Making connections for research, care and progress

CAMK2 Strategic Research Roadmap (2026 – 2031)

Executive Summary

CAMK2 Therapeutics Network Strategic Roadmap (2026–2031)

This strategic roadmap for the CAMK2 Therapeutics Network represents a unified vision developed in close partnership with families, clinicians, and researchers from around the world. Informed by extensive community feedback and shaped through a global strategic planning session, this document reflects the shared priorities of those most impacted by CAMK2-related neurodevelopmental disorders. It will serve as the guiding framework for the Network's activities over the next five years, providing a clear path from foundational research infrastructure to therapeutic readiness.

In 2026, the focus will be on establishing the essential platforms to support long-term progress. This includes launching a centralized CAMK2 Variant Portal to integrate biochemical, structural, clinical, and preclinical data, building a robust research asset platform including biospecimen repositories and genomic data, establishing a clinical center of excellence to standardize care and research integration, and formalizing a global coalition to foster collaboration, data sharing, and shared governance.

From 2027 to 2030, the Network will prioritize translational research and the development of tools needed to advance therapies. Key goals include designing and validating outcome measures, biomarkers, and clinical endpoints; screening therapeutic candidates using patient-derived models and expanded preclinical systems; and leveraging multiple model organisms to explore CAMK2 function across biological systems and identify promising compounds for further development.

By 2031, the roadmap culminates in preparation for therapeutic development and clinical trials. This includes advancing candidate therapies across multiple modalities—such as small molecules, genetic therapies, and gene expression modulators—stratifying patient cohorts based on variant-specific insights, and publishing clinical management guidelines informed by longitudinal data.

Together, these coordinated efforts reflect the CAMK2 community's deep commitment to accelerating research, improving clinical care, and delivering hope for meaningful treatments.

CAMK2 Therapeutics Network Mission and Vision

The CAMK2 Therapeutics Network is a family-led, scientifically grounded global initiative dedicated to improving the lives of individuals with CAMK2-related neurodevelopmental disorders.

Informed by the experiences and priorities of affected families and shaped through collaboration with leading clinicians and researchers, our mission is to educate the community, expand access to diagnosis and expert care, and fast-track the development of meaningful treatments.

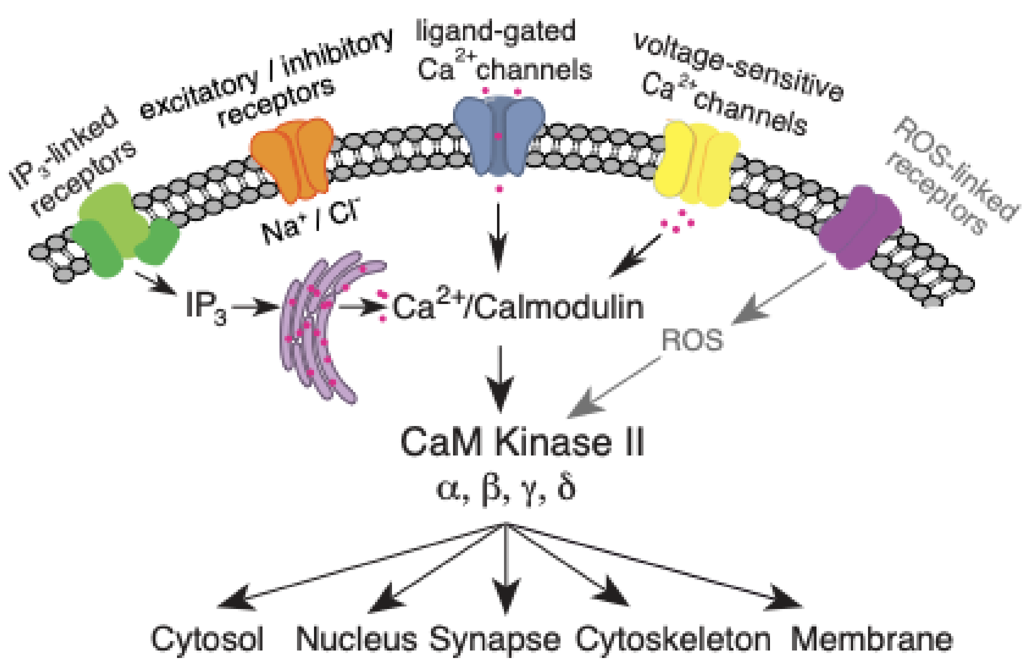
Our vision is to build a strong international CAMK2 community, advance near-term therapies through drug repurposing, and ultimately pursue a cure through precision genetic approaches.

What is CAMK2?

Calcium/calmodulin protein kinase II (CaMKII) α, B, γ, and δ are a family of proteins encoded by the CAMK2 A, B, G, and D genes.

***Critical role in learning and memory**, CaMKII plays a central role in calcium signaling through interactions with calcium channels and their effectors AND by regulating downstream calcium signaling.*

Mutations in CAMK2 genes cause dysregulation of CaMKII. Disordered calcium signaling causes significant symptoms in the brain, heart, or both—depending on where the specific α, B, γ, or δ is expressed.



Symptoms of CAMK2 Related Disorders

CAMK2-related disorders are a group of rare neurodevelopmental conditions caused by pathogenic variants in the ***CAMK2A, CAMK2B, CAMK2D****, and* ***CAMK2G*** *genes, which encode different subunits of the CaMKII protein complex—a key regulator of learning, memory, synaptic plasticity, and cellular signaling across multiple organ systems. These disorders typically present in early childhood and are associated with a broad range of symptoms, including intellectual disability, developmental delays, emotional dysregulation, pain crises, epilepsy, motor and speech impairments, autism spectrum behaviors, and, in some cases, cardiac or gastrointestinal abnormalities. Due to the functional diversity of CaMKII and the variability in mutation types and locations, individuals with CAMK2-related disorders experience a wide spectrum of clinical presentations. As a recently identified group of conditions, there are currently no targeted therapies, and treatment remains supportive, highlighting the urgent need for coordinated research and therapeutic development.*

CAMK2 Therapeutics Network Major Accomplishments

Recruitment and Logistical Support for CAMK2 Encore Natural History Study

Funded first and second International CAMK2 Summits

Close collaboration with first CAMK2 Center of Excellence in the Netherlands

Hired professional operations team

Published foundational case report and review to guide drug repurposing

Initial fundraising campaign raised over $150,000

Secured $800,000 Chan Zuckerberg Rare As One capacity building grant

Funded travel grants for patient participation in research programs

Strategic Research Roadmap Purpose

The development of the CAMK2 Therapeutics Network Strategic Research Roadmap is a critical step in aligning the CAMK2 community around a clear, actionable plan to accelerate progress over the next five years. This roadmap is essential to focus limited resources, guide research priorities, and ensure efforts are directed toward the most impactful outcomes for affected individuals.

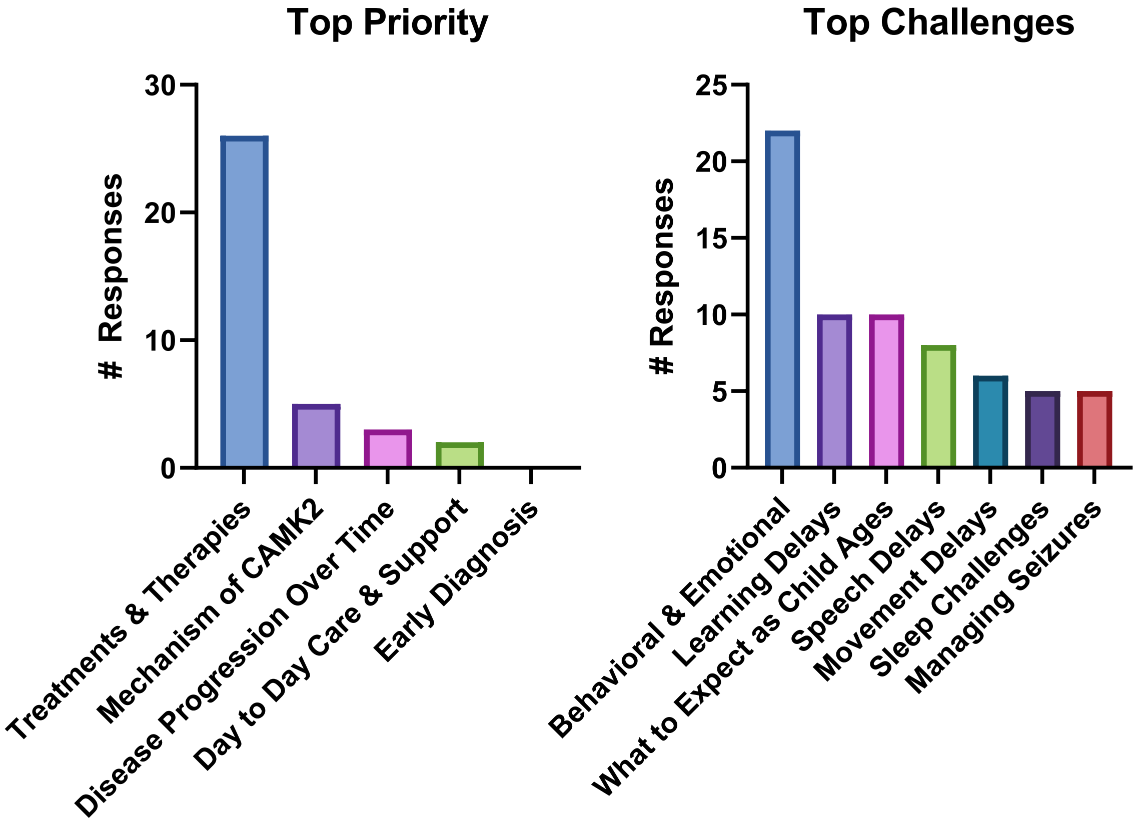
To shape this plan, we first engaged the CAMK2 community in a virtual meeting to gather input on their most urgent needs and priorities.

We then convened an in-person session with an international panel of clinicians, researchers, and families to refine these priorities and build a shared strategy for driving research, improving care, and advancing treatments.

The Voice of the CAMK2 Community

The top priorities and challenges of families and caregivers of CAMK2 Related Disorders were discerned from the Summer 2025 CAMK2 Community meeting via polling of 40+ families.

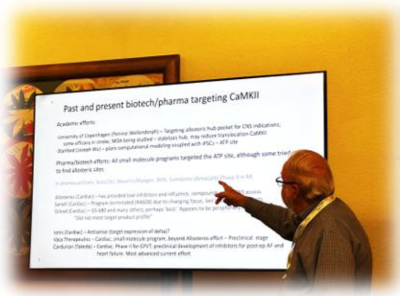
High priorities include treatments and therapies, particularly addressing behavioral and emotional challenges related with CAMK2 Related Disorders.



The Voice of International Researchers, Clinicians, and Families

The top priorities and challenges of the CAMK2 Related Disorders international research and clinical community were discerned from the Summer 2025 CAMK2 Strategic Roadmap Session held on July 9, 2025 in Orlando, Florida..

Attending this meeting were:



Bonnie Dwyer, MD
Ian Carroll, MD
Matt Gibbs
Nev Ross
Howard Schulman, PhD
Margaret Stratton, PhD
Danielle Veenma, MD PhD
Geeske van Woerden, PhD
Brad Bryan, PhD MBA
Dianne Mitchell, PhD
Nikki Stusick
Liat Vaknin-Nisan

Five Year Goal for CAMK2 Therapeutics Network

By 2031, the CAMK2 Therapeutics Network aims to establish a fully coordinated community that is clinical-trial ready and poised to advance novel therapeutics toward effectively treating CAMK2-related disorders.

Top Strategic Research Roadmap Priorities Identified

•**Establishing foundational infrastructure** including a centralized CAMK2 Variant Portal to integrate biochemical, clinical, and genetic data for variant classification and patient stratification.

•**Expanding research assets** through longitudinal natural history studies, biospecimen biorepositories, and comprehensive genomic sequencing to better understand disease mechanisms and modifier genes.

•**Building strong multi-stakeholder partnerships** via patient advocacy group coalitions to promote data sharing, collaboration, and aligned governance.

•**Creating Clinical Centers of Excellence** to provide expert, multidisciplinary care and standardize data collection across sites.

•**Developing and validating outcome measures and biomarkers** to support clinical trials and track disease progression.

•**Screening and prioritizing therapeutic candidates** using patient-derived models and expanded preclinical systems.

•**Advancing multi-modal therapy development** including small molecules, gene therapies, and gene expression modulators, supported by robust variant stratification for clinical trial readiness.

•**Publishing clinical management guidelines** to improve clinical care and prepare the community for emerging treatments.

These priorities reflect a focus on building the necessary research and clinical infrastructure to accelerate therapeutic development and improve patient outcomes.

2026: Foundation Building

Goal: Establish core infrastructure to support long-term research and therapeutic development.

•Launch **CAMK2 Variant Portal** to integrate functional, structural, clinical, and preclinical data.

•Expand the **Research Asset Platform**, including:

- Continuation of the ENCORE natural history study.
- Collection of patient biospecimens.
- Identify CAMK2 modifier genes.

•Establish a **CAMK2 Clinical Center of Excellence** at a major medical center in the US.

•Form a **Channelopathy Coalition** with governance and data-sharing frameworks.

🔹 *2027–2030: Translational Research & Outcome Development*

Goal: Turn foundational data into actionable tools, models, and therapies.

•**Design and validate outcome measures** (e.g., clinical endpoints, imaging, functional scales).

•Conduct **therapeutic candidate screening** using:

- Repurposed drugs.
- Patient-derived cellular models and biochemical assays.

•**Develop expanded preclinical models** (Zebrafish, Drosophila, Xenopus, Rodents) to study variant effects and screen for potential therapeutics.

•**Map CAMK2-related pathways** using phenotypic screens to better understand disease biology and therapeutic targets.

🔷 *2031: Therapeutic Development & Clinical Readiness*

Goal: Prepare for clinical trials and future treatments.

•Advance **multi-modal therapy development**, including:

- Small molecules
- Genetic therapies (ASOs, CRISPR, base editing)
- Gene modulators targeting expression or downstream pathways

•Define **trial-ready patient cohorts** using stratification from the Variant Portal.

•Publish **clinical practice guidelines** based on longitudinal data and expert consensus.

•Lay groundwork for **CAMK2 clinical trials** in collaboration with key academic and industry partners.

Metrics and Evaluation

- **Data Integration and Variant Classification**
  - Number of CAMK2 variants submitted, curated, and functionally annotated in the Variant Portal.
  - Percentage of variants stratified by functional and clinical impact.
- **Research Asset Expansion**
  - Number of patients enrolled and data points collected in the natural history study.
  - Volume and diversity of biospecimens collected and stored.
  - Number of whole genome/exome sequences completed and analyzed.
- **Clinical Center of Excellence**
  - Number of multidisciplinary clinical visits and standardized data entries.
  - Frequency and outcomes of multidisciplinary case reviews.
  - Patient satisfaction and engagement metrics.
- **Community and Partnership Engagement**
  - Number of active collaborators in the Channelopathy Coalition.
  - Number and geographic distribution of families and clinicians engaged through meetings and outreach.
  - Frequency of consortium meetings and data-sharing events.
- **Outcome Measure Development**
  - Number of validated clinical endpoints, biomarkers, and functional scales developed.
  - Pilot studies completed using new outcome measures.
- **Therapeutic Candidate Screening**
  - Number of compounds screened and prioritized.
  - Identification of lead therapeutic candidates with demonstrated efficacy in preclinical models.
- **Preclinical Model Development**
  - Number of new animal or cellular models established.
  - Number of phenotype screens completed and mapped pathways identified.
- **Therapeutic Development and Trial Readiness**
  - Number of preclinical safety and efficacy studies completed.
  - Defined patient cohorts prepared for clinical trial enrollment.
  - Publication and dissemination of clinical management guidelines.
- **Overall Impact**
  - Progress toward clinical trials initiation.
  - Evidence of symptom relief or improved patient outcomes in natural history or interventional studies.
  - Growth in network membership and international collaborations.

CAMK2 Therapeutics Network

Making Connections for Research, Care, and Progress