2024

Rett GAZETTE

Accelerating Research.
Empowering Families.

MECP2: The discovery that *changed* everything

International Rett Syndrome Foundation

Transforming Lives Every Day

As I reflect on the incredible strides made since our last issue, I am incredibly proud of what we have accomplished together in our fight to transform the Rett syndrome landscape. IRSF's mission is fueled by a commitment to funding trailblazing research and empowering support — and we continue to deliver results.

This year has been marked by significant advancements. We've seen the launch of two gene therapy clinical trials — offering us real hope for future transformative treatments. Today, more than 20 companies are actively developing treatments for Rett syndrome — a milestone that not too long ago seemed impossible.

IRSF's comprehensive scientific enterprise, strengthened by powerful partnerships, continues to lead the way in pursuing both genetic and non-genetic approaches in the treatment of Rett syndrome. We are funding 25 active research projects worldwide and are preparing to award our next wave of grants, continuing our commitment to support ALL innovative ideas that push our understanding of and treatment for Rett forward.

Our network of Center of Excellence clinics has expanded to 21 locations, delivering best-in-class care for individuals with Rett syndrome across the country. IRSF's rapidly growing Rett Syndrome Registry™ now includes over 800 participants and continues to provide essential data to guide new treatments. Our newly published *Comprehensive Care Guidelines* are deepening partnerships between caregivers and healthcare providers — ensuring that individuals with Rett receive the highest standard of care.

And we came together to support one another at the ASCEND 2024 Rett Syndrome National Summit. It was an honor to join over 200 expert researchers and clinicians who walked alongside hundreds of families during this meeting, reminding us of our strength and resilience, and reaffirming the essential role that our community plays in driving research forward.

On behalf of the entire team at IRSF, I want to thank you for being part of this extraordinary movement. Your commitment to creating a brighter future for everyone living with Rett syndrome is making a difference.

With hope and gratitude,

Melissa Kennedy
CEO, International Rett Syndrome Foundation

Disclaimer: All information, content, and materials provided in the Rett Gazette is intended for informational purposes only and is not intended to serve as a substitute for the consultation, diagnosis, and/or medical treatment of a qualified physician or healthcare provider. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding your specific medical condition.

IN THIS ISSUE

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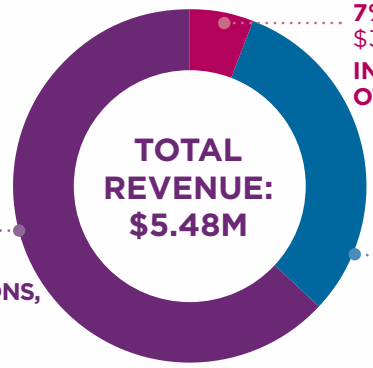
2023 IMPACT REPORT

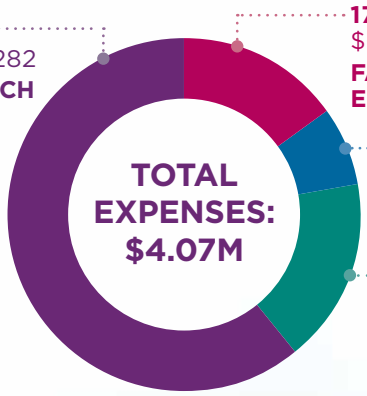
The International Rett Syndrome Foundation (IRSF) fights for families living with Rett syndrome and a world without it. We transform lives every day by funding trailblazing research seeking treatments and a cure for Rett syndrome; offering empowering support that helps families cope and offers hope; and increasing awareness of this rare disorder that affects nearly every aspect of an individual's life.



7% $374,825 **INVESTMENT + OTHER INCOME**

62% $3,409,124 **CONTRIBUTIONS, GRANTS + INDUSTRY**

31% $1,699,785 **EVENTS + CONFERENCE**



61% $2,464,282 **RESEARCH**

17% $679,293 **FAMILY EMPOWERMENT**

7% $307,432 **ADMINISTRATION**

15% $614,440 **FUNDRAISING**

$58M INVESTED IN RESEARCH TO DATE

25 ACTIVE IRSF-FUNDED RESEARCH PROJECTS

1 FDA-APPROVED TREATMENT

SCIENTIFIC MEETING:

200 ATTENDEES

77 POSTERS

NEARLY **400** INDIVIDUALS FROM 26 U.S. STATES ATTENDED THE RETTAWAY

SUPPORTED FAMILIES FROM **200+** COUNTRIES & TERRITORIES AROUND THE WORLD

147 NEW FAMILIES SUPPORTED THROUGH IRSF

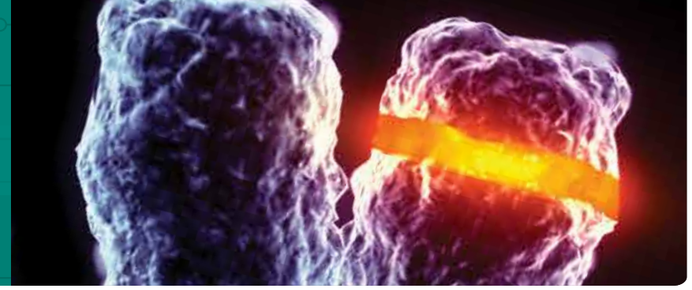
50 FAMILY-CHAIRED FUNDRAISING EVENTS

341 INDIVIDUALS ATTENDED A RETTED DAY

863 LETTERS SENT TO ELECTED OFFICIALS

80% OF EVERY DOLLAR RAISED ON AVERAGE FUNDS OUR RESEARCH AND FAMILY EMPOWERMENT PROGRAMS. WE'RE PROUD TO BE A TOP-RATED CHARITY.

MECP2:
The Discovery that Changed Everything



Twenty five years ago, the Rett research community was rocked by a landmark discovery: mutations in the MECP2 gene caused Rett syndrome. This discovery was made by Ruthie Amir, a fellow at Baylor College of Medicine in the lab of Huda Zoghbi. For Zoghbi, who encountered her first patient with Rett during her residency 16 years prior, the effort was personal.

"Every day I sat with parents and had to tell them that their child had a disorder whose cause was probably genetic, but we could not be certain," shared Zoghbi. "After seeing these girls [with Rett], I could not continue as just a clinician; I had to figure out what was happening to these patients and do something to help."*

The path forward with Rett syndrome was not easy for Zoghbi. Research funding was difficult to obtain for physicians without lab experience, and the technology available at the time made it practically impossible to study a disease like Rett that didn't affect other family members. So, Zoghbi pivoted, spending the next decade studying an inherited disorder, spinocerebellar ataxia, and establishing her lab. But she never forgot about Rett.

Amir, Zoghbi, and colleagues celebrate their groundbreaking discovery.

The Turning Point

A decade of research disappointments had made it difficult to obtain grants to study Rett syndrome and to find graduate students and fellows to work on it. Enter Ruthie Amir. A physician with no research experience at the time, Amir joined Zoghbi's lab as a postdoctoral fellow under the condition that she work on Rett. She was able to obtain critical funding from the International Rett Syndrome Association, now IRSF, and in 1999 made the discovery that would change everything.

"She showed me patient after patient with a null mutation in MECP2 that was not in the parents," said Zoghbi. "I knew this was it."

MECP2 and Rett Syndrome

The MECP2 gene, which stands for Methyl-CpG-binding protein 2, provides instructions for making the protein MeCP2. The MeCP2 protein is essential in the development of the nervous system, particularly the brain. Zoghbi's lab found that most individuals diagnosed with Rett syndrome have a mutation in the MECP2 gene on one of the X chromosomes. The mutation causes the gene to make a nonfunctioning version of the working protein so the nerve cells in the brain are not able to develop normally.

What that looks like is different for every individual with Rett. The course and severity of Rett syndrome are determined by the location, type, and severity of the mutation and X-inactivation on the MECP2 gene.

A Fundamental Transformation

This discovery of this genetic basis for Rett syndrome fundamentally changed how scientists and researchers approached the disorder. Now able to create mouse models that mimic Rett in humans, researchers were better able to study the disease's progression, gain insight into the molecular and cellular mechanics underlying it, and explore targeted therapies. Adrian Bird's 2007 demonstration that Rett could be reversed in these mouse models, funded by IRSF's legacy foundation Rett Syndrome Research Foundation, only fueled more interest in the disorder from researchers and biopharma, opening up the possibility that Rett syndrome could be treatable with therapeutic approaches.

Where We Are Now

We now have the first FDA-approved treatment for Rett syndrome, two gene therapies in phase 1/2 clinical trials, and over 20 companies involved in the Rett therapeutic pipeline. However, even 25 years after its discovery, much remains to still be understood about MeCP2's role and how exactly its disruption leads to Rett syndrome. Continuing research that aims to close these knowledge gaps is essential to both developing new treatments and improving on existing ones.

There is much reason to hope, as hundreds of scientists and researchers worldwide work tirelessly on a range of promising strategies with IRSF support, including:

- *Gene Therapy:* aims to introduce a functional MECP2 gene into cells using viral vectors to replace the defective gene and restore normal function. *(see next page)*
- *RNA-Based Therapies:* seek to correct or modify the expression of MECP2, offering potential avenues for precise genetic correction.
- *Small Molecule Therapies:* focus on enhancing the function of the MeCP2 protein or regulating its interactions with other proteins, aiming to compensate for the loss of function.
- *X-Reactivation:* targets reactivating the healthy MECP2 gene on the inactive X chromosome, providing a method to restore gene function.
- *Protein Replacement Therapy:* looks to deliver the MeCP2 protein directly to the affected tissues, aiming to compensate for the gene's dysfunction.

The discovery of MeCP2's role reshaped our understanding of Rett syndrome, but there are still many unknowns about the function of MeCP2, how its loss drives the disease process, and what treatments will be most effective. As research progresses, every new insight brings us closer to unlocking the full potential of MeCP2-related therapies.

IRSF is committed to funding trailblazing research and supporting the scientists, researchers, and the Rett community who will get us there. *Our scientific strategy will deliver.* With this continued dedication, there is hope that we will find effective treatments and, ultimately, a cure that will transform the lives of those affected by Rett syndrome.

Our Scientific Strategy

IRSF's highly comprehensive scientific program in Rett syndrome — bolstered by unprecedented industry partnerships — includes the advancement of genetic approaches and developing drugs that improve quality of life, as well as the development of a clinical research network that brings treatments to families. Our strategy focuses on three guiding pillars that cover Rett research at every level:

ADVANCING CRITICAL RESEARCH

We support fundamental research that deepens our understanding of MeCP2 and other promising targets. Filling these critical knowledge gaps is essential to helping scientists unlock new insights, develop new treatments, and improve existing ones.

DRIVING THERAPEUTIC DEVELOPMENT

We fund translational research that advances promising small molecule, gene therapy, and other approaches through the treatment development pipeline. IRSF works to expand the pipeline while helping companies and institutions developing treatments navigate it.

ENSURING CLINICAL TRIAL SUCCESS

We strengthen clinical research by creating connections between clinical trial stakeholders including clinicians, families, FDA, and trial sponsors. At the same time, we invest in essential infrastructure like patient registries and outcome measures, ensuring that potential treatments have the best chance of moving from trials to reality.

*Zoghbi is quoted from her autobiography published when she was awarded the 2022 Kavli Prize in Neuroscience. For more: kavliprize.org/huda-zoghbi-autobiography

Gene Therapy: Progress & Promising Pathways

Gene therapy holds tremendous promise for treating genetic disorders like Rett syndrome. With not one, but two gene therapy clinical trials currently underway, our community is witnessing a significant step forward in exploring groundbreaking treatment possibilities.

Gene therapy aims to treat or prevent diseases by providing or altering the genetic instructions within an individual's cells. For Rett syndrome, this means finding a way to introduce a correct copy of the MECP2 gene. As demonstrated recently in its FDA approval for other diseases like sickle cell, gene therapy gives us reason for optimism — it holds the potential to restore key functions, alleviate symptoms, and improve quality of life. We are incredibly grateful to the courageous families who participate in clinical trials and give new hope to our community.

While the promise of gene therapy is profound, it's also important to understand the challenges researchers face in developing potential gene therapies for Rett:

Complexity: The MECP2 gene is critical for brain development and function, and its role in regulating other genes and pathways makes it a complex target. Researchers are continuously working on new ways to overcome hurdles like how to cross the blood-brain barrier, target the correct brain cell types, and deliver the treatment most effectively.

Overexpression: In females with Rett syndrome, one X chromosome is silenced in each cell at random, which means that only one copy — the normal or the variant — of the MECP2 gene is active. Scientists must ensure only the correct amount of the gene is expressed and in the right cells without causing toxicity or other adverse effects.

Immune Response: Gene therapies that use AAV vectors for delivery must deliver just the right amount in one dose, as these vectors create an immune response that neutralizes further doses delivered this way and potentially cause harm. Researchers are working to minimize this response, both by optimizing viral vectors and finding new ways for delivery.

The first gene therapy clinical trials have sparked so much hope for our community, even as we await answers to questions including how long the benefits might last and how well the therapy can address various symptoms. As research continues, we look forward to sharing more insights into how gene therapy will fit into the spectrum of future treatments.

At IRSF, we believe that genetic approaches offer new possibilities for families, but are just one tool in the broader effort to address the challenges of living with Rett syndrome every day. We are committed to going further, investing in any promising science that helps deepen our understanding of Rett, expands our therapeutic pipeline, or ensures the clinical trial success that will bring more treatments to families as soon as possible.

A MUST WATCH:

To learn more about gene therapy in Rett syndrome, watch Dr. Steven Gray's top-rated presentation of "What is Gene Therapy, and What Can it Do?" from ASCEND 2024. He covers the basics of gene therapy, what it aspires to achieve in Rett, and the practical considerations researchers are facing right now.

Clinical Trial Update

Research continues to accelerate towards our goal of having multiple treatments and cures for Rett syndrome. Here are some of the most promising updates since our last issue.

Taysha GENE THERAPIES

Taysha Gene Therapies continues to recruit for its Phase 1/2 REVEAL clinical study of TSHA-102, a gene replacement therapy that uses the AAV-9 vector to deliver a functioning miniMECP2 gene to cells via an injection to the spinal canal. As of August 2024, five female patients have been dosed in the study, three in the adolescent and adult study (2 low dose, 1 high dose) and two in the pediatric study (low dose). No serious adverse events (SAEs) have been reported, and interim data from the low-dose adult patients showed clinical improvement in multiple clinician and caregiver-assessed efficacy measures, including observed new improvements in motor skills, communication, socialization, autonomic function, and seizures. The trial is currently recruiting female patients in Canada, the U.K., and the U.S. aged 5-8 for the pediatric study and 12+ for the adult study.

NEUROGENE

Neurogene has dosed four pediatric patients (3 low dose, 1 high dose) in its Phase 1/2 clinical trial of NGN-401, a gene replacement therapy that uses the AAV-9 vector to deliver a full-length MECP2 gene directly into a ventricle in the brain. Recruitment for an additional 12 female trial participants aged 4-10 is ongoing in the U.S. and Australia, with plans to expand to the U.K. soon. The treatment has been generally well-tolerated with all related adverse events (AEs) mild, and no signs or symptoms of MeCP2 overexpression toxicity to date. Neurogene plans to report preliminary clinical data from the low-dose cohort by Q4 2024.

Neurotech International

NeuroTech reported positive results from its ongoing Phase 1/2 clinical trial in Australia of NTI164, a broad-spectrum, orally administered cannabinoid drug therapy for the treatment of Rett syndrome. After 12 weeks with no SAEs, the company reported that 93% of participants showed improvement based on the CGI-I scale and the mean improvement from week 4 to 12 on the RSBQ was 205% in symptoms including communication, hand behaviors, anxiety/mood, and quality of life. The trial evaluated 14 female participants in Australia with Rett syndrome aged 5-18, with all trial participants enrolling in the ongoing 52-week extension phase.

DepYmed

DepYmed received clearance from the FDA to initiate a Phase 1 clinical trial for DPM-1003 for the treatment of Rett syndrome in the U.S. It was previously granted Orphan Drug designation and conditionally designated under the FDA's Rare Pediatric Disease program. DPM-1003 is an orally bioavailable small molecule inhibitor that targets the protein tyrosine phosphatase (PTP) family of enzymes that are disrupted in disease like Rett.

For the most up-to-date information on clinical trials and the Rett research pipeline:

2024 IRSF Rett Syndrome Scientific Meeting

In June, IRSF hosted its biggest annual scientific meeting yet, bringing together more than 200 scientists and researchers from academia and industry to share the latest research developments and discuss ways to best provide Rett patients with the care they deserve. To find a full recap of the research presented at this year's meeting, visit rettsyndrome.org/gazette.

Richard Young *explains changing views on MeCP2 during the first of five distinguished keynote presentations.*

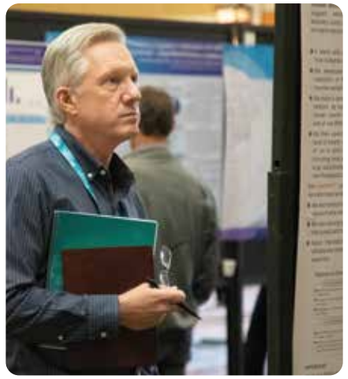
Biomarkers & Behavior Studies session speakers ***Jenny Downs and Jeff Neul,*** *discussed how to measure outcomes for the many exciting therapeutic options emerging for Rett syndrome in the final session of the meeting.*

Kicking off the session on cellular dynamics, keynote speaker ***Qiang Chang*** *discussed how astrocytes are disrupted with MeCP2 mutations.*

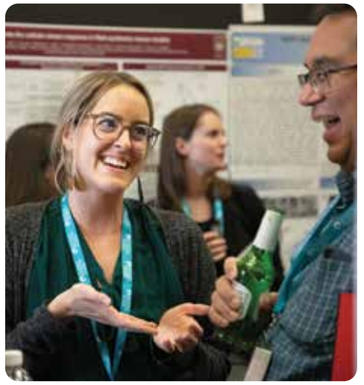
Tim Benke *asks a question during one of the meeting's lively Q&A sessions.*

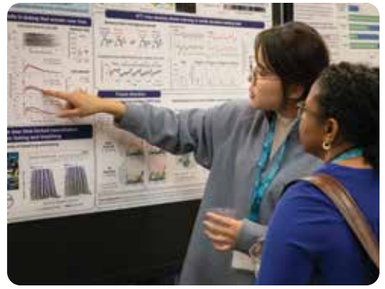
Presenters lined up for their 1-minute poster flash talk, an opportunity to briefly share their work and invite attendees to visit their poster during the evening reception.

William Lowry's *presentation during the neuronal studies session led to a vigorous debate among attendees during the Q&A.*



More than 60 researchers from around the world presented posters during the evening reception, paving the way for many in-depth conversations and networking opportunities among attendees.





Zhaolan (Joe) Zhou *shares his reflections during the concluding session of the meeting.*

Thank you to our meeting organizers (L to R): ***Vania Broccoli*** *(San Raffaele Hospital),* ***Stuart Cobb*** *(The University of Edinburgh),* ***Kathrin Meyer*** *(Alcyone Therapeutics),* ***Nupur Garg*** *(IRSF), and* ***Lucas Pozzo-Miller*** *(Michigan State University).*

Expanding the Rett Clinical Network

IRSF's new Vice President of Clinical Development, Dr. Drew Jones, is ready to help reshape the landscape of research and care for the Rett community.

As of June 2024, 21 clinics across the U.S. have received IRSF's Center of Excellence (COE) designation for best-in-class Rett syndrome care. Dr. Drew Jones is excited to build relationships with every one of them.

Joining IRSF's Scientific Leadership team in the newly created role of VP of Clinical Development, Dr. Jones is ready to make an impact for our community. He joins the IRSF team with more than 25 years of experience in clinical development, medical affairs, and pharmacovigilance in small and large pharma. His most recent work brought him to the rare disease field, advising on clinical development for giant axonal neuropathy, spinal muscular atrophy, and Rett syndrome. Dr. Jones brings a genuine interest in listening to and learning from the community and hopes to implement meaningful and relevant change.

He is hitting the ground running on several key projects already. In addition to working with the COE network, Dr. Jones will spearhead an effort to modify the content validity section of the Rett Syndrome Behaviour Questionnaire (RSBQ), one of the most widely used efficacy measures in clinical studies of Rett. Together with the COE directors, Rett experts, caregivers, and individuals with Rett syndrome, Dr. Jones will lead the effort to refine the questionnaire to better address the specific needs and characteristics of the population.

As part of IRSF's effort to create a more inclusive and comprehensive approach to research and care for individuals with Rett worldwide, Dr. Jones will also lead a sub-committee dedicated to amending critical sections of the Rett Syndrome Registry™. Here, the goal is to improve care and outcomes for the Rett community by creating a minimal dataset of essential information to capture during Registry clinic visits — from medical history and symptoms to treatments and quality of life.

"As we continue to move forward with these initiatives, I am excited about the potential impact they will have on advancing our understanding of Rett syndrome, improving clinical outcomes, and ultimately enhancing the quality of life for families living with this condition," said Dr. Jones. *"Together, we are driving change, fostering collaboration, and building a brighter future for individuals with Rett syndrome worldwide."*

New Clinical Care Resources

Find a COE Clinic:
Miami, Orange County, and San Diego just added!

Education for HCPs:
Comprehensive Rett syndrome CME library now available

Share with Your Provider:
Comprehensive Care Guidelines and Quick Reference Guide

Enroll Today:
Join the Rett Syndrome Registry

To learn more about these resources and more, visit rettsyndrome.org.

Shifting the Narrative: A Voice for Males with Rett

Brandi Spieth has spent the last 18 years caring for her son, Andrew. After his first regression at 12 months, the Spieth family did all they could to understand what was happening to their little boy. It took several misdiagnoses, second opinions, and genetic testing to receive a conclusive diagnosis of Rett syndrome more than two years later.

"Having a diagnosis of Rett syndrome is extremely challenging, but having a male with Rett syndrome is even more isolating... you are on an island by yourself," Spieth said.

Fortunately, that landscape is starting to evolve. Genetic testing has made identifying males easier, and recent studies have shown that there is a wide variability in what male Rett syndrome looks like. While the disorder was originally believed to only impact females, the community of males with Rett syndrome is steadily and rapidly growing. Still, the male Rett population has been understudied and is fraught with misconceptions.

New Hope in Understanding the Male Experience

During a candid discussion session at ASCEND 2022, many families of males with Rett shared that they experienced a delay in diagnosis and care due to misconceptions in the healthcare system. This discussion led to the launch of the Diagnostic Experience of Male Rett Syndrome study earlier this year. Led by Dr. Tim Benke and funded in part by IRSF, the study looks to better understand the lived experiences of parents and caregivers of boys with Rett syndrome in order to better inform providers and companies making inclusion decisions in clinical trials.

While the study is ongoing, the message from parents and caregivers is that more needs to be done. They want their boys to be included in all Rett syndrome research alongside their female counterparts, they want information readily available about male Rett syndrome, and they want the opportunity for their boys to participate in clinical trials as in many cases, there is no reason to believe a treatment will not work for boys too.

Speaking on a panel at ASCEND 2024, Spieth acknowledged the challenges her family has faced since Andrew's diagnosis. Sharing images of her son hitting developmental milestones as an infant nearly brought her to tears. But her message was one of hope, sharing how far they have come and her hope for the future of her son, the heartbeat of her family.

"For the past three years, we've had this [growing] community of other parents that is extremely helpful," she said. "I am very appreciative of IRSF for changing the verbiage and changing the [Rett] pronouns from she and her to they and them because all of our children matter. It's my hope that we continue to change, that we continue to evolve, and continue to include all of our males... all of our boys in research."

She then pointed to the screen and a photo of 18-year-old Andrew standing on the beach. Smiling, she said, "Rett syndrome can look just like this."

Changing the Conversation

IRSF works diligently to allocate funds aimed at better understanding Rett syndrome in all affected individuals, including males. Strategically investing in research, adapting our language to include both male and female patients, and creating a space where parents and caregivers can exchange meaningful dialogue are just a few of the ways IRSF is changing the language around male Rett syndrome.

RARE DISEASE WEEK ON CAPITOL HILL

Advocating for YOU: Rare Disease Week on Capitol Hill

By Katie Busch,
Government Relations Manager

As the longtime para and caregiver of a young woman with Rett syndrome, I've seen firsthand the strength it takes to fight every day to better the life of a loved one with Rett. That's why I was honored to represent the Rett community in Washington, D.C. this year at Rare Disease Week.

During Rare Disease Week, the EveryLife Foundation brings together more than 800 rare disease advocates to discuss policy priorities, hear inspiring stories, and raise awareness with elected officials. I was honored to represent Rett syndrome families in meetings with the staffers of 10 Congress members from my home state of Missouri and beyond, sharing stories of what living with a rare disease is like and how their policies directly affect those individuals. I was even able to join IRSF CEO, Melissa Kennedy, and board member, Steve Marconi, to advocate in person for crucial Rett research funding through the U.S. Department of Defense Congressionally Directed Medical Research Program. The CDMRP has funded more than $20M in Rett research since we started our efforts, but we must advocate every year to ensure our scientists qualify for this funding.

As I reflect on all the meetings and events one thing stands out in my mind: **the stories**. The struggles and triumphs that all the families shared. The similarities in the challenges and wins experienced by everyone whose life is impacted by a rare disease. *Our Rett community is small and mighty, but we are also a part of something much larger.* I'm inspired by the rare disease community and our Rett community, who shine clear and bright in their mission, championing their cause to improve the world. I'm thrilled to continue advocating for you.

IRSF's Promise

IRSF works tirelessly to advocate for you and your loved one with Rett syndrome. Our work takes many forms, our persistence is often unseen, and our successes are the result of countless hours spent meeting with, raising awareness, and educating key decision-makers on the needs of our Rett community. We promise to continue to advocate for:

- The federal funding needed to support researchers broadening our understanding of Rett syndrome and translating their findings to real-world treatments.
- Industry partners and biopharmaceutical companies to invest their resources in completing successful clinical trials and building the infrastructure needed to deliver treatments to patients all over the world.
- Insurance companies and state Medicaid programs to keep current and future treatments affordable and accessible so our entire community can benefit.

Visit rettsyndrome.org/advocacy or scan the QR code to learn how you too can make your voice heard for Rett:

Soaring the Summit Together: ASCEND 2024

In June, IRSF brought together families, clinicians, researchers, industry members, and Rett associations from around the world at the ASCEND 2024 Rett Syndrome National Summit in Westminster, Colorado.

Presented by Acadia Pharmaceuticals, the family conference portion of ASCEND 2024 featured 2½ full days and nights of opportunities to learn, connect, and grow together as one Rett community. We are grateful to the more than 600 attendees who made the trip for this inspiring event, traveling from 16 countries around the world and 40 U.S. states and territories. Check out the highlights!

"ASCEND was a beautiful reminder of the strength and unity within our community. It provided valuable information, support, and a sense of belonging that is so important in our journey with Rett syndrome."

~ Joshua Poulsen, Parent

The Welcome Reception brought together attendees of both the Scientific Meeting and Family Conference. Friends from all over the world reconnected, some meeting in-person for the very first time. Preceding the reception, a First Time Attendee Mixer was also held to embrace new families as part of this amazing community.

Attendees learned in nearly 60 informative, educational and, at times, emotional, presentations and panels across the plenary and breakout sessions.

"It was extremely helpful to both set our sights on future treatments as well as how we can help our [children] today. Some [sessions] were totally mind-blowing and life changing."

~ Brian Gearin, Parent

The expanded Exhibit Hall featured 27 sponsors and exhibitors ready to help families at every stage of the Rett syndrome journey.

From skating with the family to mingling with other moms, connecting with other dads, and more, there was something for everyone during the social activities night!

"It was really wonderful to get to spend in person time with people I've known online for such a long time! Having all of those experts and people who care about Rett syndrome is priceless. Having so many people speak directly to our child, so many who just 'get it'... it really heals those holes in your heart that appear from so much of the opposite in other spaces."

~ Lexy Dee, Parent

The Purple Party, a staple of ASCEND, was a time for gratitude, reflection, connection, and celebration! Families dressed in their favorite purple attire enjoyed a DJ, dancing, photo booth, and more!

My Rett Ally: It's Personal

My Rett Ally, powered by mejo, is a better way to simplify, organize, and share a child's most important medical and care information. Ryan Sheedy knows firsthand the value of tools like this for the rare disease community.

Hi, I'm Ryan Sheedy from mejo.

As a proud father of a child impacted by a rare disease, I've faced the challenges that come with being a caregiver to a medically complex loved one. I know firsthand that caregivers must become experts in their loved one's condition, but when my son was first diagnosed, there wasn't a comprehensive place to keep track of everything related to his care.

In 2018, after 15+ years in Business Development, Marketing, and Fundraising, I paused my career to become a stay-at-home dad and caregiver for my twin sons, one of whom has an ultra-rare genetic disorder. During his 103-day stay in the NICU, I began sketching out the concept of mejo — a tool designed to help caregivers like me organize their loved one's journey in a visual and meaningful way.

Bret Koncak, a friend with over 20 years of experience in healthcare technology, joined me in this mission after his own sons were impacted by sudden, acute, and severe rare diseases. In his previous executive role, Bret had regularly visited hospitals to meet with doctors, nurses, and administrators. But experiencing healthcare from the viewpoint of a caregiver rather than a provider was eye-opening for him as well. It revealed a pressing need for better tools and guidance.

Together, Bret and I created mejo to go beyond clinical data, capturing everything that makes your loved one unique. Our collaboration with IRSF led to My Rett Ally, a Rett-specific platform that has been called a "life-changer" by Rett caregivers and families. It's been an honor for both of us to be part of the Rett community and continue to grow the platform.

Being a caregiver isn't just a full-time job — it's an everyday job. I hope My Rett Ally continues to empower families to provide the best possible care for their loved ones.

My Rett Ally

Made Exclusively for the Rett Syndrome Community

Every individual with Rett syndrome is different, and so is their medical journey. With My Rett Ally, caregivers can organize and track information specifically tailored to their loved one with Rett. Some features include:

ORGANIZED MEDICAL JOURNAL

Keep the most important medical information all in one place, organized, and ready to safely share.

TRACK WHAT'S MOST IMPORTANT

You're in control of determining which tracking categories and symptoms you want to use for your caregiving needs.

STORE IMPORTANT DOCUMENTS

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Transforming Lives with Communication

It took just one encounter with an individual with Rett syndrome for Andrea Etkie, a licensed speech-language pathologist (SLP), to start down a path that would change the course of her career.

Etkie had taken a position as an SLP with the Florida public school system where she developed an expertise in Augmentative and Alternative Communication (AAC) methods. She used AAC to boost the communication skills of children with a variety of significant speech, language, and communication difficulties, but had never heard of Rett syndrome. That was until a young high school student with Rett was added to her caseload.

"When I showed up, the student's nonverbal skills were just so expressive … she was incredibly socially engaging," said Etkie. "I wasn't expecting that based on the limited research I had done on Rett."

The more Etkie worked with the student, the more questions she had on how to best support individuals with Rett. Etkie eventually saw all eight Rett students in Palm Beach and traveled across the state of Florida to perform communication assessments on Rett patients. However, she found that there was a disconnect between the published literature and her experience.

"I was seeing a group of individuals who were very engaged, who were using their on-screen keyboards to write, who were reading commensurate with their peers, who were taking standardized tests and not just scoring well … some of them were scoring in the 90th percentile," she said. "At the time, these things weren't being published."

So Etkie made the decision to do something about it. Now a doctoral candidate in the UNC speech and hearing sciences division, her goal is to publish literature that better reflects the communication abilities of the individuals she was seeing in the clinic.

One of the tools that Etkie had found incredibly helpful in her clinical work was IRSF's *Rett Syndrome Communication Guidelines*, the first publication designed to provide a common baseline for consistent, evidence-based information on Rett syndrome. Not only did this handbook prove useful in her practice, but it connected her to other professionals like Dr. Theresa Bartolotta, a co-author, Rett mom, and now, Etkie's mentor.

"What we found after the handbook was published was that there was a need to continue the conversation around communication in Rett," Bartolotta said. "To fill that need, IRSF created a certification program geared toward communication professionals who work with Rett patients. After completing the coursework, those professionals are invited to join a private, online forum where they can continue the dialogue. I was delighted when Andrea accepted my invitation to be a moderator in this forum."

The forum mostly consists of SLPs but there are other professionals — including special educators and occupational therapists — who have joined.

"A big part of our outreach efforts are focused on graduate level SLP [programs]," Etkie said. "One of Theresa's goals is for every master's student who graduates to know what Rett syndrome is. That feels very true to me. I had never heard of it until I had a Rett student put on my caseload, and I had to scramble. I don't want that to be every SLP student's experience."

Etkie recognizes this as a crucial moment in Rett research and the more professionals who know about Rett the better.

"Not all professionals who participate…will be assessing language like I am," Etkie said. "But for them to be a part of it and have that background communication knowledge, it helps them to do the best job that they can. And that's what it's all about."

SASSY SAVY

Savannah, aka Sassy Savy, prefers to use her "talker" for sassy quips rather than academics, but her teachers are as determined as her parents to ensure that she has every learning opportunity possible. With their support, she has proven that she will not only keep up with her typical peers academically but actually stay at the top of her class! Savannah finished her kindergarten year this past spring spelling her name, reading at an age-appropriate level, and doing basic addition/subtraction!

AIRBORNE EMMA

Emma took her first plane trip ever to Disney World courtesy of Make-A-Wish. It was a very special week for Emma to spend time in Orlando with her entire family — 15 in all! According to her grandmother, Cindee, "[Emma] did her first plane flight like a champ! What a fun time we had!"

WHO'S INSPIRING US!

SWINGIN' MACIE

13-year-old Macie loves to be outside and more than anything, loves to swing, but the realities of Rett mean that she can't use most of the regular swings at the park. But her dad wasn't going to let Rett stop her from doing something she loved. For Christmas this last year, he built Macie her very own swing, one that can accommodate her chair!

BALLERINA EMMA

Emma was awarded her Five Year Dancer status by her dance company! Emma has been dancing in a non-profit adaptive dance group every Saturday since she was three. Each week she joins her other special friends, alongside typical ballerinas, to share an hour of dance, and multiple times a year they also get to perform together at recitals.

RUBY'S WATER SKIING ADVENTURE

When Ruby was diagnosed with Rett her parents were devastated to think of what Ruby might not get to experience. But Ruby is 6-years-old now, and their perspective has completely changed. Though it might take a little more effort, nothing is out of reach for Ruby, even water skiing! "If you told me when she was diagnosed that she would be water skiing 5 years later I'd have never believed you, but here we are!" shared mom, Amanda. "Rett is hard and stinks, but it doesn't stop us and her from doing our darndest to find things and adapt stuff so she can experience the same things as every other kiddo out there."

JOHANNA'S PASSION FOR FASHION

At 7-years-old, Johanna is making a name for herself on the runway, capturing accolades for her resilience and achievements with her mom by her side. Recently, Johanna has even been gracing the stage at several regional and international fashion shows! Her confidence and style always shine through, capturing the attention of prominent news outlets in India that have shared her story and brought awareness of Rett syndrome in her country. Johanna recently added even another achievement to her growing list: modeling for a photo shoot!

Ellie & Kiara

Asha & Avi

SISTER ACT

Ellie & Kiara

Even on the darkest days, Ellie's big sister Kiara brings her so much joy. "Their love is pure and is a privilege to witness," shares mom, Shannon. "They love each other so big. Kiara is definitely Ellie's favorite person."

Asha & Avi

Asha was diagnosed with Rett syndrome right before her little sister Avi was born. The sisters immediately had a beautiful relationship and now just love each other so much. Avi helps her sister, always encourages her, and makes sure that she is never left out. Mom, Ashley, can't wait for them to grow up together. "The sweetest things we hear are 'Go sissy!' [from Avi] while Asha giggles and smiles."

Help give hope to families all over the world with Rett syndrome. Share your story at rettsyndrome.org/share.

The Next Generation of Fundraisers

Teens Ellie Morgan and Melissa Nues are channeling their personal experiences with Rett syndrome into powerful fundraising efforts that inspire hope and action.

For the past few years, Ellie Morgan has been stepping out of her comfort zone. Entering her senior year of high school, the Idaho teen has gone through various stages of grief since her sister, Megan, passed away in 2017. Megan had Rett syndrome, and while she couldn't speak, Megan and Ellie developed their own way of communicating. They were best friends.

Morgan Family

"Her laugh was definitely my favorite," Ellie recalls with a smile. "It was a laugh that got everyone's attention in the room. Megan's favorite thing was watching me and my brothers get in trouble."

The loss of her sister and that infectious laugh left a void in Ellie that few people in her small hometown could understand. She channeled a lot of her grief inward, leaning on her family and close friends to get her through difficult days.

"At first, I didn't want to talk about Megan," she said. "Looking back, that was a really hard time. But then, I started to realize how much my parents loved talking about her and keeping her memory alive. It really made them happy. And slowly I started doing that too."

As she worked through her grief, Ellie looked for ways to celebrate Megan that could also aid in her healing process. With her senior year of high school on the horizon, she thought that a Strollathon might be a good way to do that.

"I'm not a social person, so this is completely out of my comfort zone," Ellie said. "But, I live in a really small town of 3,000 people. Most of them don't know anything about Rett syndrome. I want them to know about it. I also want them to know that no matter what they are going through, there is a community out here who is going to support them."

Ellie envisions welcoming attendees to the park with purple archway balloons and tables set up where businesses and non-profits can share their services with community members. She hopes that the money raised helps advance research for Rett and assists families who are battling the disorder in real-time. So far, she has been overwhelmed by the support of IRSF and her community in Idaho.

"A big part of my healing process has been to put myself out there even if I feel uncomfortable, even when it's hard," she said. "I've found that once I take that first step, it gets easier. And I just remember that I'm doing this for my sister. That has given me strength."

Nues Family

For college-bound Melissa Nues, strength is a trait that she has built following the example of her parents and sister, Katie, who has Rett syndrome.

"My parents have always been 'doers,'" Melissa said. "They meet every challenge with a brainstorm session and a solution. Growing up, their trailblazing efforts felt like an everyday occurrence — ordinary, even. When I heard women in NorCal wanted to organize a Stroll, I just thought, 'What would my parents do?'"

The obvious answer is that they would help. So Melissa did just that. Together with Rett moms Rachael Linford and Natalie Gifford, Melissa helped organize a Strollathon that not only reengaged a community of Rett supporters, it exceeded the group's fundraising goals by more than $50K.

Melissa attributes the event's success to the community that came together to make it happen.

Melissa with her Strollathon co-chairs

"From tears during the butterfly release in memoriam of those we lost during COVID to the matching butterfly necklaces Natalie gifted us that I still wear every day, every moment of this event was filled with the beauty of our community," she said. "There is no way to sum up the family that this Rett community is, and those bonds were palpable that day."

Together, the organizing committee and volunteers across Northern California put together an event that truly embraced the spirit of community. Melissa shared her joy in being able to interact with others who understand the unique challenges of caring for a loved one with Rett syndrome. She also shared the unexpected ways that people showed up in support.

"A surprising aspect of the process was spreading awareness among people I'd known at school for years," she said. "A girl who I hadn't spoken with since sophomore year history class donated. It really does take a village... sometimes that village just needs to know what's needed."

Melissa was proud to have her entire family in attendance at the event, including Katie.

"Katie's story alone inspires people," she said. "The way she can pick her head up and carry on, even with all the odds stacked against her, is nothing short of a miracle. I figured if she can do the impossible every day, then what's stopping me from helping make her journey a little easier by helping to raise funds for research and care."

Melissa is proud that her involvement helped to make the event a success, and vows to continue her philanthropic efforts as she heads off to her freshman year at Cal Poly in the fall.

"I always thought philanthropy had to be something big and world-altering," she said. "The reality is that sometimes the smallest actions are the most impactful. There is always a person or a community in need of something — find what cause you are passionate about and just start to research! There is a calling out there for you, just keep asking questions until you find it."

Strollathon

For over two decades, Strollathons have been a beacon of hope in the fight against Rett syndrome, raising more than $17 million for vital research and uniting thousands of advocates and families. These events are more than just fundraisers — they are vibrant, community gatherings where individuals affected by Rett syndrome can connect, share stories, and find support.

Each Strollathon is a peer-to-peer fundraising event, empowering participants with personalized pages to rally support from family, friends, and their communities. Many of these events have become long-standing traditions in their community, with some running for over a decade and contributing hundreds of thousands of dollars to the cause.

Last year alone, more than 2,000 people joined Strollathons across the country. To date, these events have taken place in over 33 states, and the 2024 lineup promises even more opportunities to get involved.

Visit rettsyndrome.org/strollathon to find a Stroll near you, or email events@rettsyndrome.org to learn how IRSF can help bring one to your community!

Harnessing the Power of Your Network

By Tim Frank,
IRSF Development Director

When my daughter Ella was diagnosed, so many people offered to help. In addition to wanting to support my family directly, many wanted to give to a foundation that was helping families like mine and working toward a cure. For me, IRSF has always been the perfect organization to encourage my community to support.

IRSF is focused on accelerating all promising research for treatments and cures and providing support for families to better care for their daughters and sons.

Harnessing the power of your network to support IRSF is very easy. Your dedication and enthusiasm have always been the backbone of IRSF's success, and now, with a few simple steps, you can amplify your impact even further.

No matter where you start, ***always share your personal connection to Rett syndrome.*** Whether it's a heartfelt post on social media, an email to friends and family, or a blog post, your story can inspire others to give.

Virtual Giving

Create a Fundraising Page: IRSF has a revamped online platform that makes it easier than ever to create a personalized fundraising page. Customize your page with your story and then share it widely.

Go Social: Platforms like Facebook and Instagram are powerful tools to share your efforts and tag friends who might be interested. The more you share, the more visibility you gain.

You've Got Mail: Send personalized emails to your contacts. Include compelling reasons why they should support Rett syndrome research and provide our link to donate.

In-Person Giving

Do you love to bake? Start a bake sale. Like running? Consider starting a community 5K for Rett. Like working out? One friend in St. Louis started a POUND event to support her friend's son with Rett syndrome.

Hosting an event can take your fundraising one step further. It's incredibly special for your network to hear directly from you when you share your story and how their contributions can make a difference.

From organizing small get-togethers, cocktail parties, or dinners to going bigger with a Strollathon, golf event, or gala, IRSF has the tools to support your fundraising efforts at any event you can dream up.

Thank You

We are incredibly grateful for how our community has rallied together to leverage their friends, family, and network. Because of their support through these online and in-person giving opportunities, we have invested more than $58 Million into research and counting.

If you have an idea and need help, please reach out. We'd love to help make your idea a reality in honor of someone you love with Rett syndrome.

The 3 Keys to Fundraising Success

BE GENUINE
People respond best to authentic, heartfelt appeals. Share why Rett syndrome research matters to you personally.

BE CLEAR AND CONCISE
Make it easy for people to understand how they can help and where their money is going.

FOLLOW-UP
Don't hesitate to follow up with people who have shown interest. A friendly reminder can go a long way.




UPCOMING RETT EDUCATIONAL EVENTS

Make plans to join us for one of our upcoming virtual or in-person RettEd events! For more information on the events listed below, scan the QR code:

RettEd

Live Webinars

RettEd Live Webinars are held periodically on the topics most important to families living with Rett syndrome. For the full video library of past webinars, please visit our YouTube channel.

October 24, 2024
Epilepsy Treatments in Rett Syndrome
Speaker: Robin Ryther, MD, PhD

December 12, 2024
IRSF Research Update
Speakers: IRSF's Scientific Team, Nupur Garg, PhD, and Drew Jones, MD, MPH

2025 Webinar Series Announcement
Coming Soon!

RettEd Day
CONNECT. SHARE. GROW.

RettEd Days

Held at IRSF-designated Centers of Excellence for Rett syndrome care, RettEd Days are full-day sessions designed to provide information, enrichment, and connection for anyone involved in the care of a loved one with Rett syndrome.

November 15, 2024
Children's Hospital of Philadelphia

April 5, 2025
Nationwide Children's Hospital

May 3, 2025
Children's Hospital Los Angeles

TBD Fall 2025
University of Alabama at Birmingham
Boston Children's Hospital

2025 RettAway

July 2025 | San Diego, California

Get ready! IRSF's RettAway is a destination vacation for families to spend time together and build connections with other members of our Rett community. It's an exclusive opportunity for families to "learn by doing" that adventures can be pursued and enjoyed by all — no sitting on the sidelines here. Stay tuned for more information!

RettAway

International Rett Syndrome Foundation

4500 Cooper Road, Suite 204
Cincinnati, OH 45242

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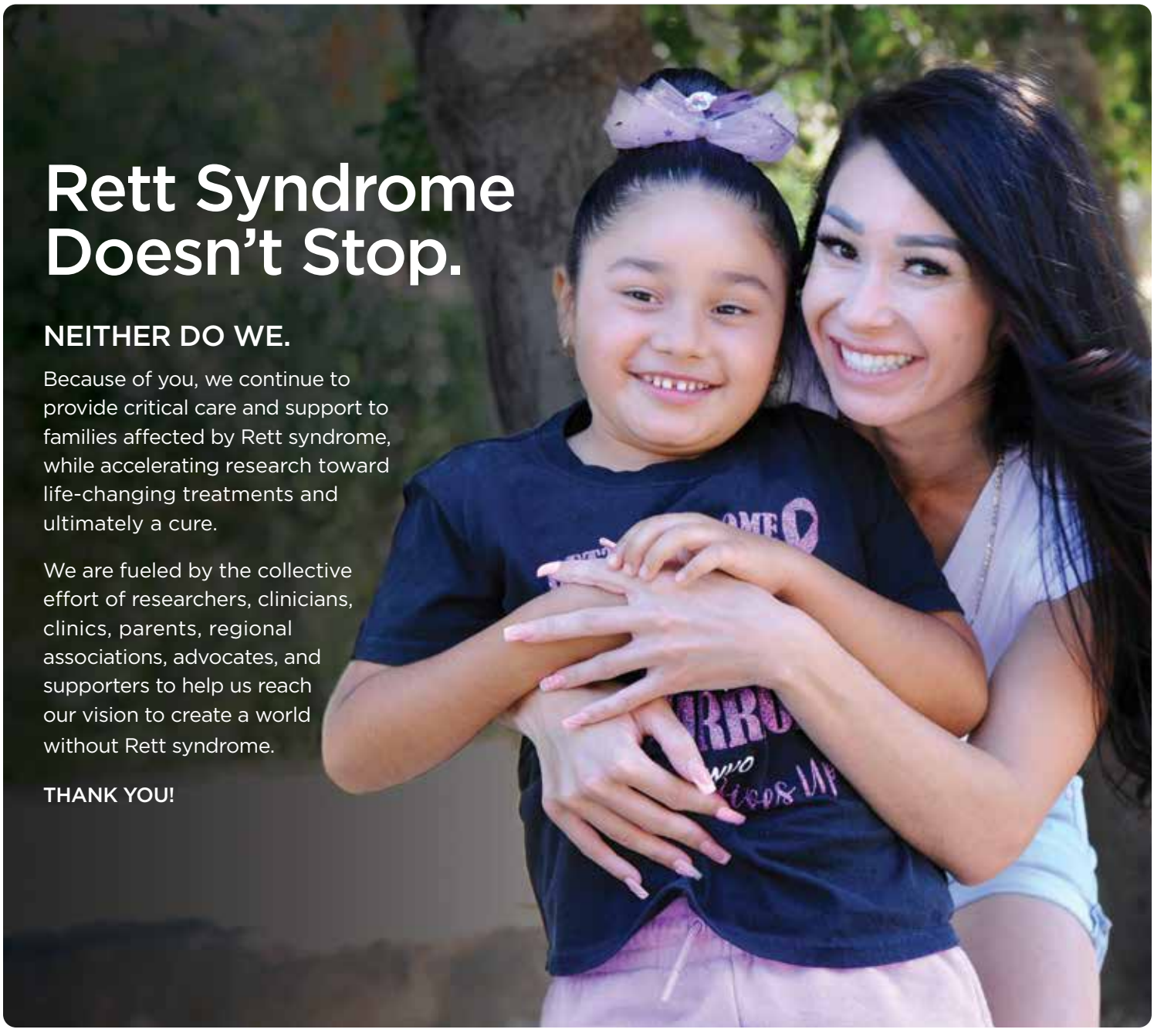

Rett Syndrome Doesn't Stop.

NEITHER DO WE.

Because of you, we continue to provide critical care and support to families affected by Rett syndrome, while accelerating research toward life-changing treatments and ultimately a cure.

We are fueled by the collective effort of researchers, clinicians, clinics, parents, regional associations, advocates, and supporters to help us reach our vision to create a world without Rett syndrome.

THANK YOU!