Barth Syndrome Foundation®

How We Did It

Family Voices & Scientific Data Win Approval for First Barth Treatment

And other news from the Barth Syndrome Foundation, 4th Quarter, 2025

For families affected by Barth syndrome, waiting is a constant part of the experience: waiting for answers, waiting in emergency rooms, waiting to recover from debilitating exhaustion, waiting for treatments that might give their loved ones a chance at life.

But our community doesn't just wait.

We act.

This year, your support helped achieve something remarkable: regulatory approval of the first treatment for Barth syndrome and the first mitochondrial treatment of its kind.

This story is about more than one treatment approval, but it starts here:

Over a decade ago, researchers developed elamipretide, now trademarked as FORZINITY™.

Our Executive Director, Emily Milligan, hugs Kevin W. following a meeting with American health officials.

The drug's science made sense. It fixed the broken machinery in the cells caused by Barth syndrome so the body's cells could produce more energy.

And the treatment worked.

In clinical trials (research studies

with people), most patients with Barth syndrome gained muscle strength — a result that meant participants could play with their friends, climb stairs, or work jobs.

Participants' lives changed.

The science was strong.

The data was positive.

Yet we faced an unexpected challenge.

Typically, American health regulators look for evidence that a drug works for thousands of people before they approve it for the public.

If a drug works for thousands of people, they can be reasonably confident it will work for hundreds of thousands more.

But there are fewer than 150 living individuals in the United States with Barth syndrome and fewer than 300 confirmed cases across the globe.

Regulators examining data from large disease communities can rely solely on math and statistics to interpret evidence. For the Barth community, that wasn't possible.

We had to show leaders a different way to interpret the evidence.

This is a story about how we helped officials understand that with strong science, compelling data, testimonies of real improvements in daily living, and few other options, our small community deserved access.

It's about how a handful of committed people took on processes that weren't built for them and won.

It's about how your time, generosity, and advocacy created tangible change for families with Barth.

This is how we did it.

Understanding the Stakes

We need to zoom in to a microscopic part of your cells: the mitochondria.

The mitochondria are like factories that turn nutrients into energy.

In someone with Barth syndrome, mitochondria don't function properly. They can't produce the energy needed for the body's cells.

The results are often life-altering and devastating.

Hearts struggle to pump effectively. Crushing fatigue is common. Immune systems are weakened. Feeding and digestion are difficult. Historically, many

Our Director of Research, Dr. Lindsay Marjoram, PhD, and Board Member, Steve Graessle, in Washington D.C. to advocate for the community.

children with Barth died by age three from heart failure or infection.

Today, improved diagnosis and management offer some children brighter futures, but many babies born with Barth syndrome still don't survive to become adults. Adults with Barth commonly face progressive and life-limiting symptoms, the constant threat of medical crises, and early mortality.

> "I just want to live as normally as possible."

Although in some cases Barth syndrome appears spontaneously in the womb without prior family history, it is usually passed from parents to children.[1]

One mother, Kristi P., described, "This disease doesn't just impact the child. It devastates entire families — financially, emotionally, generationally. My grandmother buried both of her sons. I have a nephew and a cousin with Barth. This is our family history."[2]

While the disease may be ultra rare, the worries and hopes of the families affected are universal.

They want their kids to play with friends, dream about the future, and grow into strong adults who live vibrant and full lives.

"I just want to live as normally as possible," Jacob W., who is now 24, said. "I want to have kids. I want to have a life."[3]

The Barth Syndrome Foundation (BSF), the first and only advocacy organization solely established for those affected by Barth syndrome, champions a robust pipeline of treatments. A "typical" individual with Barth really doesn't exist. Because Barth syndrome affects multiple systems in the body, a single therapy may not offer improvement for everyone or for every aspect of the disease.

Our hope is that every individual

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BSF Is Building a Robust Portfolio of Treatments

Families living with Barth syndrome deserve access to multiple approved, effective, and safe therapies.

The drug development process has five main stages, and they all require funding, time, and advocacy. Here's a short summary of treatments currently in development.

Discovery Research and Preclinical Research

BSF is currently watching or engaged in:

- ABHD18 inhibitors (Jason Moffat, Sick Kids, Toronto; Scenic Bio, Amsterdam; Mindong Ren, New York University): Restores mitochondrial function by inhibiting ABHD18 and preventing toxic buildup of monolysocardiolipin, the primary consequence of TAFAZZIN mutations in Barth syndrome.
- TAFAZZIN Gene Therapy (Barry Byrne, University of Florida; Bill Pu, Boston Children's Hospital; Michael Chin, Tufts University; Jim Wilson, Gemma Bio): Gives TAFAZZIN protein back to the body; would be a 1x infusion-based treatment
- Myotropes (Leo Ferreira) and MA-5 (Takaaki Abe, Japan): Medicines that increase energy output of cells, most likely in the form of daily pills

Clinical Research

Treatments listed below are either about to start or are already in the clinical stage. BSF has supported their efforts financially, as a thought partner, or both:

- Nicotinamide riboside (Riekelt Houtkooper, Amsterdam): Medicine that increases energy output of cells. Would likely be a daily pill.
- XOLREMDI / mavorixafor (X4 Pharma): Medicine that increases the number of neutrophils to improve immune system function. A once-daily pill.

Approval and Post-Approval Monitoring

As our community learned with elamipretide, approval often requires sustained advocacy, family testimony, and demonstration that patient experiences constitute valid evidence alongside traditional statistical data. Even after approval, we must continue to invest resources in ensuring and expanding access and helping families navigate financial and healthcare concerns.

Today, FORZINITY is the only FDA-approved treatment for Barth syndrome, although the current approval includes only about half of those with the disease due to the weight requirements.

The Drug Approval Process

1	Discovery Research	Researchers identify promising drugs and study how they work.
2	Preclinical Research	Laboratory and animal testing address FDA concerns about safety, dosing, and side effects before human studies begin.
3	Clinical Research	Under FDA guidance, researchers study drugs' effects on people over many years to ensure they are safe and effective for their intended use.
4	FDA Review & Approval	The FDA examines all submitted data related to the drug and decides whether to approve it for commercial use.
5	Post-Approval Monitoring & Access	The FDA monitors drug safety. FDA labeling requirements, insurance issues, or a lack of physician awareness may still limit access.

Continued from page 3

will one day have access to multiple therapies, allowing them to live long, full lives.

Looking for a Future in Science

With this mission in mind, we began working with Stealth BioTherapeutics (Stealth), a biotechnology startup focused on mitochondrial diseases, in 2014.

Stealth was developing a drug called elamipretide, now called FORZINITY.

Early research suggested the drug was generally very safe and the mechanism of action (the way the drug works) showed promise for our community.

Scientific research confirmed that the treatment targets a core problem in Barth syndrome and improves the

Families Share Their Experiences in a 2018-2019 Report for the FDA[7]

"What I wish I could do: Work full or part time in a career. Take classes if needed for said career. Do more than one activity a day without having to rest after. Have the stamina to play actively with my niece; and have the energy to do normal everyday things without being exhausted."

"I've been plagued with this fatigue all my life and for any new treatment to have any positive effect, that's the aspect it needs to tackle—something to improve my ability to do things I love to do in life so I can spend the day or even an afternoon working and out with friends and not have to suffer."

"As a mother who has lost two children, I want more moments."

structure of mitochondria, therefore increasing their ability to produce energy for the body.

A Pivotal Clinical Trial

One of the most critical parts of the scientific process is collecting evidence about how a treatment works with real people.

So Stealth launched a pivotal clinical trial called the TAZPOWER study in 2017.

This study included 10% of all the known, US-based individuals with Barth syndrome, a remarkable contribution from our tiny community, since many members were excluded due to their age or having had a heart transplant or an implanted internal defibrillator.

The study results were encouraging across multiple measures: hearts pumped more blood, muscle strength improved, and patients reported meaningful changes in their daily lives.

"It changed my life completely," one participant, Walker B., said. He continues on the therapy today. "I wasn't just existing — I was finally living. Because of the drug, I'm able to live the life I could only dream about before."[4]

Importantly, research continued to indicate that elamipretide is low risk. Data came from both Barth patients and large studies in non-Barth individuals.

The Challenge of Drug Approval for Ultra-Rare Diseases

For any drug to become commercially available to Americans with Barth syndrome, it needs to be approved by the United States Food and Drug Administration (the FDA).

The FDA, drug developers like Stealth, and BSF all want the same thing: safe and effective therapies for the families who need them.

However, FDA review processes are generally designed for treatments affecting large numbers of people. The FDA typically demands multiple phases of clinical trials involving increasing numbers of participants, from hundreds to many thousands.

These large studies allow regulators to look for mathematical evidence to indicate if a drug is definitively effective. If regulators see that a drug is safe and effective for several thousand people, they can be reasonably confident the

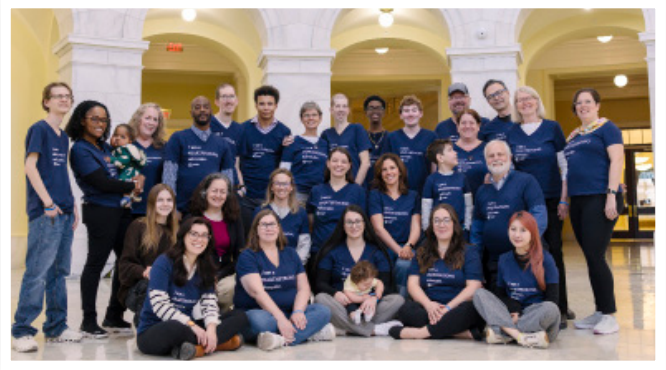
drug will be safe and effective for the whole group, possibly hundreds of thousands of people. This data collection can take 12 to 15 years.

But what if there aren't thousands of people suffering from a disease?

What if a community of fewer than 150 people could never meet the requirements of processes designed for large populations?

Our challenge wasn't the science — it was solid and promising. The science was the basis of our advocacy. Congress had even established an approval pathway for cases like ours.

Whether they approved the drug or not, we needed the FDA to act from a deep understanding of the realities of our community.



A group photo of our advocates during Rare Disease Week.

Jacob W. and his family at the 2024 Barth Conference.

Our Solution: Listen to Families

We believe that when the science is strong but mathematical certainty is impossible, the answer shouldn't be to reject the treatment.

The answer is to listen to families.

The newfound ability of many people in the clinical trial to run, play, work, live full lives — those weren't just anecdotes.

They were evidence.

"In ultra-rare diseases without an adequate, approved, and available therapy, a 'totality of the evidence' approach needs to be taken," Dr. Emil Kakkis, Ph.D. wrote in an article for STAT on October 9, 2024.

Or in the words of Jacob, a young adult with Barth, "I know doctors have all

these degrees, but I know my disease. I know what works. And I know I deserve a chance."[5]

We Mobilize the Community

The Barth Syndrome Foundation has a history of taking action.

In July 2018, we hosted the first FDA off-site Externally Led Patient-Focused Drug Development Meeting as part of our biennial international conference.

The turnout was extraordinary. More than 25% of the world's Barth community was represented. Twenty-two individuals living with Barth and 182 caregivers attended, many of them in person. They came from 12 countries.

> "I know my disease... And I know I deserve a chance."

Our volunteers and staff centralized the family feedback into reports, testimonials and later, petitions, that we could submit alongside clinical trial data.

For the next three years, while more data was being accumulated, we continued to educate FDA officials on the realities of small disease communities even as the pandemic shuttered much of the world.

We hosted listening sessions so regulators could hear from families directly, ran a half-day FDA workshop on Barth syndrome and rare-disease regulatory challenges, and launched a community petition that collected thousands of signatures.

We were preparing regulators — and our community — for success.

Years of Setbacks and Persistence

In 2021, Stealth submitted elamipretide's first New Drug Application (NDA), the formal process required to request approval.

This massive and costly application compiled all the data that Stealth had obtained from the trial, including the outcomes our families had experienced, formalized into the Barth syndrome symptom assessment.

Unfortunately, we then faced years of setbacks and unnecessary delays.

Between 2021 and 2025, the FDA declined to review the drug application, asked Stealth to find more patients, and demanded additional trials and application resubmissions.

Regulators wanted data that would meet mathematical and statistical standards achieved by studies with large populations.

It was impossible.

While the FDA insisted on unattainable thresholds, our children were dying.

Families struggled. Financial pressures threatened Stealth's survival, even risking trial participants' continued access to elamipretide.

And yet, our community persisted.

During the setbacks from the FDA, your support powered our advocacy on multiple fronts:

- We launched public campaigns to raise visibility of our predicament, including hand delivering a petition to the FDA with nearly 20,000 signatures at the end of 2023 after bureaucratic delays.
- We mobilized support from Congress, with our advocates holding hundreds of meetings on Capitol Hill and virtually to educate regulators about the plight of those with Barth syndrome and other ultra-rare diseases and to urge timely action. We recognized 16 members of Congress for their unwavering advocacy as Champions of Progress.[6]
- Our physicians exerted consistent pressure during setbacks, collaborating on three different expert physician letters requesting accelerated access.
- We fought for more effective regulatory processes specific to ultra-rare diseases, collaborating with the FDA in a 2022 workshop to establish Barth-specific regulatory pathways and advocating for accelerated approval pathways that fit our data and needs and the use of pathways already established by Congress.
- We continued highlighting families' real-life experiences to health officials, bridging the knowledge gap between families and regulators.
- We created strong, agile, advocacy-focused relationships

among our families by hosting consistent calls, ensuring our families were updated and could pitch in with their talents.

Our community did not do this work alone.

We are grateful to peer organizations like the EveryLife Foundation for Rare Diseases, the United Mitochondrial Disease Foundation, MitoAction, the PoIG Foundation, and many other individuals for their partnership.

The Breakthrough

Our persistent education paid off.

On September 19, 2025, the FDA granted accelerated approval to FORZINITY as a treatment for Barth syndrome for individuals weighing more than 30 kg or 66 pounds.

If the drug is accepted for coverage by their insurance companies, Barth syndrome patients will finally have access to a treatment that proved life-changing in clinical trials.

What The Approval Means

The approval recognized the strong scientific foundation, the positive data

results, and our families' experiences.

Where traditional statistical methods (designed for studies with thousands of participants) couldn't provide complete certainty, our families' experiences helped regulators understand the data they had.

Our community's experience will serve as a foundation for other ultra-rare groups. In a complex

Where the science is strong but the data is too small to provide complete certainty, the lived experiences of patients and families can make decisions more clear for regulators. This is especially true in situations like ours when data demonstrate the drug is safe.

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the lived experiences of patients and families can make decisions more clear for regulators. This is especially true in situations like ours when data demonstrate the drug is safe.

The approval was its own type of evidence: a small number of transformed lives are meaningful evidence.

The voices of our community matter.

Our Work Continues

We celebrate this very important success. But our work isn't finished.

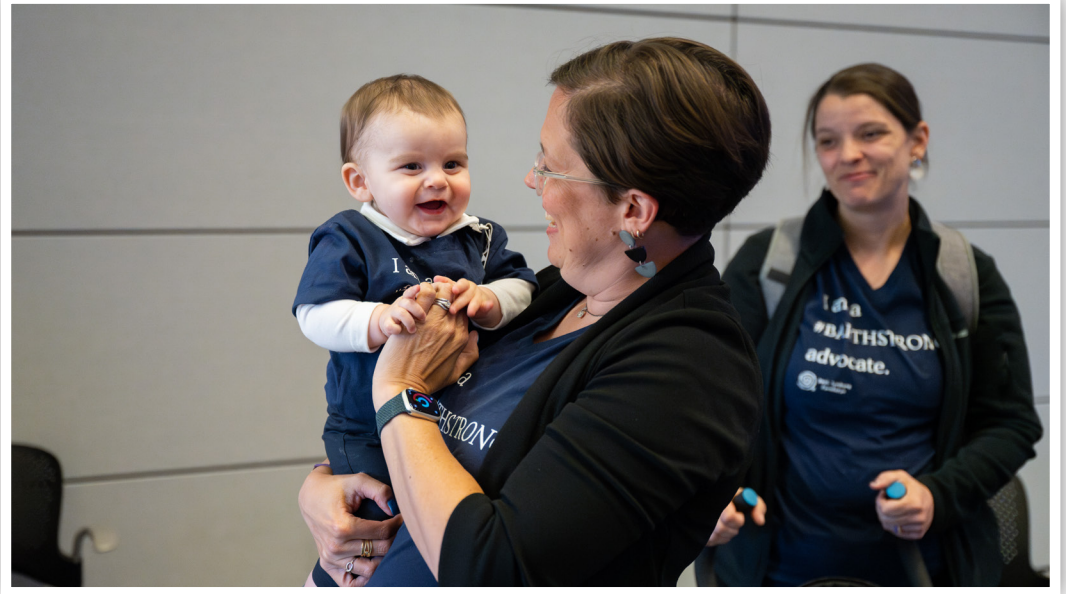
We hope for a world where all Barth individuals have access to multiple safe, effective, and affordable therapies.

We need the drug label to be expanded to younger ages and ultimately for approval to be granted in other geographies.

We will continue to push for post-approval processes that reflect our realities, for affordable access to treatment for our families, and for a robust pipeline of treatments.

As we advocate for the futures of all people with Barth syndrome, we look back with pride and immense gratitude.

"This achievement belongs to our families," Emily Milligan, Executive



Dr. Lindsay Marjoram, PhD enjoys a moment with the Enroughty family after an FDA committee meeting.

Director of the Barth Syndrome Foundation, says. “They refused to accept that being ultra rare means being overlooked. Together, we proved that a tiny community’s truth can change a system built for thousands. Lived experience must shape drug development for every rare disease. That’s what we are building, together.”

You proved that hope isn’t as rare as Barth is. Small communities power big movements. Family voices save lives.

This is how we did it.

And this is how we’ll continue.

Your donations make this possible.

Give today

Thank you for your generosity!

How You Can Get Involved

Your involvement makes a real difference for the rare disease community. Here's how you can support our work:

Volunteer with us

Our volunteers help in a range of ways: writing to policymakers, organizing our conference, raising awareness or funds in their community, engaging with the press, and coordinating programs. Whatever you're good at, your support is valuable!

Participate in clinical trials and research studies

Clinical trials move us from promising research to accessible treatments. With such a small number of people diagnosed with Barth syndrome, every individual who volunteers for clinical trials makes a critical difference. BSF's biennial international conferences offer opportunities to participate in research studies as well as enroll in or update the registry.

Wear the swag

Raise awareness about Barth syndrome and show you are #BARTHSTRONG by purchasing, giving, or wearing our swag.

Share your story and raise awareness

Use your voice on social media, in your community, and with your networks to educate others about Barth syndrome, especially during Rare Disease Week or Barth Syndrome Awareness Day, and help us amplify the experiences of those living with Barth.

Get involved

(click here)

It's the GivingTuesday Season

Our GivingTuesday campaign continues! GivingTuesday is a global movement to make the world a better place. While GivingTuesday itself was December 2, we continue our fundraising through the end of the year.

Your donations power:

- Advocating for broad and inclusive FORZINITY™ approval and access for all who need it
- Educating public and private payers about the Barth lived experience to ensure drug coverage
- Planning our 2026 International Family, Scientific and Medical Conference and providing financial assistance to families who want to attend but cannot afford to do so
- Supporting the entire pipeline of potential therapies so individuals can live longer and fuller lives
- Raising awareness about our rare disease community with the public, lawmakers, payers, and regulators

Whether you contribute $5 or $5,000, every single dollar moves us closer to more answers, more treatments, and more time for families.

Thank you for your generosity!

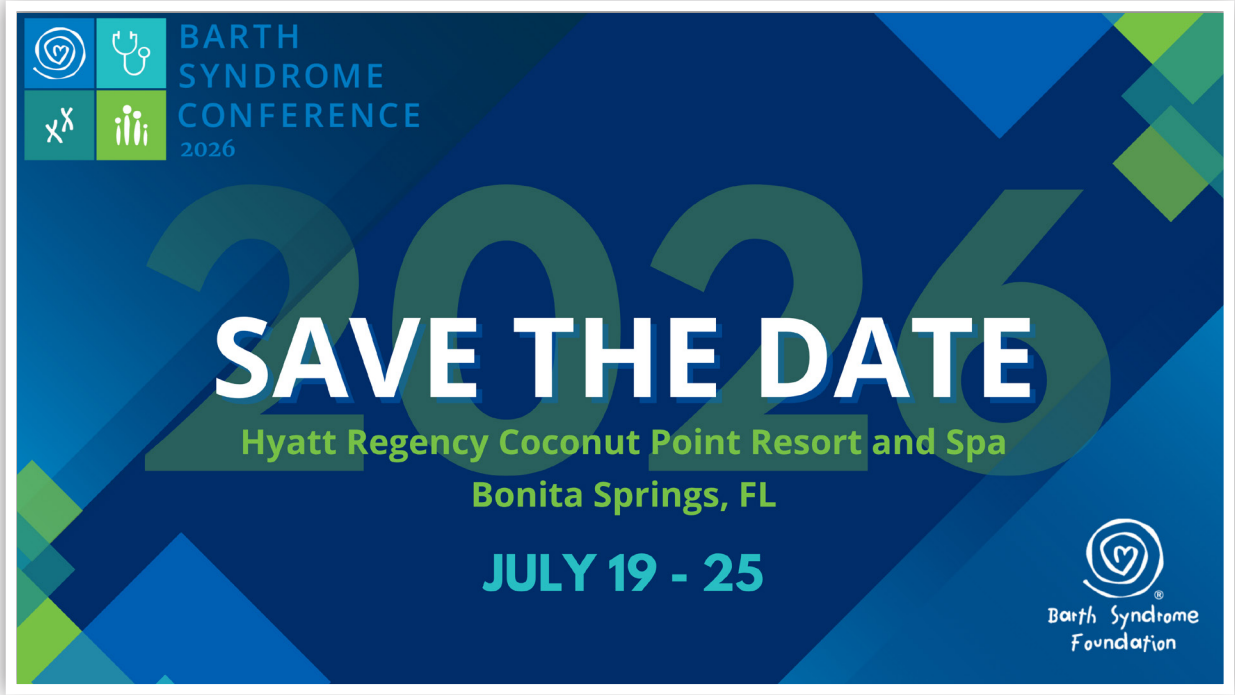
Be part of the giving season

(click here)

Join Us for Our 2026 Conference

Our 2026 Biennial International Scientific, Medical, and Family Conference is a unique and vital opportunity that brings together the entire Barth community — patients, researchers, caregivers, health care professionals, and regulators — to advance Barth syndrome research and reinforce our dedication to affected individuals and the community.

With multiple tracks tailored to healthcare providers, researchers, caregivers, and affected individuals, this event fosters collaboration and innovation within the field.



Executive Director's Note
Emily Milligan

I'm writing to you today with profound gratitude and pride.

The first FDA approval of a treatment for Barth syndrome is a success that belongs to every affected individual who participated in the clinical trials, every patient or family member who shared their story, every weary traveler who visited Capitol Hill, every donor who funded trials and advocacy, and every person who amplified BSF's mission on social media.

You made this possible.

And our work continues with urgency today. We listen to our families and respond in real time to what they need.

We must set our community up for success with FORZINITY (elamipretide) and future treatments.

This means educating insurance companies and payers to cover the costs so eligible families can access the drug.

This means participating in or supporting studies that are required by the FDA to confirm previous trials' results.

This means doing our best so that every person with Barth syndrome, regardless of weight or age, who can clinically benefit from treatment can access it.

Beyond this treatment, we must work hard for the next generation of therapies. We work toward a world where families can access multiple safe and effective options.

As we approach year end, we hope your winter includes spending time with those who mean the most to you. You mean so very much to us.

Thank you for everything you do.

Emily Milligan, Executive Director

References

You'll find references from this newsletter below.

1 You can read more about Barth syndrome at www.barthsyndrome.org/barthsyndrome.

2 Read Kristi's story in "Mississippi's Heartbeat: One Mother's Mission to Keep Her Son Alive", published on May 13, 2025, on www.barthsyndrome.org/newsevents

3 Read Jacob's story in "A Life Measured in Milligrams", published on May 20, 2025, on www.barthsyndrome.org/newsevents.

4 Read Walker's story in "The Drug That Gave Me My Life Back", published on May 20, 2025 on www.barthsyndrome.org/newsevents.

5 You can read about the Champions of Progress on our website at www.barthsyndrome.org/article/2025/03/05/barth-syndrome-foundation-recognizes-congressional-champions-of-progress-for-rare-disease-advocacy.

6 Read Jacob's story in "A Life Measured in Milligrams."

7 You can read the report, "The Voice of the Patient: Barth Syndrome", on ourwebsite at www.barthsyndrome.org/advocacy/pfdd/voiceofthepatient.html

Thank you
for everything you do
for our community!

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