalon, face every day and their hopes for the future as research moves forward. The attendees, many of whom had never heard of Fragile X before the event, were captivated as Edward talked about his son. People read the FRAXA materials with interest and grew enthusiastic about the hope of a cure.

Jackson, 6, was in attendance this year and happily mingled among guests as the person of honor.

The Fennesseys look forward to this annual event and hope that it can provide a model for wine tasting fundraisers in other parts of the country.

For more information contact Holly Roos at hroos@fraxa.org.



2000

With FRAXA funding, Mark Bear, PhD, and Kim Huber, PhD, formulate the **mGluR theory of Fragile X**.

2001

With a FRAXA grant, Robert Darnell, MD, PhD, and Jennifer Darnell, PhD, discover and publish list of targets of FMRP with FRAXA grant.

2002

FRAXA funds **first clinical trial of an investigational new drug** (a smart drug, Ampakine) by Elizabeth Berry-Kravis, MD, PhD and Randi Hagerman, MD.

2005

FRAXA funds Clinical trial of the available drug lithium by **Elizabeth Berry-Kravis, MD, PhD**.

A FEW OF OUR RECENT FUNDRAISERS *Thank you!*



Hall Golf Tournament

Haverhill, MA

Brothers Pete and Dave Hall host an Annual Charity Golf Tournament. For the fifteenth consecutive year the money raised has gone to FRAXA, raising over \$262,000 for Fragile X research!



Poker Run

Sparta, NC

For over 15 years the Charlton Family has hosted their annual Poker Run. Over 100 motorcycles travel through 4 states along the Blue Ridge Parkway raising money for FRAXA.



Walk & Raffles for Fragile X

Derry, NH

Fragile X grandparents Darlene and Pat Donovan host an annual Fragile X 5K in honor of Elias. With the support of family, friends, and the community, raffles top off this great event.



Boston Bruins 50/50

Boston, MA

Each year the Boston Bruins Foundation invites FRAXA to host a 50/50 raffle with all proceeds going to fund Fragile X research. FRAXA is proud to partner with the Bruins!



VLM Company Match Week

New York, NY

Fragile X father Lou Barbera and his partners at VLM Commodities challenged staff and clients to donate their earnings to Fragile X research, raising \$10,000 in 1 week!



3 Peaks Challenge

North Wales, UK

Fragile X father Michael Leonard and his friends climbed the peaks of the United Kingdom's 3 highest mountains: Ben Nevis in Scotland, Scafell Pike in England, and Snowdon in Wales—all in 24 hours! Michael saw taking on the 3 Peaks challenge as an ideal opportunity to raise funds for FRAXA in honor of his son, Cole.



Flatbread Fundraiser

Amesbury, MA

This family-friendly fundraiser brought one family over 3 hours to meet others with Fragile X (and enjoy delicious pizza!) It was a tasty event filled with laughter and new friendships.

Celebrating 29 years of Outstanding Research

2005

Roche, Novartis, and Seaside Therapeutics all join the Fragile X syndrome field, hunting for mGluR antagonists to treat Fragile X.

2007

Doris Buffett Challenge "The sky is the limit!" Unlimited matching gift challenge enables FRAXA to double Fragile X research funding.

2010

New York Times front page reports success of first Novartis trial, features FRAXA. Bloomberg News and NPR also cover the story.

2011

FRAXA-DVI funded to provide a standard platform to test potential treatments using mice. Goes on to complete preclinical testing of 100+ compounds.

MEET OUR Donors

Robert & Ardis James Foundation

An introduction from longtime FRAXA family friend and advocate, William (Ted) Truscott, laid the groundwork for a strong partnership between FRAXA and the Robert & Ardis James Foundation that is propelling Fragile X research forward.



Robert G. James and Ardis (Butler) James

Ardis (Butler) James grew up in Lincoln and Omaha, Nebraska and married Robert G. James of Ord in 1949. In leading the foundation that bears their parents' names, the James children seek to support causes that will honor their parents' passions.



Ralph James

Siblings Ralph and Cathy James have long supported numerous nonprofits and educational institutions through their family foundation. After meeting with Ted Truscott, they were invigorated by what they saw as FRAXA's "thoughtful, well-executed philanthropy at work."

The FRAXA community is grateful to and energized by people like Cathy James, Ralph James, and Ted Truscott who — while not personally impacted by Fragile X — understand that the work we do now will also advance treatments for individuals living with autism and intellectual disabilities beyond Fragile X syndrome. This trust and understanding drives us to succeed.

Mary Higgins Clark

Best-selling author Mary Higgins Clark, known as the 'Queen of Suspense', had a knack for keeping readers up late into the night, eagerly turning the pages. She was also a tireless champion for Fragile X research in honor of her grandson, David Clark, who lives with Fragile X syndrome.

Mary put FRAXA on the map in 1997 when she made a 1 million dollar donation over five years to solve, as she said, "the mystery of Fragile X syndrome" in her grandson, David's name. At a time when FRAXA was just a few years into operations, her support was an enormous boost to the entire Fragile X community.

Over the next decade, Mary traveled around the country, appearing at FRAXA fundraising events in Boston, New York, Washington DC, Chicago, Pittsburgh, and Newport Coast, CA. At every event she loved to talk with everyone and share wonderful stories about her grandson, brimming with love, pride, and sparkle.

The passion for FRAXA's cause runs deep in Mary Higgins Clark's family, and it shows in their active involvement in the foundation. Mary's husband, John Conheeney, their children, Dave Clark, Carol Higgins Clark, Judge Marilyn Clark, and Warren Clark, as well as granddaughter Elizabeth Clark and her mother, author Mary Jane Clark, have all been inspired by her commitment to the cause.



Mary Higgins Clark

Mary was a member of FRAXA's Honorary Board. After Mary's passing in January of 2020 at the age of 92, the Mary Higgins Clark Foundation continues to support FRAXA's efforts on behalf of her grandson, David, and everyone living with Fragile X worldwide.



Mary Higgins Clark with Michael Tranfaglia and Katie Clapp, FRAXA Co-Founders



Mary Higgins Clark with the Shelly sisters

2015

FRAXA starts working with Tetra Therapeutics to test their PDE4D inhibitor for Fragile X. **PDE4 inhibitors** are also potential treatments for Alzheimer's.

2016

First use of AI in Fragile X. FRAXA funds Healx to use Artificial Intelligence to identify the most promising available drugs to treat Fragile X.

2019

FRAXA launches **collaboration with Purposeful**, a drug repurposing company based in Athens, Greece, to develop Fragile X treatments.

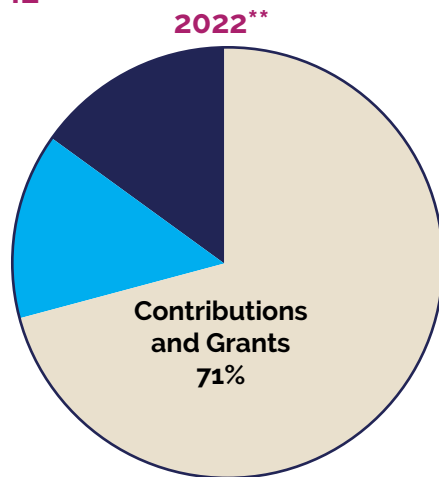
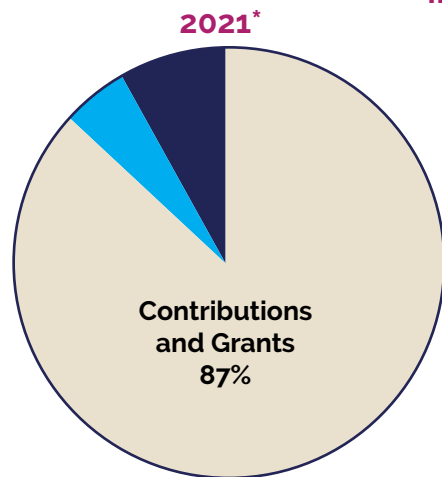
2020

FRAXA-funded Phase 2 **Tetra trial**. PDE4 inhibitor reports positive results: improves cognition significantly.

FINANCIAL Highlights

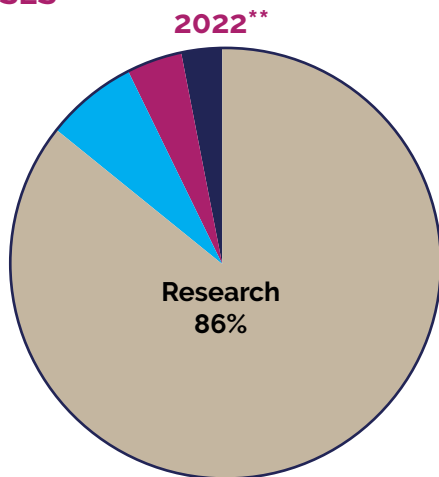
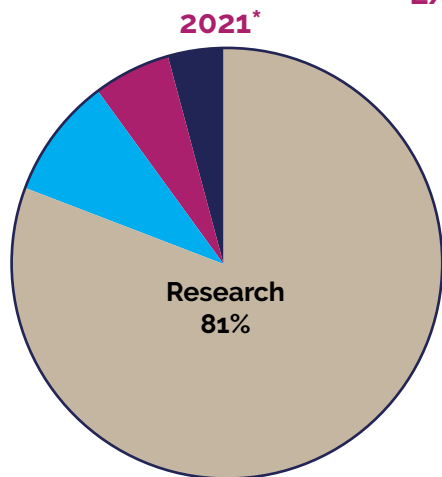
FRAXA recognizes the responsibility that comes with your contribution and is proud to be continually recognized as one of the most reliable stewards of donor gifts. We earn the highest possible marks from major nonprofit rating agencies. Please visit fraxa.org/about for more information.

INCOME



FRAXA's funding comes from individuals and organizations who believe in our mission. We receive no government funding.

EXPENSES



FRAXA's priority is research, with over 80% of our budget supporting research grants and clinical trials — even during the pandemic! Over 90% of FRAXA's funding goes directly to our programs.

INCOME

	2021*	2022**
Contributions and Grants	1,915,294	1,539,712
Fundraising Events	116,223	214,258
Interest & Investment Income	165,723	-222,495
Total Revenue and Support	\$2,197,240	\$1,531,475

EXPENSES

	2021*	2022**
Research	1,126,798	1,629,831
Education	124,390	138,551
Fundraising	85,498	72,858
Administration	57,958	56,623
Total Expenses	\$1,394,644	\$1,897,863

ASSETS

	2021*	2022**
Change in Net Assets	802,596	-366,388
Net Assets - Start of Period	3,099,475	3,902,071
Net Assets - End of Period	\$3,902,071	\$3,535,683

*2021 Audited financial statements and 990s can be found at fraxa.org/about

**2022 numbers are unaudited and preliminary



Celebrating 29 years of Outstanding Research

2020

FRAXA-DVI successfully tests available medicines predicted by Purposeful to be effective for Fragile X.

2021

FRAXA launches **World Fragile X Day** to celebrate individuals affected by Fragile X and their families, and to raise awareness worldwide.

2021

FRAXA funds clinical trial of ergoloids/5-hydroxytryptophan combination predicted by Purposeful and validated in the mouse model by FRAXA-DVI.

2021

FRAXA passes the \$30 million mark in direct research funding.

HOW YOU CAN HELP FRAXA

Ways to Give

Help Advance Fragile X Research

Donating to FRAXA Research Foundation accelerates groundbreaking research to find effective treatments and ultimately a cure for Fragile X.

"FRAXA lives and breathes its mission to help the Fragile X community through funding cutting-edge research. I know when I support and donate to FRAXA, they will be excellent stewards of my contributions. The research they are funding will ensure a bright future for my son."

Sara Hamilton, parent, Missouri



Donate Online
fraxa.org/donate

Mail Donation

FRAXA Research Foundation
10 Prince Place, Suite 203
Newburyport, MA 01950-2657

Recurring Donation

fraxa.org/monthly

By becoming a monthly donor to FRAXA, you can support families affected by Fragile X syndrome and make a significant impact with a small monthly gift.

Company Matching Gift

Maximize the impact of your donation by checking if your company offers a matching gift program. By donating to FRAXA, you may be able to double your contribution thanks to your employer's matching gift.



2022

FRAXA funds collaboration between Kantify, an Artificial Intelligence company, and Frank Kooy, PhD, lab to build new drug testing platform in Belgium to evaluate Fragile X treatments.

2023

Last subject completes *ergoloid/5-HTP* combination trial (results soon!)

2023

FRAXA hosts special Banbury meeting to discuss breakthroughs in gene reactivation and gene therapy for Fragile X.

2023

Large phase 3 clinical trials are recruiting participants for *Tetra's PDE4D inhibitor* and *Zynerba's CBD gel*.

"Now there is an industry-wide pipeline of programs in development across many companies. It is a simple truth that without FRAXA, this would not be the case. The initiatives FRAXA has in place have been, and continue to be, crucial to this critical mass of effort to find new options for people with lives touched by Fragile X."

Michael Snape, PhD, AMO Pharma, Ltd



"It's hard to overestimate the impact of FRAXA in advancing Fragile X research toward treatments. From the get-go they were unwilling to accept defeat."

**Mark Bear, PhD,
Massachusetts Institute of Technology**



"FRAXA Research Foundation has been a light for us. I have a son with full mutation Fragile X, and FRAXA's nonprofit not only works hard to fund finding a cure, they also connect families through social media posts, raise awareness, and make families like mine feel not so alone in this fight. They are amazing!"

April Godwin, parent, Alabama



"FRAXA has given our family so much hope. We've reached out to their leadership for advice about medications and research trials. We are enrolling our teenage son in one and really excited about its potential. FRAXA helped designed this trial and funded its early phases. If they hadn't built relationships and expertise like they have, we wouldn't have access to groundbreaking studies like this. We are so excited."

Jennifer Frobish, parent, Missouri

WHY WE SUPPORT FRAXA?



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