Sunitha Malepati, CACNA1A Foundation & The Buffalo Initiative

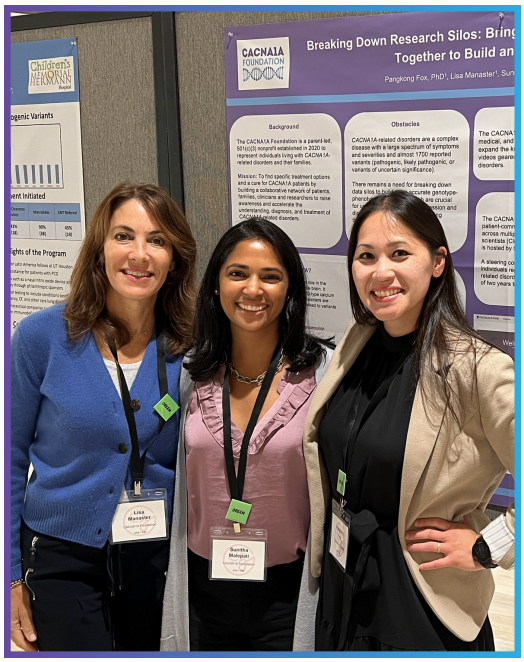
"We're bringing together researchers, funders, regulatory experts, translational research experts, to coalesce around these high-impact, high-potential projects in the rare disease space that are faltering right now because they have a lack of funding, they have a lack of guidance, and they really need some accelerant to take them through that valley of death to the first in human trials."

When Sunitha's daughter was born, she immediately sensed something was off based on the way her daughter's eyes moved. Her concern grew as her daughter faced delays in reaching developmental milestones and experienced febrile seizures. Raising these concerns with her pediatrician set off a long journey of referrals and specialist visits. After two and a half years, they finally had an answer: genetic testing revealed a mutation in the CACNA1A gene. This gene encodes a protein essential for normal neuronal activity, and when impaired, it can lead to a range of symptoms, including ataxia (a balance and coordination disorder), migraines with temporary weakness or paralysis, eye movement disorders, epilepsy, and neurodevelopmental delays. For Sunitha, the diagnosis aligned with what she had observed in her daughter.

The CACNA1A Foundation

In 2020, the year Sunitha's daughter was diagnosed, the CACNA1A Foundation was formed by parents of children with CACNA1A-related disorders who met through a Facebook community. They created the organization simply because the research was not moving fast enough for their kids. Sunitha explained that in the rare disease space, the standard way of thinking—"leaving the science up to scientists and medicine up to doctors"—does not work. She clarified, "When you are faced with this diagnosis of your own child, or maybe it's yourself, and you realize there's no one working on it, you've got to take matters into your own hands...no one was focused on finding a treatment, and we had to do something."

That "something" became a flurry of activity. The foundation established a scientific advisory board and dedicated its resources to accelerating research into treatments. "We've developed cell lines that different modalities can be tested on, we've invested in new mouse models, and we've built a collaborative research network of 60 of the world's renowned researchers," Sunitha shared. Equally important, the foundation sought guidance from pharmaceutical companies and regulatory experts and provided a vehicle for patient data to be aggregated and analyzed through natural history studies.



"What I think is really important for people to understand is that when you develop research agendas and they're not tied to the communities that are living with the impacts of these diseases, you're not going to necessarily be working on the same scientific problems that matter to patient communities. Patient communities care about treatments. They care about quality of life. They care about what happens to my kid when I pass away."

These early efforts of the CACNA1A Foundation were a step toward making research translatable, or, as Sunitha shared, "de-risking the disease" by building a community, gathering patient data, and funding research necessary for the subsequent development of a treatment. Now, approaching their 5th anniversary, these efforts have established a foothold with commercial partners interested in CACNA1A-related disorders. However, for many disease advocacy organizations, gaining commercial interest is not yet in sight. "These [advocacy] groups are heartbreakingly pouring so much time, energy, and money into de-risking, and then they just get stuck," Sunitha explains. "They have a promising proof of concept, meaning there is promising data in a lab somewhere saying that this might work in humans, but they don't have the funding to take it forward."

The Buffalo Initiative

For Sunitha, the path to more treatments for rare disorders is patient-centric and patient-driven. It's this mindset that led to the creation of The Buffalo Initiative, a philanthropic organization dedicated to partnering directly with patient leaders to bring promising therapies to clinical trials.

As founder, Sunitha has assembled a team of advisors with expertise in science, strategy, investment, and commercial development, many of whom are directly connected to the rare disease patient community. And though she believes Buffalo will prove beneficial to those affected by CACNA1A-disorders, Sunitha indicated that Buffalo is more broadly focused on the genetic drivers of epilepsy, intellectual disability, and autism. The Buffalo Initiative is interested in "elevating this to a bigger set of stakeholders who might be interested in funding, but also enabling pattern recognition across disease groups, so a breakthrough in one disease could potentially be applied across diseases."

By building a bridge to clinical trials, Sunitha believes Buffalo can fast-track the creation of clinically impactful medicines that would have otherwise been stranded in the drug development "valley of death."

> *"We put together a 10-year timeline to take as many programs as we can support to clinical trials, but [also] to change how funders think about funding science... [to put] more money into translating innovations into something that impacts human lives."*

BUFFALO INITIATIVE
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While the focus is on the financial challenge to treatment development, Sunitha and her team are well aware of the regulatory hurdles to address. However, there is optimism, as recent years have demonstrated increasing interest and flexibility from the FDA when it comes to small-sample rare diseases and trial approaches. Per Sunitha, "The new FDA Rare Innovation Hub, where they're going to be tackling these issues—there are just so many talented stakeholders that are working on the regulatory side of things, and so that gives me a lot of hope that we're going to face a more favorable regulatory environment when we start to push more programs to the clinic, because there actually is a lot of appetite for innovation at the highest levels of the FDA."

Research, Reflect, Act

Sunitha is the first to acknowledge that what she's accomplished is only possible because of her support system. "I have an amazing, amazing family. I could not do this work without my spouse, my parents, and my in-laws," Sunitha stated, continuing, "I have an enormous number of advisors, mentors, partners, a robust team, and great champions in the community, too, that fuel you."

When asked what others could do to support these efforts, Sunitha gratefully acknowledged those who have previously contributed funds while asking those who would like to help to contribute in a pointed manner, by considering how money may be best used. "When you're thinking about making a donation in this space, look to patient groups that are research-focused and mission-oriented... Buffalo is one of those entities, [a] spot for people to put their money, to see the results that we're hoping to drive for, which is treatments in these kids' lifetimes."

CACNA1A FOUNDATION

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To learn more

The https://www.cacna1a.org/ and https://buffaloinitiative.org/ websites provides a host of resources for families, researchers, clinicians, advocates, and other healthcare stakeholders. Other resources suggested by Sunitha include:

- National Organization for Rare Disorders - https://rarediseases.org/
- Global Genes - https://globalgenes.org/
- Once Upon A Gene Podcast by Effie Parks - https://effieparks.com/
- Rare Awareness Radio - https://rareawarenessradio.org/
- Principled Research Resources - https://www.principledresources.com/rare-awareness-radio

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