PATH TO TREATMENT
Two-Year Plan to First Clinical Trial

Contact: impact@kif1a.org
KIF1A.ORG is a parent-led organization established in 2017 to launch the world’s first translational research program dedicated to discovering treatment for people affected by KIF1A Associated Neurological Disorder (KAND). There is no cure or treatment for this neurodegenerative disorder. Yet.

Our organization supports researchers who engage in collaborative and translational work to rapidly discover treatment for this generation of KAND patients. We have made tangible progress over the last three years, but time is running out. 2020 is a transformational year for KIF1A with a clear path to clinical trials.

This Path to Treatment outlines our immediate therapeutic strategy with defined objectives and resources needed to bring treatment options to families affected by KAND.
The first step toward treatment: identify the disorder and find patients.

- **2011**
  - First KIF1A patient identified

- **2016**
  - Dr. Wendy Chung of Chung Lab (Columbia University, NYC) sees her first KIF1A patient, Susannah
  - Susannah’s family starts building KIF1A.ORG

- **2017**
  - Chung Lab launches world’s first pre-clinical research program for KIF1A Associated Neurological Disorder (KAND) & becomes a center of excellence

- **Present**
  - 200–300 known KAND patients today
  - Tens of thousands likely misdiagnosed or undiagnosed
In order to develop KAND treatment, we must understand the disorder and create a longitudinal clinical picture of the disease. Our natural history study (NHS) gathers patient information to track how the disorder develops over time without treatment.

Chung Lab manages the world’s only KIF1A NHS. In this comprehensive, longitudinal study, patient data is continuously collected from enrolled families to track how KIF1A mutations affect patients’ development & health over time.

Information collected includes genetic test results, developmental & medical history, symptomatic treatment, MRI, EEG, medical records, & patient/caregiver-reported data. KIF1A families are highly engaged in the NHS.

The KIF1A NHS has 150+ enrolled patients & continues to enroll newly diagnosed families. We have learned much about how KIF1A affects patients since starting the NHS in 2017. For the latest information, visit kif1a.org/nhs.
# OUTCOME MEASURES & BIOMARKERS

Our goal is to create treatment that is safe, effective, and meaningful to families.

### OUTCOME MEASURES
What are meaningful therapeutic changes for KAND families?

- Seizure reduction?
- Improved cognition?
- Reduced spasticity?

### BIOMARKERS
What can we measure in the body to evaluate change from baseline?

- Brain waves through EEGs?
- Cerebrospinal fluid?
- Neuron density/function?

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**What’s Next**

KAND families play a crucial role in research & development by providing valuable input on meaningful outcome measures. Our active community regularly provides samples needed to build a robust KIF1A biobank at Chung Lab. These samples are freely accessible to members of the scientific community, including biotech. Developing early biomarkers & outcome measures readies our community for clinical trials with appropriate endpoints.
Researchers can also produce miniature 3D brains that closely resemble full-size brains of KIF1A patients.

Mouse models with KIF1A mutations have been developed by The Jackson Laboratory & Chung Lab. These animal models are available to the scientific community.

With a diverse & expanding resource of KIF1A models, researchers are understanding more about the disease. These tools allow researchers to test existing compounds (medicines) & new therapeutics in the lab before starting clinical trials in humans.
Scientists believe KAND is caused by dominant negative mutations in KIF1A. This rare mechanism of disease means mutations in KIF1A damage the protein encoded in the gene. This damaging effect prevents healthy function of the KIF1A protein, a protein that is vital for brain & nerve function.

For a basic science introduction to KIF1A, visit kif1a.org/what-is-kif1a.
Three therapeutic approaches, or modalities, are the focus of our pipeline: small molecule, gene therapy, and antisense oligonucleotide therapy (ASO). Our strategy is to pursue multiple approaches in parallel, and rapidly bring treatments to the clinic in 2021.

**Small Molecules** include most drugs on the market today. In 2020, KIF1A researchers will conduct high-throughput drug screening, using technology to rapidly test thousands of compounds & identify possible drug candidates for KAND. This includes repurposing existing drugs with an established safety record that have already been developed to treat other diseases. This repurposing can save time & money in the therapeutic development process.

**Gene therapy** is the process of replacing defective genes with healthy ones, adding new genes to help the body fight or treat disease, or deactivating problem genes. Learn more from the FDA. There are several gene therapy approaches to consider for KAND, like replacing defective KIF1A genes with healthy copies, or recruiting a different gene or pathway to compensate for the dysfunctional KIF1A protein caused by mutations in the gene.

**ASOs** or antisense oligonucleotides are synthetic strands of nucleic acids that can bind to messenger RNA (instructions for protein production) to alter a gene’s expression. For example, if a KAND patient has a healthy copy of KIF1A & a mutated copy of KIF1A (heterozygous), an ASO could reduce, or “knock down,” disease-causing proteins without interfering with the body’s healthy copy of KIF1A.
Before we start clinical trials in humans, we’ll test our best therapeutic options in the lab to evaluate safety. Preclinical research takes place *in vitro* and *in vivo*.

**In Vitro**
Latin for “in glass”—think of experiments taking place in petri dishes or test tubes using organism components like iPS cells.

**In Vivo**
Latin for “within the living”—think of experiments with animals like mice living with KIF1A mutations.

Preclinical trials allow us to make informed decisions before designing clinical trials for humans. How might the drug affect the body? Does the drug have any toxic effects? Does the drug provide therapeutic benefit? What is a safe dosing strategy? Regulatory agencies (FDA) will not allow clinical trials in humans without strong preclinical data.
Our objective is to create global clinical trials and bring treatment to this generation of KAND patients. With increased resources, KIF1A researchers & clinicians will have the capacity to pursue, research & develop treatments for KAND before we lose any more children to this degenerative disease.

KAND families have a significant unmet therapeutic need. Our objective is to create global clinical trials and bring treatment to this generation of KAND patients. With increased resources, KIF1A researchers & clinicians will have the capacity to pursue, research & develop treatments for KAND before we lose any more children to this degenerative disease.
WE HAVE A BOLD AND ACHIEVABLE PLAN TO MAKE TREATMENT A REALITY IN 2021.
Together with our research partners and clinicians, KIF1A.ORG is positioned to translate our robust preclinical work into real treatment. Visit our [Tools for Development](#) page at KIF1A.ORG for details. Every day we go without KAND treatment our children lose skills and abilities they work so hard to gain. Some children never develop skills so many of us take for granted. Together, we can #StopTheClock on KAND.

### KAND CLINICAL FUNDS NEEDED TODAY

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<thead>
<tr>
<th>Target Therapeutic Options</th>
<th>Manufacture Viral Vector, ASO &amp; Small Molecule</th>
<th>Preclinical Safety Trials</th>
<th>1st KAND Clinical Trial/Treatment</th>
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#### Year One

**Required staff**
- 2 Research nurses: $260,000
- 2 Research assistants: $170,000
- 2 PhD research fellows: $160,000
- MD research fellow: $150,000
- Bioinformatics PhD fellow: $80,000
- Administrative assistant: $80,000
- Research administrator: $55,000

**Research infrastructure**
- Computer server space: $80,000
- Patient assistance: $50,000
- Travel costs: $50,000
- Biorepository: $30,000
- Clinical/disease database: $25,000

**Total** $1,190,000

#### Year Two

**Required staff & infrastructure**
- Continue Year One resources: $1,190,000
- Assistant professor: $200,000
- Wet space (300 Sq Ft): $40,000
- Dry space (500 Sq Ft): $40,000

**KIFIA mutation cell line & screening**
- High throughput drug screen: $1,000,000
- 2 Research scientists: $300,000
- Gene editing postdoc fellow: $90,000
- Maintain mouse colony: $50,000
- Mouse model (3 generations): $45,000
- Cell-based disease models (3 mutations): $27,000
- Reagents/Labware: $20,000

**Total** $3,002,000
LEARN MORE AND JOIN OUR MISSION AT KIF1A.ORG

Contact: impact@kif1a.org