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CAMK2-Related Neurodevelopmental Disorders

A GIVING SMARTER GUIDE

Nadia Penrod, PhD; Elizabeth Burke, PhD; Cara Altimus, PhD; and Caitlyn Barrett, PhD

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The Milken Institute is a nonprofit, nonpartisan think tank focused on accelerating measurable progress on the path to a meaningful life. With a focus on financial, physical, mental, and environmental health, we bring together the best ideas and innovative resourcing to develop blueprints for tackling some of our most critical global issues through the lens of what's pressing now and what's coming next.

About Milken Institute Strategic Philanthropy

Milken Institute Strategic Philanthropy tackles persistent societal challenges by guiding individuals and foundations with the insights and tools to develop strategies, implement giving programs, and foster collaboration to create a better, more equitable world.

About the Science Philanthropy Accelerator for Research and Collaboration

Milken Institute Strategic Philanthropy's Science Philanthropy Accelerator for Research and Collaboration (SPARC) works to develop, launch, and lead initiatives that fund medical research and invest to accelerate the development of tools and treatments that will bring better health to millions of people. Our expertise lies within a number of medical research fields, including neuroscience, mental health, oncology, rare disease, and immunology. We partner with philanthropists, leading them through complex medical research and clinical systems and guiding pathways for philanthropy to create a healthy, equitable world.

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Foreword

For years, my family lived without answers. My daughter Sienna is full of light—playful, affectionate, and deeply intuitive—yet she faced struggles no one could explain. Relentless gastrointestinal problems, profound sleep disruption, and constant behavioral challenges, including aggression beyond her control, dominated our lives. She lived in a state of extreme fight-or-flight, a neurological storm that affected every part of her day.

For years, doctors and therapists tried to help but couldn't connect the dots. I fought for Sienna because I knew her potential; when regulated, her wit, warmth, and intelligence shone. At 18, genetic testing finally gave us the answer: a rare condition caused by a mutation in the **CAMK2A gene**.

CAMK2 is a master gene that controls learning, memory, and communication between brain cells. Many children with CAMK2 mutations do not walk or talk, and most will not live independently. Some face seizures, profound developmental delays, and daily behaviors that overwhelm families. And yet, hope persists.

CAMK2 is well studied and considered targetable, with treatments—from medications to gene-based therapies—within reach. **But a critical treatment window may exist, and children like Sienna risk missing breakthroughs if action is not taken quickly.**

With Sienna's diagnosis, I refused to accept that nothing could be done. I engaged the Milken Institute to learn how to build a community, raise awareness, and accelerate research. When I confessed to guilt about dedicating myself to a condition affecting fewer than 400 known children, they reminded me: *Philanthropy is often personal.*

That resonated deeply because rare genetic neurodevelopmental disease **is personal**. It is also prevalent: An estimated **three in 1,000 people** live with such a condition, yet more than half go undiagnosed due to **limited access to genetic testing**. Without a diagnosis, children miss effective treatment, and families and schools are left to struggle in the dark.

Now 19, Sienna is living proof that with the right supports, children can improve and flourish. But only targeted treatments can make true independence possible.

Our community may number only in the hundreds, but our vision reaches millions. By advancing CAMK2 research, we are building a road map for many other neurodevelopmental diseases. We aim to raise awareness, expand access to genetic testing, and inspire other rare disease communities to see what's truly possible. With your help, we can turn research into real treatments—giving children like Sienna, and so many others, a chance not just to survive, but to **thrive**.

Dina Friedman, PsyD
Founder, Limitless Pathways

Executive Summary

CAMK2-related disorders are rare genetic conditions that disrupt fundamental brain processes essential for learning, memory, and development. These disorders, caused by mutations in the CAMK2 genes, lead to a range of profound neurodevelopmental symptoms. Affected individuals may experience developmental delays, intellectual disabilities, speech and language impairments, motor dysfunction, and severe emotional dysregulation. In some cases, epilepsy further complicates care. The severity of these symptoms varies by mutation, but one common thread runs through every case: the absence of effective, targeted treatments.

For families, the impact is immeasurable. Children and adults living with CAMK2-related disorders often require lifelong support to navigate communication, learning, and daily tasks. Caregivers face immense challenges in accessing specialized care and educational resources that meet each affected individual's unique needs. There are no treatments approved by the Food and Drug Administration (FDA), and while speech therapy, physical therapy, and behavioral interventions can provide meaningful benefits, they address only symptoms, rather than the underlying biological cause.

Decades of research have mapped CAMK2's critical role in brain development and function, giving scientists a strong foundation to explore targeted therapies. But the link between CAMK2 mutations and neurodevelopmental disorders was recognized only recently, and progress remains constrained by minimal disease-focused funding. Over the past decade, no National Institutes of Health (NIH) grants and only a handful of international awards have directly supported CAMK2-related disorder research, limiting therapeutic development. Strategic philanthropic investment now could take advantage of existing models, molecular tools, and expertise to accelerate therapy development, turning decades of foundational knowledge into tangible, life-changing treatments for affected individuals and their families.

Opportunities for Strategic Philanthropic Investment

The Friedman family partnered with the Milken Institute SPARC to identify areas where strategic investment could accelerate progress for CAMK2-related disorders. This report reviews the current scientific landscape and funding trends and highlights CAMK2-specific investment opportunities, informed by leading experts and stakeholders in and beyond the field. These opportunities aim to unify efforts across the CAMK2 ecosystem to accelerate research, enhance collaboration, and drive therapeutic development.

Establish Networked Centers of Excellence for CAMK2 Disorders

Fund networked centers that integrate expert clinical care, patient support, and research. These hubs would enable decentralized trials; generate high-quality, real-world data; accelerate therapy development; and directly improve the quality of life for affected families.

Invest in Shared Preclinical Tools and Resources

Support a coordinated research ecosystem by funding shared models, standardized assays, variant databases, and a collaborative infrastructure. This will accelerate understanding of CAMK2 variants, uncover therapeutic targets, reduce duplication of efforts, and enable the development of patient-specific treatments.

Advance Therapeutic Discovery and Development

Fund coordinated efforts to identify and develop targeted treatments, including drug repurposing, antisense oligonucleotides (ASOs), gene therapies, and precision approaches guided by patient molecular data. These investments will accelerate therapies that address the full spectrum of CAMK2-related disorders and de-risk early-stage development.

Catalyze Biomarker and Outcome Measure Development

Fund the discovery and validation of molecular, imaging, and patient-reported biomarkers, along with standardized clinical outcome measures. These tools will enable well-designed clinical trials, support regulatory readiness, and speed the delivery of therapies to families.

Establish a Bridge Team and Shared Data Ecosystem

Fund dedicated staff and a centralized data platform to coordinate research, clinical care, and patient engagement. This infrastructure will sustain collaboration, prevent siloed efforts, and ensure discoveries are efficiently translated into meaningful therapies.

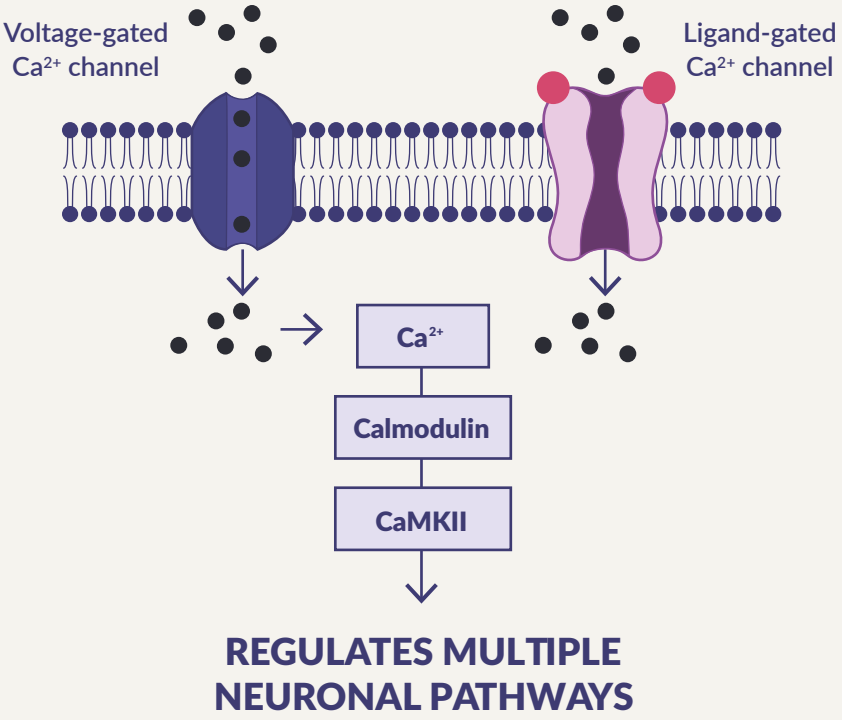
Philanthropic investments in these five areas offer a path to strengthen the CAMK2-related neurodevelopmental disorders field. By connecting research, clinical care, and patient communities, we can accelerate development of impactful therapies. To date, around 300–400 individuals worldwide have been diagnosed with CAMK2-related disorders, though this number is expected to rise as genome sequencing becomes more routine. Targeted therapies are urgently needed for today's patients—and to spare future families from facing the devastating challenges these disorders bring.

This report provides an overview of the scientific landscape, current funding trends, and actionable opportunities to guide high-impact, strategic investment.

CAMK2 and Neurodevelopmental Disorders

Understanding CAMK2-related neurodevelopmental disorders begins with recognizing the critical role of calcium signaling in the brain. Calcium ions (Ca^{2+}) act as messengers that coordinate communication between neurons and regulate processes within cells—including neuronal growth, synaptic connectivity, and plasticity or adaptation—that shape the strength and structure of synapses, the specialized junctions where neurons send and receive signals. As shown in Figure 1, calcium/calmodulin-dependent protein kinase (CaMKII) is a key mediator of calcium signaling, translating short bursts of calcium into long-term changes in neuronal structure and function. These processes are fundamental not only to brain development but also to learning, memory, and behavior throughout life.

Figure 1. CaMKII Links Calcium Signals to Long-Term Changes in Neurons



Source: Modified from Daoud et al. (2023)

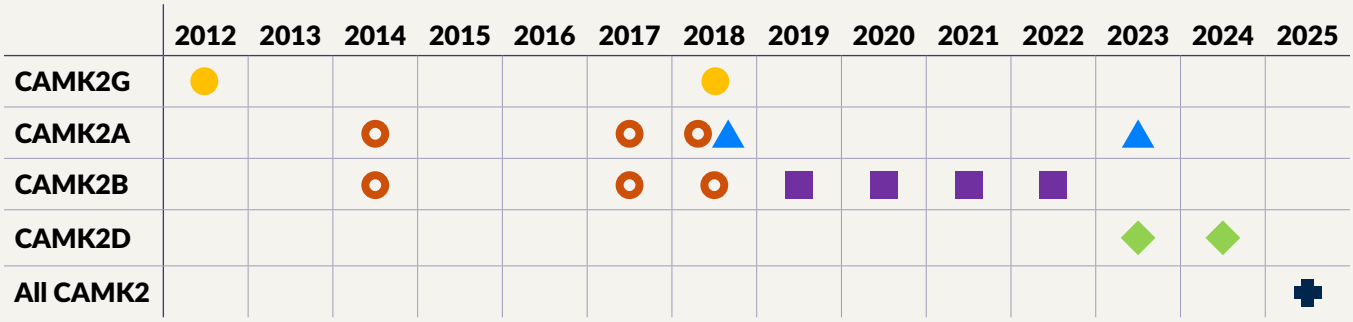
Mutations in the genes that encode CaMKII can disrupt these finely tuned systems, leading to a recently recognized group of disorders known as CAMK2-related neurodevelopmental disorders. These disorders are typically characterized by intellectual disability, developmental delay, speech and language impairment, and motor impairment. Although individually rare, CAMK2-related disorders belong to a growing class of genetic neurodevelopmental conditions, some of which are increasingly recognized as contributing to autism spectrum disorder or presenting with autism-like features. Research into CAMK2-related disorders is still emerging, but early findings are shedding light on how specific molecular disruptions impact brain development and function; these insights may guide future approaches to clinical care and treatment.

Identification of CAMK2 Gene Variants

In just over a decade, the CAMK2 gene family has gone from being known for its essential role in learning, memory, and synaptic signaling to being recognized as harboring mutations that cause severe neurodevelopmental disorders in humans. Rapid progress in genome sequencing, case discovery, and early functional studies have established this association. These discoveries began in 2012, when the first CAMK2 gene variant linked to intellectual disability was identified. By 2014, additional variants were found in individuals with autism spectrum disorder, and by 2017, a landmark study confirmed that these mutations directly disrupt brain development.

Since then, the number of known cases has steadily increased. Children and young adults with CAMK2-related disorders experience a wide range of symptoms, including intellectual disability, developmental delays, seizures, and behavioral challenges (e.g., irritability, hyperactivity, anxiety, aggression, autistic traits). The type and severity of symptoms can vary significantly, depending on which gene is affected and the specific mutation involved. Parents report that exaggerated fight, flight, and freeze responses are among the most difficult behaviors to manage, and for some, these reactions dominate daily life. Additional features like cardiac abnormalities, structural brain differences, or facial and skeletal anomalies have also been observed.

Table 1. Studies Linking CAMK2 Gene Variants to Neurodevelopmental Disorders



Notes: Colored symbols show studies linking CAMK2 genes to neurodevelopmental disorders. There are 17 symbols representing 14 unique studies because a few studies reported results for multiple genes. Symbols correspond to the genes identified in the study: CAMK2G (yellow circle); CAMK2A + CAMK2B (orange ring); CAMK2A (blue triangle); CAMK2B (purple square); CAMK2D (green diamond); All CAMK2 genes (navy plus sign).

Source: Milken Institute (2026)

A 2025 review of known cases marks a turning point in the field. For the first time, researchers are beginning to see patterns between specific CAMK2 genes and the symptoms they cause, opening the door to precision diagnosis and, potentially, targeted therapies. However, progress is still early, and more research is urgently needed to understand these disorders, improve clinical care, and pursue treatments.

Understanding the full spectrum of genotype–phenotype correlations will require larger patient cohorts. To this end, an ongoing natural history study is deeply phenotyping affected individuals and systematically characterizing the functional consequences of specific variants. As each newly identified variant provides additional insight into CAMK2-related pathophysiology, these findings may ultimately reveal converging mechanisms and potential therapeutic targets to reverse or mitigate the associated neurodevelopmental phenotypes.

To contextualize the significance of individual variants and guide future diagnostic and therapeutic efforts, it is essential to explore the demographics and clinical profiles of individuals with CAMK2-related disorders. This requires estimating overall prevalence, understanding the rate and mechanisms of individual mutations, and describing the natural course of the disorder across diverse populations and developmental stages.

Epidemiology and Natural History

CAMK2-related disorders are not typically inherited. Instead, they are caused by spontaneous (*de novo*) mutations that occur during early development. Mutations in any one of the four CAMK2 genes (CAMK2A, CAMK2B, CAMK2D, CAMK2G), described in Table 2, can lead to a CAMK2-related disorder with a wide range of cognitive, motor, and behavioral symptoms, as illustrated in Figure 2.

WHY ARE SO MANY UNDIAGNOSED?

- Most CAMK2 mutations are not inherited, so they often go undetected without a family history to prompt testing.
- Signs and symptoms overlap with more common disorders, leading to misdiagnosis of autism, epilepsy, or global developmental delay.
- CAMK2 genes are not yet included on many standard genetic diagnostic panels for autism or intellectual disability.
- There is still low awareness of CAMK2-related disorders among most health-care providers, especially those outside of specialist clinics.

To date, more than 200 unique mutations have been identified across these genes. Most distinct mutations have been identified in only one or very few individuals, though a few recurring mutations, such as one in CAMK2B, have been identified in several unrelated individuals with similar symptoms. The type and severity of symptoms can vary significantly, depending on which gene is affected and the specific mutation involved.

Fewer than 400 cases have been diagnosed worldwide, but the actual number is likely far higher. Many individuals remain undiagnosed or misdiagnosed when genetic testing is unavailable, or when it is available but not pursued. Because CAMK2 mutations typically occur spontaneously, we can expect them to arise at similar rates across all populations. Therefore, the current case count likely reflects disparities in both access to and use of diagnostic tools rather than true geographic or demographic variation.

In some cases, a genetic diagnosis may be overlooked when clinical features resemble more common conditions, such as autism spectrum disorder, leading clinicians to stop short of ordering more comprehensive genetic testing. Many families spend years navigating a "diagnostic odyssey," cycling through evaluations, referrals, and uncertainty before learning the root cause of the disorder and potentially missing key windows for intervention.

Most children with CAMK2-related disorders show signs within the first year of life. A common early indicator is low muscle tone (hypotonia), which may cause a baby to appear floppy or struggle to hold up their head, sit, or crawl. As they grow, many experience delays in motor development and speech, which are typically among the earliest and most persistent symptoms.

Across published cases, more than 75 percent share a core set of clinical features:

- intellectual disability
- impaired speech and language (both understanding and use)
- motor impairment
- global developmental delay
- atypical behaviors, including irritability, aggression, and autism-like traits

CAMK2-related disorders are not progressive, meaning affected individuals do not lose skills as they age. However, the developmental gap often becomes more pronounced over time as their peers grow, advance, and become more independent. Many individuals require ongoing support across all areas of daily life, and most families face significant emotional, financial, and logistical strain. With no approved treatments and limited clinical research, families face uncertainty at every stage.

Seizures and epilepsy are relatively common in CAMK2-related disorders and can further complicate the clinical picture. In these cases, early and consistent treatment of seizures is critical to improving long-term outcomes. In a subset of individuals with CAMK2D mutations, cardiac complications may influence life expectancy, making heart health an additional concern and underscoring the need for specialized coordinated care. Additional issues such as persistent low muscle tone, sleep disturbance, and gastrointestinal problems can have a profound impact on quality of life for both the patient and their family.

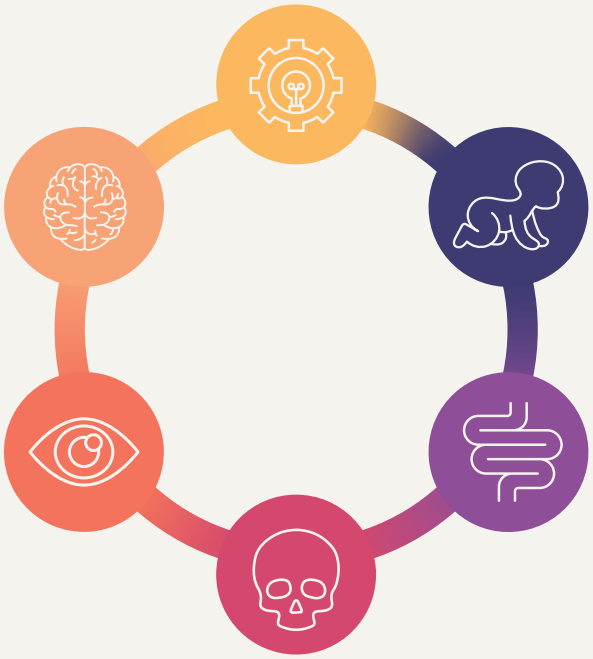
Figure 2. The Symptoms of CAMK2-Related Neurodevelopmental Disorders Are Often Systemic

Cognitive and Behavioral

- Intellectual disability
- Impaired speech and language
- Global developmental delay
- Atypical behavior

Neurological

- Seizures
- EEG abnormalities



Motor Function

- Motor impairment
- Hypotonia
- Involuntary movements

Sensory Function

- Visual impairment

Systemic and Other

- Digestive tract abnormalities
- Skin abnormalities
- Cardiovascular abnormalities

Craniofacial and Physical Anomalies

- Facial dysmorphisms
- Abnormal brain morphology
- Microcephaly or macrocephaly
- Limb abnormalities

Source: Milken Institute (2026)

Because CAMK2-related disorders were only recently recognized, researchers are still working to understand how clinical presentation changes with age and how specific gene variants influence symptoms and outcomes. Natural history studies (see information box), which follow individuals over time, are essential to developing future treatments and improving clinical care.

WHY NATURAL HISTORY STUDIES MATTER

What Is a Natural History Study?

A natural history study systematically tracks how a disease develops and changes over time in real patients. It gathers detailed clinical, genetic, and patient-reported data such as age at diagnosis, symptoms, test results, and quality-of-life measures from patients, caregivers, and clinicians.

Why Does It Matter?

By showing how a condition progresses and varies across individuals, natural history studies provide the foundation for therapy development. They help researchers define meaningful trial endpoints, identify biomarkers, and understand which patients might benefit most from specific treatments.

Biomarkers and outcome measures provide the proof needed to show that a treatment truly improves disease symptoms. Without this evidence, the FDA cannot approve new therapies for patients.

Impact for Rare Disease Communities

- Speeds development of diagnostic criteria and clinical care guidelines
- Improves design and readiness for clinical trials
- Strengthens the science and patient community voice in research
- Builds a shared evidence base that attracts industry and academic partners

Philanthropic support can make these studies possible by funding coordination, data management, and patient engagement, which are rarely covered by traditional research grants.

Mechanisms of Pathogenesis

Mutations in the CAMK2 genes disrupt the function of CaMKII proteins, which are essential for brain development and maintaining communication between neurons. These mutations can affect the protein in different ways: Some reduce or eliminate its activity (loss of function), others make it overactive (gain of function), and some interfere with the function of normal CaMKII proteins in the cell (dominant negative effects). While these categories help classify mutations, they don't fully capture how these changes disrupt complex brain development and function. To understand this, it helps to explore CaMKII's role in three critical brain functions.

Building Neural Circuits During Development

CaMKII is essential for constructing the brain's neural circuits during early development. It guides how neurons grow, branch out, and form connections with other cells to create the complex networks that support cognition, communication, and movement. Mutations in CAMK2 genes can disrupt neuron growth, branching, and connection formation, leading to atypical brain wiring. These disruptions are associated with conditions such as intellectual disability, autism spectrum disorder, and epilepsy. Because these processes occur early in development, understanding and targeting them offers a crucial window for intervention and an opportunity to develop more effective treatments.

Coordinating Neuronal Communication

After neural circuits are established, CaMKII remains essential for ongoing brain function. It helps neurons communicate by regulating key proteins involved in sending signals and by supporting the structure of synapses—the specialized junctions between neurons. To perform these roles effectively, CaMKII must be present in the right amounts, properly assembled, and localized at synapses where it helps anchor other important proteins in place and carries out its signaling functions. Some mutations in CAMK2 genes can reduce the levels of functional CaMKII by disrupting its production or speeding its degradation. Other mutations interfere with its ability to reach synapses or interact with partner proteins. These disruptions weaken communication between neurons and are linked to difficulties with attention, motor coordination, and behavior.

Fine-Tuning Neural Networks

CaMKII plays a key role not only in neuron communication but also in adjusting the strength of connections between neurons over time. This process, known as synaptic plasticity, is fundamental for learning, memory, and adapting to new experiences. Inside neurons, CaMKII acts like a molecular switch, turning other proteins on or off to strengthen or weaken synaptic connections. Mutations in CAMK2 genes can disrupt this balance; some reduce CaMKII's normal activity, while others cause it to become overactive. When this delicate balance is disturbed, the brain's ability to reshape its connections is compromised, negatively impacting learning, memory, and behavior.

By disrupting how the brain is built, how it operates, and how it learns, CAMK2 mutations contribute to the wide range of observed symptoms. Each mutation may have distinct effects, but they all interfere with the critical roles CaMKII plays in developing and maintaining healthy brain function. As researchers learn more about these molecular mechanisms, they move closer to developing targeted therapies that could correct or compensate for these disruptions, offering hope to individuals and families affected by CAMK2-related disorders.

Table 2. CAMK2 Gene Family—Four CAMK2 Genes with Unique Patterns of Expression and Roles Across Tissues and Developmental Stages

	CAMK2A	CAMK2B	CAMK2D	CAMK2G
Gene Name	Calcium/ calmodulin-dependent protein kinase II alpha	Calcium/ calmodulin-dependent protein kinase II beta	Calcium/ calmodulin-dependent protein kinase II delta	Calcium/ calmodulin-dependent protein kinase II gamma
Chromosomal Location	5p32	7p13	4q26	10q22.2
Protein Isoform Name	CaMKIIα	CaMKIIβ	CaMKIIδ	CaMKIIγ
Tissue Expression	Brain	Brain, skeletal muscle, small intestine, and endocrine tissues	Brain, heart, skeletal muscle, intestine, and lung	Ubiquitous: highest in brain and skeletal muscle
Expression Timing	Postnatal	Late prenatal to postnatal	Early prenatal	Early prenatal
Developmental Role	Forming and fine-tuning connections between neurons	Migration and branching of neurons	Migration of neurons	Development and branching of neurons
Functional Specialization	Strengthening connections between neurons, learning, and memory	Strengthening connections between neurons, learning, and memory	Memory persistence and maintenance	Spatial learning, long-term memory storage

Source: Milken Institute (2026)

Treatment

There are currently no therapies that directly address the underlying causes of CAMK2-related neurodevelopmental disorders. Today, treatment focuses on managing symptoms and supporting development through a combination of medical, therapeutic, and educational interventions. Care plans are highly individualized and often require coordination across multiple specialties.

Current efforts can be broadly divided into pharmacological and nonpharmacological approaches, with the goal of improving outcomes and quality of life.

Pharmacological Interventions

Some individuals with CAMK2-related disorders experience seizures, mood instability or neuropsychiatric episodes, and significant behavioral challenges. In these cases, clinicians may prescribe medications such as antiepileptic drugs (e.g., lamotrigine, valproic acid) to manage seizures or mood stabilizers or antipsychotics (e.g., lithium, risperidone) for mood or behavioral symptoms.

However, these medications are not specifically designed or tested for CAMK2-related disorders, and finding a safe and effective regimen requires trial and error, as treatment outcomes vary and may depend on the type of mutation.

Many commonly prescribed drugs—including some used to manage seizures, mood, or behavior—can affect calcium levels and calcium signaling pathways, or they can directly or indirectly influence CaMKII activity. Because CaMKII plays such a central role in brain development, plasticity, and neuronal communication, individuals with CAMK2 mutations may have atypical or unpredictable responses to drugs that modulate these pathways. A treatment that helps one patient may be ineffective or poorly tolerated in another. More research is needed to understand how different types of mutations influence drug response and to guide safer, more effective prescribing.

As our understanding of CAMK2 mutations and their impact on brain function grows, so does the opportunity to develop targeted, disease-modifying treatments that could change the course of these conditions.

Nonpharmacological Interventions

While medications can help manage certain symptoms, nonpharmacological therapies are essential for supporting development, communication, learning, and daily functioning.

Speech and language therapy: Because speech relies on precise coordination of brain, nerve, and muscle function, early intervention with a speech therapist is essential. Speech therapy can improve delayed language comprehension and challenges, producing clear, coordinated speech with specialized approaches that incorporate appropriate communication tools, such as visual aids, and focus on motor coordination and sound or word production. Improving verbal and nonverbal communication skills can significantly enhance quality of life for individuals with CAMK2-related disorders and their caregivers.

Occupational therapy: Occupational therapy assists in developing fine motor skills, improving daily living activities, and enhancing sensory processing abilities. Occupational therapy specialized for neurodevelopmental disorders and tailored to individual patients can promote independence, improve access to learning and play, and strengthen the ability to adapt and cope.

Physical therapy: Early intervention with physical therapy is essential for improving muscle strength, coordination, and gross motor skills. Individualized exercises are important for supporting better mobility, preventing joint stiffness, and improving overall physical development and function. For individuals with persistent muscle tone issues, periodic evaluation by a pediatric rehabilitation specialist is recommended to ensure appropriate support and mobility aids are in place.

Educational interventions: Specialized educational programs tailored to the individual's cognitive and developmental level are important. These programs often include individualized education plans that provide structured learning environments and appropriate accommodations. To guide educational placement and long-term planning, psychological or neuropsychological assessments are recommended at key stages of development (ages 3–4, 7–8, 11–12, and 15–16), ideally at centers experienced with intellectual and developmental disabilities.

Behavioral therapy: Behavioral interventions, such as Applied Behavior Analysis, can be beneficial in managing behavioral abnormalities and improving social skills. When tailored to an individual's specific needs, these therapies can help reduce problematic behaviors and enhance adaptive functioning.

Psychological support: Counseling and other psychological support for affected individuals and their families can help in managing the disorder's emotional and psychological impact. This support can include individual therapy, family therapy, and support groups.

Even with these interventions, many families report persistent unmet needs and challenges, including difficulty accessing services, uncertainty about prognosis, limited guidance on treatment, and significant emotional and financial stress. These gaps reflect a need for broader access to developmental and behavioral services; more precise, mutation-informed treatment strategies; and adequate psychosocial support for the entire family.

Funding for CAMK2-Related Neurodevelopmental Disorder Research

To identify where philanthropic investment could have the greatest impact, we analyzed a decade of public and private funding related to CAMK2. This review highlights current funding priorities, areas of scientific momentum, and, most importantly, critical gaps where targeted philanthropic support could accelerate progress.

While data limitations (e.g., incomplete reporting, restricted access to project-level details) prevent a fully comprehensive view, the available data offer valuable insights into how resources are currently allocated and where targeted investment could drive progress for the CAMK2-related disorders community.

NIH Funding for CAMK2 Research

Over the past decade, the NIH has awarded more than $55 million across 51 research grants related to CaMKII. While this reflects sustained scientific interest, annual investment has remained relatively modest, averaging just over $5 million per year. In the context of the NIH's nearly $48 billion annual budget, this represents only a small fraction of public funding, even as evidence linking CaMKII mutations to atypical brain development and function continues to grow.

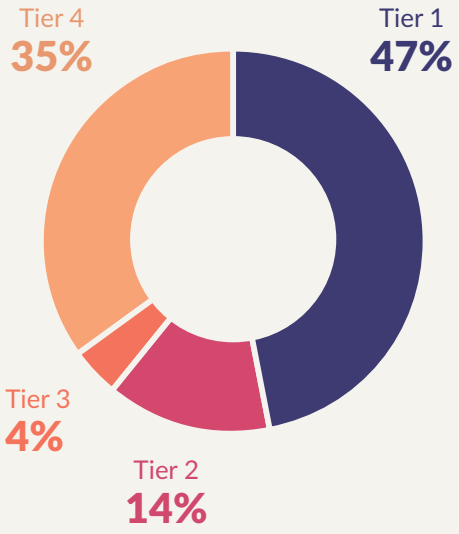
The following sections explore how public funding for CaMKII-related research has been distributed, including the types of studies supported, the NIH institutes involved, and the extent to which the portfolio advances translational goals—that is, efforts to move basic scientific discoveries toward new diagnostics or treatments. Together, the analysis reveals a critical gap: Despite a strong scientific foundation, CAMK2-related disorders remain underrepresented among federal research priorities.

What Is Being Funded

To better understand the focus and potential impact of NIH-funded CaMKII research, we reviewed all 51 publicly funded grants and assessed how closely they align with disease-relevant or translational goals. Figure 3 summarizes these results. While NIH investment has been steady over the past decade, the majority of funded projects are not focused on the brain. Instead, about half of all grants support either basic research into CaMKII's molecular function (14 percent) or studies on systems outside the brain, including studies of CaMKII in the heart, blood vessels, bones, and metabolism (35 percent), where it also plays a role.

Figure 3. US Public Funding Categorized by Relevance to CAMK2-Related Neurodevelopmental Disorders

Domestic Publicly Funded Research			
Relevance Tier	**Category**	**Description**	**Number of Grants**
Tier 1	Neuro-Relevant Research	CaMKII research relevant to brain function, cognition, or neurobehavior (directly or indirectly)	24
Tier 2	Basic Mechanistic Studies	Molecular-level studies of CaMKII signaling, structure, and activation	7
Tier 3	Non-Neuro Drug Development	CaMKII as a therapeutic target, focused on cardiac indications	2
Tier 4	Non-Neuro/ Systemic Research	CaMKII research in heart, vascular, bone, metabolism, or other non-neural systems	18



Source: Milken Institute analysis of NIH RePORTER, fiscal years (FY) 2016–2025 (2026)

Of the 51 NIH-funded CaMKII research grants, 24 (47 percent) were categorized as neuro-relevant—a term used here to describe studies focused on brain-related functions such as learning, memory, behavior, or synaptic signaling. While this subset includes some of the research most likely to inform future treatments, none of the funded projects directly target genetic CAMK2-related neurodevelopmental disorders. These conditions have been defined as distinct clinical entities with well-established links between CaMKII dysfunction and atypical brain development, but they remain absent from the current NIH funding portfolio.

Which NIH Institutes Are Investing in CaMKII Research?

Over the past decade, CaMKII-related research has been supported by 11 institutes within the NIH. However, nearly 75 percent of funding has come from just two: the National Heart, Lung, and Blood Institute (NHLBI) and the National Institute of Neurological Disorders and Stroke (NINDS). NHLBI has invested almost $22 million across 17 grants, indicating sustained interest in CaMKII's role in cardiac signaling and vascular biology. NINDS follows closely with over $18 million, focused largely on CaMKII's role in neuronal signaling, synaptic plasticity, and cognition—areas in which its biological significance is well established.

Beyond NHLBI and NINDS, several other NIH institutes have provided limited support for CaMKII research. The National Eye Institute, National Institute on Aging (NIA), and National Institute of General Medical Sciences have each contributed moderate funding, primarily for studies on CaMKII's role in vision, aging, and basic biology. In contrast, institutes with a focus on mental health, neurodevelopment, or rare diseases, such as the National Institute of Mental Health, National Institute on Drug Abuse, and National Institute of Diabetes and Digestive and Kidney Diseases, have made only minimal investments.

Table 3. US Public Funding by NIH Institutes and Centers

Institute/Center	**Funding (USD)** FY 2016–2025	Number of Grants
National Heart, Lung, and Blood Institute	$21,951,915	17
National Institute of Neurological Disorders and Stroke	$18,001,136	17
National Eye Institute	$3,535,802	2
National Institute on Aging	$3,477,059	7
National Institute of General Medical Sciences	$3,146,808	3
National Institute of Allergy and Infectious Diseases	$2,899,045	1
National Institute of Arthritis and Musculoskeletal and Skin Diseases	$571,800	1
National Institute of Diabetes and Digestive and Kidney Diseases	$243,415	1
Office of the Director	$236,725	1
National Institute on Drug Abuse	$178,866	2
National Institute of Mental Health	$28,702	1
Total	**$54,271,273**	**53***

**Number of grants exceeds the total number of unique grants funded because of supplements. The Office of the Director provided a supplement to an NIA-funded grant; NIA provided a supplement to an NINDS-funded grant.*

Source: Milken Institute analysis of NIH RePORTER data, FY 2016–2025 (2025)

This distribution suggests that CaMKII research is largely being funded for its role in general biology or in specific organ systems like the heart and brain, rather than through disease-focused initiatives aimed at specific patient populations. The limited engagement from institutes most aligned with neurodevelopmental disorders or genetic disease exposes a critical gap and highlights an opportunity to better align future funding with the emerging clinical relevance of CaMKII mutations.

Global and Emerging Funding for CAMK2 Research

Although CAMK2-related neurodevelopmental disorders have not yet attracted large-scale public funding in the US, early investment from international research agencies and philanthropic organizations signals growing recognition of their scientific and therapeutic relevance. These efforts, though still limited in number, are laying essential groundwork: advancing disease-focused research, supporting early-stage therapeutic development, and building the infrastructure needed to move the field forward.

The following subsections provide a brief overview of this early activity, highlighting international public investment and philanthropic support driven by patient advocacy and translational urgency.

International Public Funding

An analysis of international funding shows that several countries, including Canada, Australia, Japan, the Netherlands, and Germany, have made public investments in CaMKII-related research. Collectively, these international grants represent millions in public research dollars and underscore widespread scientific interest in CaMKII's role across systems such as the brain, heart, and immune function.

A few notable international research projects have begun to focus specifically on CAMK2-related neurodevelopmental disorders, marking early and important steps toward understanding disease mechanisms and therapeutic potential:

- **In the Netherlands**, the Dutch Research Council is supporting a project titled "Unravelling the Function of CAMK2 in Brain Development and Its Role in Neurodevelopmental Disorders," directly investigating the pathway's role in early brain development.
- **In Japan**, the Japan Society for the Promotion of Science is funding a research project titled "Elucidation of the Disease Mechanism of Neurodevelopmental Disorders Caused by CaMK2β Mutations," targeting a specific genetic subtype of the disorder.
- **In Canada**, a doctoral project funded by the Canadian Institutes of Health Research explores how disease-associated CaMKII variants affect synapse assembly and function, using *C. elegans* as a model.

These efforts represent a promising shift toward disease-focused, translational research outside the US, but they remain rare. Greater coordination and investment will be essential to sustain and expand this momentum.

It's important to note that global research funding data are often incomplete. Many countries do not publish centralized or searchable records of funded projects, and available information may lack key details such as disease focus, project titles, or funding amounts. To partially address this, our analysis also drew from scientific publications where funding acknowledgments confirm investment by various public agencies, particularly in East Asia, Europe, and Canada, not otherwise visible in public databases.

While this means the true scale of global investment in CAMK2-related research is likely underrepresented, the available data confirm widespread and sustained international scientific interest in CaMKII. The data also suggest additional disease-relevant efforts may already be underway, reinforcing the need for better tracking and coordination across borders.

Philanthropic Investment

While public investment in CAMK2-related neurodevelopmental disorders remains limited worldwide, early support from philanthropic and nonprofit funders is beginning to shape a new, more targeted research landscape. These initial grants reflect growing awareness of unmet needs and a commitment to building the infrastructure required for therapeutic progress.

Two foundations are currently leading philanthropic investment in translational research:

- **CAMK2 Therapeutics Network**—This recently established foundation focuses on advancing therapies for CAMK2-related disorders. In 2022, it awarded $27,000 in targeted research grants to generate patient-derived induced pluripotent stem cells (iPSCs) as a research tool and is currently building capacity to significantly increase its investment in translational research and clinical care. The foundation also received a Chan Zuckerberg Initiative Rare As One grant, which is supporting network and infrastructure development.
- **Dutch Hersenstichting (Brain Foundation)**—In 2024, this national brain foundation awarded €600,000 (~$699,000 USD) to support preclinical development of ASO therapies for CAMK2-related disorders, representing a significant investment in therapeutic and translational research.

These examples represent the only identified philanthropic funding streams supporting CAMK2-related research. Driven by a mix of patient advocacy, scientific initiative, and translational urgency, they are laying the groundwork for expanding the research ecosystem, catalyzing early-stage therapeutic work, and helping to position the field to attract larger-scale public and private funding. While the primary goal of these investments is to accelerate progress for individuals with CAMK2-related neurodevelopmental disorders, insights generated from this work may also have relevance for other disease areas in which CaMKII plays a pivotal regulatory role, including other neurodevelopmental or psychiatric conditions, cardiac and metabolic disorders, and aspects of digestive system function.

Together, these efforts mark a pivotal shift in CAMK2 research funding—from broad basic research to a more coordinated and disease-specific approach with a strong translational focus. Scaling philanthropic investment at this stage is essential to turning basic scientific discoveries into the real-world treatments affected individuals urgently need.

Therapeutic Pipeline Investment

While no industry programs directly target CAMK2-related neurodevelopmental disorders, recent advances in drug development have helped validate CaMKII as a viable therapeutic target in humans. Cardurion Pharmaceuticals has brought the first CaMKII inhibitor into clinical trials and is testing its lead compound in early-phase studies for a rare genetic heart condition. Although focused on cardiovascular diseases, this work establishes an important precedent by demonstrating that CaMKII modulation can be safely and effectively pursued in a clinical setting, a key milestone for future therapeutic applications.

Separately, public-private investment has also begun supporting CaMKII-targeted drug discovery in other areas. Notably, a 2018 initiative funded by the Lundbeck Foundation awarded kr10 million (~$1.56 million USD) to study CaMKII modulation in the context of stroke. This project, supported in collaboration with the Novo Nordisk Foundation and several international government agencies, explores the effects of gamma-hydroxybutyrate and related compounds on CaMKIIα. While not aimed at neurodevelopmental disorders, this research reflects increasing interest in small molecule modulation of CaMKII and may yield tools or mechanistic insights useful to other therapeutic efforts, including those focused on rare genetic conditions.

Together, these efforts demonstrate that CaMKII is a clinically actionable pathway. This progress lays a foundation that funders in the rare disease and neurodevelopmental space can build on to help de-risk and accelerate disease-specific therapies.

Philanthropic Opportunities for Advancing CAMK2-Related Neurodevelopmental Disorder Research

Our analysis of CAMK2 research and funding reveals some clear gaps: There is not enough coordinated investment or clinical infrastructure to drive progress efficiently. At the same time, there are some exciting opportunities to push toward new treatments. Decades of foundational work on CaMKII biology, combined with recent breakthroughs in genetic medicine, have positioned this field for meaningful therapeutic advances.

The opportunities shown in Figure 4 offer a strategic pathway for philanthropic and institutional funders to help translate discoveries into treatments. With targeted investment, the next phase of CAMK2 research can strengthen, align, and expand ongoing collaborations among clinicians, scientists, and families to drive innovation, improve care, and ultimately bring transformative therapies to those affected by CAMK2-related disorders.

Figure 4. A Strategic Pathway for Funders of CAMK2 Research

Networked Clinical Infrastructure

Support integrated care models and expand patient registries to improve clinical outcomes and enhance trial readiness. The ENCORE CAMK2 Center of Excellence offers scalable models that combine research, care coordination, and patient engagement.

- Establish a transatlantic Center of Excellence network.
- Fund natural history and real-world data collection.
- Support development of patient registries with deep phenotyping.
- Enable remote monitoring tools and decentralized trial capabilities.

Shared Preclinical & Biological Tools

Support unified efforts to functionally validate CAMK2 variants and develop high-throughput tools that bridge basic biology with clinical insight. Funding in this area will help uncover actionable genotype–phenotype correlations, laying the groundwork for patient-specific treatment strategies.

- Fund early-stage functional genetics to assess pathogenicity of variants.
- Support target validation and therapeutic mechanism studies.
- Create a modular preclinical pipeline (i.e., models + assays) adaptable to different genes/variants.

Bridge Team and Shared Data Ecosystem

Sustained progress in CAMK2-related disorders requires coordination, data integration, and translational alignment across the growing research and clinical community. A dedicated bridge team and shared data ecosystem will strengthen all other investments by fostering collaboration, supporting consistent data collection and use, and ensuring continuity across projects over time.

Biomarkers and Outcome Measures

Fund initiatives to identify, validate, and standardize disease-relevant biomarkers and clinical endpoints. These tools are essential for efficient trial design, regulatory approval, and ultimately, effective therapies and help to identify molecular targets and evaluate the efficacy of new therapeutic candidates.

- Pilot biomarker discovery and validation of molecular, imaging, and digital biomarkers.
- Support early surrogate endpoint qualification with regulators.
- Invest in development of patient-reported outcomes and quality-of-life metrics.

Therapeutic Development

Invest in development of targeted small molecules or genetic therapies tailored to CAMK2-related pathophysiology. Early-stage support for therapeutic pipelines, including drug repurposing and platform-based screening, can shorten the timeline from discovery to clinical application.

- Promote portfolio approaches (small molecules, ASOs, gene therapy).
- Explore targeted therapeutics for individual mutations and groups of mutations.
- Fund a precision repurposing initiative.

Source: Milken Institute (2026)

Establish Networked Clinical Infrastructure

Families affected by CAMK2-related disorders often struggle to find coordinated, expert care, while researchers lack the integrated clinical infrastructure and shared data needed to translate discoveries into therapies. The ENCORE CAMK2 Center of Excellence at Erasmus Medical Center in the Netherlands has demonstrated a successful model that brings clinical care, research, and patient engagement together under one roof. Expanding this model to additional sites, particularly in the US, could significantly increase access to coordinated care and create a more robust, data-rich environment for research. For a rare disease like CAMK2-related disorders, connecting families, clinicians, and scientists is essential to build the critical mass of patients, expertise, and data needed to advance both care and therapeutic development.

More such centers of excellence could serve as hubs for longitudinal data collection, decentralized clinical trials, and translational research, while improving daily care and building community trust. By embedding research and care within one clinical ecosystem, this network would accelerate discovery while ensuring scientific progress remains closely aligned with the real-world needs of patients.

Strategic Investment Opportunities

Philanthropic investment should focus on three complementary areas, each building a critical component of a connected ecosystem for care and research:

- **Expand Centers of Excellence**—Fund global centers modeled on ENCORE to provide expert coordinated care, integrate research and family support, and follow patients over time.
- **Strengthen data and registries**—Connect and expand patient registries and natural history studies that link genetics, clinical data, and outcomes, creating the foundation for future trials and biomarker development.
- **Enable digital tools and decentralized trials**—Support remote monitoring, telehealth, and decentralized trial infrastructure to make participation easier for families worldwide and generate high-quality, real-world data.

Impact and Strategic Value

These investments will immediately expand access to expert care, significantly improving quality of life for families while generating the high-quality data needed to accelerate therapy development. Over time, they will establish the integrated clinical and research infrastructure required to launch future trials and lay the groundwork for the first transformative treatments for CAMK2-related disorders.

Invest in Shared Preclinical and Biological Tools

While scientific momentum is building and dedicated researchers are actively engaged, progress toward therapies for CAMK2-related disorders remains limited by fragmented funding and insufficient shared infrastructure. A growing number of rare genetic variants are being identified as drivers of CAMK2-related

disorders, each causing distinct, and sometimes opposing, effects on protein function and neuronal signaling. For example, some variants cause excessive activation of CAMK2 signaling, while others suppress it. Understanding how these variants alter molecular pathways is essential in uncovering therapeutic targets and designing precision treatments.

A small but highly committed network of researchers is already collaborating to characterize CAMK2 variants, develop models, and test interventions. However, because these groups rely on individual grants and project-specific funding, coordination happens informally and on a limited scale. The absence of dedicated shared resources slows progress and makes it difficult to sustain collaboration over time. Strategic philanthropic investment can unify and scale existing research efforts by creating a shared, modular preclinical pipeline that links variant biology to patient characteristics (phenotype) and therapeutic discovery. By supporting access to validated models, standardized assays, and collaborative infrastructure (for example, a variant database), funders can help accelerate functional interpretation of variants and uncover actionable genotype–phenotype relationships, paving the way for patient-specific therapies.

Strategic Investment Opportunities

Targeted philanthropic investment can strengthen the CAMK2 research ecosystem by building shared tools, common infrastructure, and collaborative capacity across the field. Together, these four complementary areas form the foundation for a coordinated preclinical pipeline, offering the greatest potential for impact:

- **Functional assessment of variants—**Expand high-throughput testing platforms and standardize approaches to evaluate and classify CAMK2 variants, linking genetic changes to their functional impact and clinical relevance.
- **Model and assay development—**Create validated animal and cell-based models that represent key variant types and symptoms and make these tools broadly available to accelerate translational research.
- **Therapeutic mechanisms and target discovery—**Support studies that identify and validate therapeutic targets, investigate shared disease mechanisms, and connect academic and industry drug discovery efforts.
- **Coordination and data sharing—**Fund the coordination of collaborative working groups, establish a centralized data platform, and host regular meetings to align priorities, share results, and reduce duplication.

Impact and Strategic Value

Investments in shared preclinical and biological tools will immediately strengthen the research ecosystem, reduce duplication of efforts, and increase transparency and collaboration. Over time, these investments will establish a scalable, modular pipeline linking variant biology to therapeutic development. This will produce validated models and assays, uncovering convergent disease mechanisms and laying the foundation for patient stratification, trial design, and precision therapies. By de-risking early infrastructure development, philanthropic investment can attract subsequent public and industry funding, multiplying the return on impact.

Ultimately, these shared resources will transform independent discoveries into collective progress, bringing new treatments closer to families affected by CAMK2-related disorders.

Advance Therapeutic Discovery and Development

The ultimate goal for families affected by CAMK2-related neurodevelopmental disorders is the development of targeted therapies that address the underlying molecular and cellular dysfunction. As scientific understanding of these disorders improves, there is increasing urgency to identify and test potential treatments that can meaningfully improve outcomes. Multiple therapeutic strategies hold promise, including small molecules, ASOs, gene therapy, and repurposed drugs. However, a lack of coordinated investment and a systematic approach to advancing these strategies is limiting progress.

Philanthropic investment at this stage can be transformative. By supporting portfolio-based approaches that recognize the biological complexity of CAMK2-related disorders, funders can help de-risk and accelerate the development of new therapies. These investments can enable both broad, platform-based discovery efforts and patient-specific solutions to move forward and create a more comprehensive therapeutic pipeline that delivers precision treatments to all affected individuals.

Strategic Investment Opportunities

Philanthropic support can drive progress by advancing a coordinated, multipronged approach that accelerates both broad therapeutic strategies and treatments tailored to individual patient needs. Key opportunities include:

- **Therapeutic screening and drug repurposing—**Support high-throughput screening platforms, such as fly or cell-based models, to identify compounds that rescue CAMK2-related dysfunction. This will include funding for drug repurposing studies, with a focus on FDA-approved compounds that may have potential CAMK2-relevant mechanisms. Leveraging existing genetic models and compounds could quickly identify new therapeutic options.
- **ASO development for gain- and loss-of-function mutations—**While ongoing efforts focus on gain-of-function mutations, there is a critical need to develop ASOs for loss-of-function mutations in CAMK2-related disorders, which are currently underexplored. Investment here could support lead optimization, in vivo studies, early regulatory planning, and preclinical toxicology studies, helping prepare these candidates for potential investigational new drug (IND)-enabling work.
- **Gene therapies—**Gene therapy approaches, such as gene editing and gene replacement, hold long-term promise to correct underlying genetic dysfunction in CAMK2-related disorders. Although these strategies are not yet actively pursued, they offer a promising investment in future targeted therapies. Support for preclinical research and early-stage feasibility studies will help establish the foundation for gene therapies.
- **Precision repurposing fund using patient molecular (multi-omic) data—**Establish a precision repurposing initiative that leverages patient molecular data, such as transcriptomic, proteomic, and metabolomic profiles, to identify shared molecular pathways and drug candidates. Where feasible, data from accessible tissues, such as nasal swabs, can provide valuable insights into systemic changes linked to neuronal dysfunction, even if the tissue is not directly neuronal. Integrating these complementary data types across diverse patient populations may uncover converging molecular mechanisms and prioritize existing drugs that target those pathways, enabling more personalized treatments for subsets of patients.

Impact and Strategic Value

Investments in therapeutic discovery will accelerate the development of precision treatments for CAMK2-related disorders. By supporting high-throughput screening, ASO development, and gene therapies, funders can help identify and optimize therapies targeting the full spectrum of genetic variants. Incorporating patient molecular data will ensure drug repurposing efforts remain grounded in real-world biology. These investments will create a coordinated, adaptable pipeline, de-risking the field and laying the groundwork for the first targeted therapies.

Catalyze Biomarker Discovery and Outcome Measure Development

Although researchers are making progress in understanding CAMK2-related neurodevelopmental disorders, the field lacks validated biomarkers and clinical outcome measures needed to support trials for new therapies. Designing trials, selecting meaningful endpoints, and meeting regulatory requirements are especially challenging given the small and geographically dispersed patient population. Advancing this work requires coordinated efforts to collect and standardize clinical and molecular data, test potential biomarkers, and engage early with regulatory authorities.

A small but dedicated network of clinicians and investigators is generating important patient data, but there has been little investment in systematically developing the tools needed for trial readiness. Strategic philanthropic support can establish validated biomarkers and outcome measures, create the infrastructure for clinical studies, and expedite regulatory preparation. By funding pilot studies, patient-reported outcomes, and early biomarker validation, funders can lay the groundwork for the first clinical trials, helping to ensure that new therapies reach families without unnecessary delay.

Strategic Investment Opportunities

Philanthropic investment can accelerate clinical trial readiness by supporting the identification, validation, and standardization of disorder-relevant biomarkers and clinical outcome measures. Three complementary actions will establish the infrastructure needed to enable well-designed and actionable CAMK2 clinical trials:

- **Foundational data and sample collection**—Support expanded collection of clinical, molecular, and imaging data and biological samples across patient populations. Establish advisory groups to guide priorities, standardize methods, and integrate existing data.
- **Pilot biomarker and outcome measure development**—Invest in early studies to evaluate molecular, imaging, and digital biomarkers. Develop patient-reported outcomes and quality-of-life metrics. Refine clinician-reported assessments and link biomarkers with clinical data to explore potential trial endpoints.
- **Regulatory and trial readiness preparation**—Engage with regulatory authorities to align biomarker and outcome measure development with their qualification pathways. Develop clinical trial protocols and feasibility studies to test data collection processes and endpoint usability.

Impact and Strategic Value

Investments in biomarkers and outcome measures will immediately create the tools needed to design and evaluate clinical trials for CAMK2-related disorders, while also supporting translational research to identify and prioritize therapeutic candidates. By funding pilot biomarker studies, patient-reported outcomes, and early regulatory engagement, funders can generate standardized, high-quality data to inform trial endpoints and feasibility. Over time, these efforts will establish a coordinated infrastructure for clinical research, enabling rigorous evaluation of new therapies and accelerating the path from discovery to impactful therapies for patients.

Establish a Bridge Team and Shared Data Ecosystem

As progress accelerates across research and clinical efforts in CAMK2-related disorders, the need for continuous coordination and data management grows. The systems and staffing needed to connect discoveries, manage shared data, and sustain collaboration rarely receive dedicated, sustained funding, but without this support, even the most promising efforts risk becoming siloed, redundant, or disconnected from long-term impact. These behind-the-scenes structures are often treated as temporary or secondary, despite being essential to translating scientific progress into outcomes for patients.

Critically, the early stages of a research program are the most important for establishing this infrastructure. Building data sharing and coordination into the foundation enables rapid data collection and analysis, minimizes duplication, and fosters continuous collaborative learning. Few rare disease areas have the opportunity to design these systems from the outset; CAMK2-related disorders are early enough in their development that investing in these frameworks now will save significant time and resources later.

Strategic philanthropic investment can address this gap by establishing a bridge team and shared data ecosystem that connects researchers, clinicians, and families across the CAMK2 community. Embedding dedicated experts in operations, translational research, and data management and analysis will create the backbone that links discovery to therapy. By ensuring that information, resources, and relationships are coordinated over time, this investment will amplify the impact of every other effort in the field and build a foundation for sustained progress.

Strategic Investment Opportunities

Philanthropic investment can ensure long-term success in CAMK2-related disorders by providing the infrastructure needed for sustained collaboration and data integration. The following efforts will prevent siloed work and enable a seamless, coordinated flow of information and resources that will drive innovation and long-term impact across the field:

- **Dedicated bridge team**—Fund the hiring of key personnel to manage collaborative grants, track progress, align efforts across institutions, and oversee data entry into a shared platform. This team will include translational research coordinators to bridge communication among basic scientists, clinicians, and patient communities, ensuring seamless coordination and data flow across the CAMK2 ecosystem.
- **Shared data ecosystem**—Develop a centralized data platform to store, share, and curate genetic, clinical, and functional datasets. Establish data governance aligned with FAIR principles (findable, accessible, interoperable, and reusable) and support multimodal data entry from clinical sites, research labs, and patient platforms.
- **Community building and coordination**—Support the organization of an annual CAMK2 Scientific Meeting to align research priorities, share findings, and foster collaboration, while acting as a hub for integrating new collaborators and partnerships within the ecosystem.

Impact and Strategic Value

Investing in a bridge team and shared data ecosystem will establish a sustainable foundation for long-term collaboration and data integration across the CAMK2 ecosystem. This strategic investment will enhance coordination across research, clinical, and advocacy efforts, ensuring alignment and optimized use of data. By facilitating the exchange of information and supporting collaboration, funders will help drive continuous progress and accelerate the translation of research into treatment for patients.

Conclusion

CAMK2-related disorders are rare genetic conditions that profoundly affect brain development, learning, and daily functioning. Scientific understanding of CAMK2 biology is extensive, but research focused specifically on CAMK2-related neurodevelopmental disorders is recent and remains severely underfunded. Today, only a handful of research groups worldwide focus on these disorders, and translational efforts toward targeted therapies are still in their early stages.

This report identifies strategic opportunities where philanthropic investment can have an outsized impact. By supporting coordinated centers of excellence, shared preclinical tools, targeted therapeutic discovery, biomarker and outcome measure development, and a centralized data infrastructure, funders can accelerate research, enhance collaboration, and move the field from basic discovery toward a pipeline of tangible therapies. These investments would address the urgent needs of the hundreds of individuals diagnosed today while laying the groundwork to prevent future families from facing the immense challenges these disorders bring.

With timely and focused investment, the CAMK2 field has the opportunity to translate decades of research into therapies that meaningfully improve the lives of affected individuals and families.

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About the Authors

Nadia Penrod, PhD, leverages her interdisciplinary scientific expertise in biomedicine and informatics toward initiatives in SPARC's Rare Diseases focus area. Previously, as an academic scientist, she built a diverse research portfolio spanning cancer genomics, molecular pharmacology, and mind-body medicine; as a science writer, she covered topics in sustainable agriculture and food for health. Penrod holds a PhD in experimental and molecular medicine from the Geisel School of Medicine at Dartmouth College and a bachelor's degree in biochemistry from Indiana University of Pennsylvania.

Elizabeth Burke, PhD, focuses on philanthropic investment in rare diseases and cancers, leveraging her expertise in rare disease research, including neurodevelopmental and neurodegenerative disorders. Previously, Burke was a scientist in the NIH Undiagnosed Diseases Program, where she managed patient matching, data sharing, and biospecimen repository and coordinated research focused on extremely rare or novel disorders. She holds a PhD in molecular medicine and translational science from Wake Forest University and a bachelor's degree in biology from Carleton College.

Cara Altimus, PhD, leads SPARC at the Milken Institute. She is also the Managing Director of Breakthrough Discoveries for thriving with Bipolar Disorder (BD2), a philanthropic initiative launched out of SPARC. Previously, Altimus led the Neural Interfaces Laboratory at the FDA. She serves as the chair for the Trainee Advisory Committee for the Society for Neuroscience and as an advisor to the Ontario Brain Institute. Altimus holds a PhD in biology from Johns Hopkins University and a bachelor's degree in genetics from the University of Georgia.

Caitlyn Barrett, PhD, manages SPARC's work in the Rare Diseases and Cancer focus areas. She also serves on the Board of Directors of the Coalition Against Childhood Cancer. Previously, Barrett was the senior director of research and programs at CureSearch for Children's Cancer. She also established the Human Cancer Models Initiative at the Office of Cancer Genomics at the National Cancer Institute and completed postdoctoral research training at the Pittsburgh Institute for Neurodegenerative Disease at the University of Pittsburgh. Barrett holds a PhD in cancer biology from Vanderbilt University.


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