REQUEST FOR PROPOSALS

RARE EPILEPSY PARTNERSHIP AWARD

CURE Epilepsy's grant programs seek to accelerate promising research leading to new treatments and cures for people living with epilepsy. CURE Epilepsy prioritizes innovative projects that address our mission, affirming our core belief that the only acceptable final goal is "no seizures, no side-effects."

CURE Epilepsy: Our mission is to cure epilepsy, by promoting and funding patient-focused research.

We identify and fund cutting-edge research that may lead to new approaches for curing epilepsy, challenging scientists worldwide to collaborate and innovate in pursuit of this goal. Our commitment is unrelenting.

We encourage applications from groups identified as nationally underrepresented in the biomedical sciences. These groups include individuals with disabilities, veterans, persons from underrepresented racial and ethnic groups and gender-diverse groups, women in biomedical-related disciplines, or any other characteristic protected by federal, state, or local law.

Researchers outside the U.S. are also encouraged to apply. U.S. citizenship is not required.

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PRIORITY AREAS

CURE Epilepsy funds research that has the potential to truly transform and save lives. The purpose of this funding opportunity is to stimulate and accelerate discovery on rare epilepsies through the development of necessary research tools, techniques, model systems, and data collection platforms. Applications that are strictly focused on basic research including but not limited to gene discovery, understanding cellular pathways and mechanisms, basic electrophysiology, etc., without a research tool-building component will be given lower priority. This award is not intended to fund research focusing solely on a comorbid condition associated with a rare epilepsy without also seeking to develop tools to understand the causes and treatments for the accompanying seizures.

Each award will be co-funded by CURE Epilepsy and one or more of the rare epilepsy advocacy groups (partners) identified below. Applications must focus on one or more of the specific rare epilepsies that are represented by each group as well as address CURE Epilepsy's mission to cure epilepsy. Applications must clearly identify the rare epilepsy(ies) that the research is directed towards.

General priority areas for this program include:

- Development of rare epilepsy-specific cellular models including but not limited to patient-derived stem cells, iPSC lines, 3D organoid models or fused organoid models.
- Development of appropriate genetic animal models.
- Development of novel *in-vitro* or *in-vivo* assays or techniques, for example, drug screening platforms, to enhance research in a rare epilepsy.
- Development of research tools and novel techniques to enhance understanding of the cellular, molecular, genetic, and systems-level biology that leads to rare epilepsy, as well as facilitate the investigation of disease-modifying or preventative strategies.
- Supporting registries to better understand the natural history of one or more rare epilepsies or to look across rare epilepsies to identify common therapeutic targets and/or pathways. Projects utilizing existing registries or databases are allowed and must clearly articulate the specific rare epilepsy that will be studied. The use of registry platforms that ensure patient access to their data and when appropriate integrate with existing data collection platforms to enable data sharing with researchers and patient advocacy groups is strongly encouraged.
- Use of Electronic Health Record data to better understand the disease burden of rare epilepsy and develop therapeutic strategies.
- Development of technologies that will accelerate accurate diagnoses for rare epilepsies.

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An overarching goal of this funding mechanism is to develop resources and data that will be made available to the research community to accelerate research on rare epilepsies.

Research priorities for each partner are described below. *Preference will be given to projects that specifically address one or more of these priorities.*

ASXL Rare Research Endowment (ARRE) Foundation
https://www.arrefoundation.org/
The additional sex combs-like (ASXL) family of genes, comprised of ASXL1, ASXL2, and ASXL3, are involved in epigenetic and transcriptional regulation. Pathogenic variants in the ASXL genes lead to three distinct syndromes that have overlapping features:

1. Bohring-Opitz Syndrome (BOS) is caused by mutations in the ASXL1 gene.
2. Shashi-Pena Syndrome (SPS) is caused by mutations in the ASXL2 gene.
3. Bainbridge-Ropers Syndrome (BRS) is caused by mutations in the ASXL3 gene.

Individuals diagnosed with ASXL-related disorders share several clinical features including characteristic facial features, feeding difficulties, developmental delay, and hypotonia. They also have a significant seizure burden, some individuals more than others. The ARRE Foundation's mission is to support research and education that lead to improved quality of life for individuals with ASXL syndromes.

Specific research priorities include:

a. Identifying unique and shared biomarkers of disease in individuals with ASXL1, ASXL2, and ASXL3-related disorders. Projects related to this priority would facilitate establishing new biorepositories or expanding existing ones. Preliminary data suggests that individuals diagnosed with ASXL1-related disorder have a unique EEG signature. Similar patterns may exist in individuals diagnosed with ASXL2- and ASXL3-related disorders. In addition, patient biological samples are also being collected through a patient registry and biobank to facilitate the identification of blood-based or other physiological biomarkers of ASXL-related disorders www.reach-biobank.org.
b. Developing tools to characterize the impact of ASXL gene variants on neuronal development and function. To date, there has been a lack of understanding regarding the functional impact (whether gain of function, dominant negative, or loss of function) of select variants in the ASXL genes. One first critical step in designing future treatment strategies is to further elucidate the impact of select variants on protein expression levels and select readouts of cellular pathology such as aberrant neuronal firing.
c. Develop screening platforms and assays to facilitate the identification of small molecules and/or FDA-approved repurposed drugs that can alter ASXL protein levels. The ARRE Foundation has

invested in developing several patient-derived cell lines that are publicly available to researchers for screening experiments https://www.reach-biobank.org/.

FAM177A1 Research Fund

https://www.fam177a1.org/

Family With Sequence Similarity 177 Member A1 (FAM177A1)-related disorder is a rare neurological disorder that includes treatment-resistant seizures. FAM177A1-related disorder is caused by bi-allelic mutations resulting in loss of function of the FAM177A1 gene and absent or truncated protein. The FAM177A1 protein is ubiquitously expressed and locates to the Golgi complex. The function of the protein is mostly undefined, and the mechanism of this disease is unknown. There is an urgent demand for treatments for this life-limiting genetic disease. The FAM177A1 Research Fund has identified the elimination of seizures as a top priority based on caregiver surveys.

Specific research priorities include:

a. Developing patient-derived neuronal, glial, and muscle cell lines to facilitate understanding of the cellular mechanisms of FAM177A1 loss-of-function, conducting drug repurposing screens and hit validation, and testing the efficacy of gene therapy in reversing cellular phenotypes.
b. Establishing drug repurposing screening assays to identify promising therapeutic candidates and developing gene therapy strategies to counteract FAM177A1 loss-of-function. To further these initiatives, the FAM177A1 Research Fund has assembled a suite of disease models including patient-derived cells (CombinedBrain biorepository), FAM177A1- deficient flies (University of Utah), FAM177A1 knockout zebrafish (Washington University), and a FAM177A1 knockout mouse model available through Jackson Labs.
c. Studies utilizing and expanding on existing patient databases established through RARE-X and Ciitizen to define clinical phenotypes and natural history, develop biomarkers of disease, and capture baseline symptomatology. Biosamples from patients, including serum, urine, and plasma are available to researchers through the Stanford Biobank. (DevonBonner@stanfordhealthcare.org).

HNRNP Family Foundation

https://www.hnrnp.org/

Heterogenous Nuclear Ribonucleoproteins (HNRNPs) Related Neurodevelopmental Disorders (HNRNP-RNDDs) are a group of distinct, rare neurodevelopmental disorders caused mostly by *de novo* variants in

the HNRNP genes. Epilepsy is prevalent in several of the HNRNP-RNDDs but little research has focused on it. HNRNP genes code for a large family of about 30 RNA-binding proteins that play an important role in nucleic acid metabolism including alternative splicing, mRNA stabilization, and transcriptional and translational regulation. The HNRNP Family Foundation is an umbrella organization covering all the HNRNP-RNDDs.

Specific research priorities include:

a. Developing patient-derived neuronal models to assess and characterize seizure phenotypes. While it is estimated that 57% of individuals with HNRNP-RNDDs have seizures, some of the existing animal models have not recapitulated the seizure phenotype.
b. Generating new animal models to study the seizure phenotype in HNRNP-RNDDs. Many of the HNRNP-RNDDs lack animal models, and as mentioned above, some of the existing models do not recapitulate the seizure phenotype seen in humans.
c. Developing novel strategies to investigate the genotype-phenotype associations and structural brain differences that cause epilepsy in individuals with HNRNP-RNDDs. There is limited evidence to suggest that there are structural differences in the brain of many individuals with HNRNP-RNDDs but their contribution to epilepsy has not been evaluated.

IDefine, the Kleefstra Syndrome Foundation

https://www.idefine.org/

Kleefstra Syndrome (KS) is a rare genetic disorder characterized by intellectual disability, childhood hypotonia, severe expressive speech delay, and a distinctive facial appearance with a spectrum of additional clinical features including seizures in about 30% of individuals. While not all KS patients have seizures, those who do often have Lennox-Gastaut Syndrome and/or intractable seizures. It is poorly understood why some KS patients have seizures and others do not, and it is also not clear how to optimally treat KS patients who present with seizures, with different anti-seizure medications seeming to work better in different patients. KS is caused by haploinsufficiency of the gene Euchromatic Histone Methyltransferase 1 (EHMT1), due to a deletion/rearrangement on the long arm of chromosome 9 containing the EHMT1 gene, or a pathogenic variant in EHMT1 itself. IDefine's mission is to discover and bring to market life-changing treatments for Kleefstra Syndrome patients. Understanding the underlying mechanisms by which some KS patients have seizures and some do not could potentially deepen our understanding of the underlying pathology of KS, opening the door to improved treatments. To further this mission, IDefine has invested in developing resources available to researchers including patient plasma samples and two patient-derived cell lines from non-epilepsy KS patients. To apply for access to existing plasma samples and patient-derived cell lines contact grants@idefine.org.

Specific research priorities include:

a. Understanding, at a cellular level, the mechanisms that may cause seizures to develop in KS patients. Projects related to this priority would facilitate the development and characterization of neuronal cell, organoid, or other models from patients with KS and epilepsy as well as those with KS and no epilepsy.
b. Developing new techniques, models, or datasets to help identify genetic, epigenetic, brain morphology, or other factors that are associated with epilepsy in KS. Limited clinical data suggests that seizures are more common in patients with copy number variants (CNVs) versus pathogenic variants in EHMT1 but the mechanisms driving this are unknown.
c. Establishing assays or platforms to screen for novel compounds or approved drugs for the treatment of seizures in KS.

KCNT1 Slack Epilepsy Foundation

https://kcnt1epilepsy.org/

KCNT1-related epilepsy refers to a spectrum of epileptic syndromes that are rare, severe, and are caused by mostly *de novo*, pathogenic mutations in the potassium sodium-activated channel subfamily T member 1 (KCNT1) gene. The two main phenotypes are early onset seizures known as Epilepsy of Infancy with Migrating Focal Seizures (EIMFS) and later onset seizures known as Autosomal Dominant Sleep-Related Hyperkinetic Epilepsy (ADSHE) that typically manifest after the first six months of life. Core symptoms include migrating focal seizures, multifocal seizures, severe neurodevelopmental delay and regression after seizure onset, severe impairment of motor function, multifocal seizures, and multiple daily seizures at a young age. The mission of the KCNT1 Epilepsy Foundation is to accelerate research and drug development efforts focused on finding a cure for KCNT1-related epilepsy.

Specific research priorities include:

a. Exploring KCNT1's connection to other rare channelopathies including SCN8A-related epilepsy and SCN1A-related epilepsy. Recent research suggests that ASOs against KCNT1 can improve phenotypes in SCN8A and SCN1A models. Projects related to this priority would facilitate the development of assays/techniques to test novel KCNT-1 targeting small molecules or anti-sense oligos in cellular and/or animal models of SCN8A or SCN1A channelopathies and assessing seizure phenotypes.
b. Developing novel assays or strategies to understand the relationship between illness/fever and seizures in KCNT1-related epilepsy. This patient-generated research question springs from the reports of KCNT1 patient caregivers, who have noticed that KCNT1 patients experience fewer seizures during illnesses that include fever, and following recovery, seizures are often worse.

c. Developing novel assays or strategies to understand the relationship between acquired epilepsy and KCNT1. A recent study showed upregulated KCNT1 expression surrounding the lesion in patients with a traumatic brain injury (TBI) who went on to develop epilepsy. Examples of studies addressing this priority include the evaluation of KCNT1 expression in TBI brain tissue or exploring downregulation of KCNT1 in animal models of TBI and assessment of seizures.

ELIGIBILITY REQUIREMENTS

This award is available to both established and early-career investigators. Established investigators are university faculty at the associate professor level or above, or investigators who hold an equivalent position in a non-university research organization. Early career investigators are defined as a) university faculty at the assistant professor level or hold an equivalent position in a non-university research organization, b) researchers with an appointment as an instructor or research assistant professor, c) post-doctoral fellows with at least three years of post-doctoral experience or d) clinical fellows. Early career investigators must have a mentor committed to advising the applicant. A clearly articulated mentorship statement from the mentor must be submitted along with the application. See Letter of Intent and Full Proposal Instructions for details.

Members of CURE Epilepsy's Scientific Advisory Council and their research team members are not eligible to apply. Scientific advisors named by partners during the registration process and their team members are not allowed to submit applications in this cycle. Other advisors not named during the registration process and their team members are, however, eligible to apply.

All materials must be submitted in English.

AWARD TIMELINE

Activity	**Key Dates**
Open call for Letters of Intent	Tuesday, May 14, 2024
Letter of Intent deadline	Tuesday, June 11, 2024, 9 PM ET
Full proposal invitations	Friday, July 26, 2024
Full proposals due	Wednesday, August 28, 2024, 9 PM ET
Anticipated awardee notification	December 2024-January 2025
Anticipated award start date	Spring 2025

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BUDGET

Funding requests must be itemized and based on specific, milestone-defined scientific aims. Requests may be made for up to a maximum of $100,000 paid over one year. CURE Epilepsy reserves the right to fund only select specific aims or stage funding of proposals based on the achievement of milestones.

Budgets may include salary support for the Principal Investigator (PI), technical staff and/or co-PIs, supplies, animal costs, vendor costs, limited equipment costs, and travel to an epilepsy-related conference only if the PI is presenting his/her CURE Epilepsy-funded research. **Indirect costs are not supported.**

LETTER OF INTENT INSTRUCTIONS (TWO-PAGE LIMIT)

All applicants must submit a Letter of Intent (LOI). The LOI should clearly and succinctly outline the specific aims and include a brief description of the justification and research plan according to the guidelines in this announcement.

Letter of Intent Instructions:
Below are instructions for the required **scientific summary** and **future directions** sections, which together can be no longer than two pages in length. LOIs exceeding two pages of text will not be reviewed.

1) **Scientific Summary:** Clearly and succinctly outline the milestone-based specific aims and anticipated research outcomes. Include a brief description of the proposed research plan and how it aligns with CURE Epilepsy's mission and the needs of the partnering organization who collectively seek to find a cure for epilepsy by accelerating research forward by leaps rather than by incremental steps (one and a half-page maximum). Early Career Investigators must identify a mentor who will advise on the development and execution of the research project.

2) **Future Directions:** Describe what next steps will be taken once the goals of your proposed project have been achieved (one half-page maximum, including spaces). This must include clear steps to critical next stages in development or implementation of the research findings to advance research on the rare epilepsy syndrome. This section must also include a resource and data-sharing plan to make data, research tools, databases, animal or cellular models, and assays that result from this funding readily available to the research community. Examples of data and laboratory repositories where results and resources emanating from the work will be deposited are strongly encouraged.

A few points to note:

- Lower scores will be given to proposals that are not milestone-based and not achievable within a

one-year timeframe.

- Preliminary data is not required for this grant but may be submitted, if available. Graphs, figures, figure legends, and charts do not count toward the two-page text description of your project.
- References are not required at the LOI phase. However, if you decide to include references, they do not count towards the page limit.

FORMATTING GUIDELINES

- Type font: 12-point.
- Type density: No more than 15 characters per inch (including spaces). For proportional spacing, the average for any representative section of text should not exceed either 15 characters per inch or 114 characters per line.
- Spacing: Single-spaced between lines of text, no more than five lines of type within a vertical inch.
- Margins: Minimum of 0.5-inch top, bottom, right, and 1-inch left.

PROPOSAL CENTRAL INSTRUCTIONS

LOIs must be submitted through proposalCENTRAL (https://proposalcentral.altum.com). To begin an application, applicants will need to create a professional profile, if one does not already exist.

Instructions for each section of the application in proposalCENTRAL:

1) *Title Page:* Enter proposal title (maximum 150 characters, including spaces).

2) *Download Templates and Instructions:* Download LOI guidelines and other available instructions (if provided) as needed.

3) *Enable Other Users to Access this Proposal:* Use this optional section to grant access to a collaborator or co-investigator.

4) *Applicant/PI:* This section should auto-populate from the applicant's professional profile. Double-check that the information is complete and correct. If it is not, click *Edit Professional Profile* to update the information. Indicate whether you are an early-career or established investigator. An early career investigator must have a committed mentor to advise on development and execution of the research project. *A letter of commitment from the mentor is required if invited to submit a full proposal.*

5) *Institution and Contacts:* Information should auto-populate from applicant's profile.

6) *Co-Principal Investigator (Co-PI)/Collaborators:* Please enter information for any co-PIs or collaborators, if applicable.

7) *Rare Epilepsy syndrome(s):* Please select the specific rare epilepsy syndrome your project will address from the list. You may select up to three.

8) *Keywords:* Select at least three keywords from the list that best describe the specific focus of your research proposal.

9) *Current and Pending Support*: List all current and pending support for you and any co-investigators. Pending support includes any grant applications that you have submitted, but for which decisions have not yet been communicated. Current and pending support is required for the PI and co-PI but is not required for collaborators.

10) *Upload Attachments:* Once the LOI is finalized, attach it by uploading the PDF into this section of proposalCENTRAL.
Biosketch for PI: Applicants may use NIH biosketch format if preferred over the provided template.
    i. ***Please include a statement that clearly articulates the specific rare epilepsy(ies) that your work targets. Also describe your interaction(s) with a rare epilepsy-related patient community and how your proposed work will benefit them.***
    ii. *Optional: Applicants are encouraged to provide statements regarding their commitment to fostering diversity, equity, and inclusion in their research environment (100 words).*
    iii. *Optional: Applicants may include a one-half page section describing any life events or circumstances that contributed to delays or gaps in their career trajectory. This may include information that may not otherwise be apparent to reviewers and can help provide context as they evaluate your professional trajectory and achievements. Examples include but are not limited to: being a member of a community underrepresented in biomedical research, having experienced a life event that impacted career trajectory (such as parenthood, family, or medical leave), COVID-19 pandemic-related effects, having a learning or other disability, coming from a low-income family, and being the first in your family to go to college.*

11) *Validate:* The system will check for required components that have not been completed. Applicants will not be able to submit until all required components are completed.

12) *Submit: Click Submit* after your application has been successfully validated.

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FULL PROPOSAL NARRATIVE INSTRUCTIONS (10-PAGE LIMIT*)

Invited applicants should submit full proposals and include the following in the proposal narrative:

Specific Aims: Clearly state the specific aims that will be addressed by this work. Each specific aim should be associated with a clearly articulated, measurable milestone in the research plan. Each aim and milestone must have a clearly identified budget.

Background: Describe the project background including the biological rationale and patient population for which the research is intended. Describe how the proposed approach will significantly enable treatment or prevention strategies.

Preliminary Data: Provide any preliminary data available at the time of submission.

Research and Development Plan: Detail the experiments that will be done to address each specific aim, details of research design and methods, the expected outcomes, potential pitfalls, and how results will be interpreted. If this is a collaborative proposal, briefly describe how the collaboration adds value to the application.

- CURE Epilepsy strongly encourages the use of Common Data Elements (CDEs) in your research. Pre-clinical CDEs increase rigor, data standardization, and transparency across research studies. Please include a statement in your grant application that depicts the incorporation of CDEs. *Guidance for Integration in Grant Proposals*: Researchers are strongly urged to state in their grant applications, where applicable, the procedure specific CDEs that will be used in their pre-clinical studies. An example of the language is suggested below:
  "Data collection for all *in vivo* experiments were captured using Case Report Forms (CRFs) specific to each procedure. CDEs that will be used are listed and recorded as a supplemental file". This statement can be listed in the protocol section of your application. Files can be in .doc or .xlsx format, or how the researcher sees most appropriate for their study. Data standardization tools can be found here for the relevant pre-clinical CDEs. (https://cureepilepsy.org/research-resources/).

Statement of Relevance: Include one paragraph describing how the proposed research addresses the goal of curing epilepsy.

References: Please list all literature cited within the proposal. References do not count toward the page limit.

Proposals will be evaluated for innovation, feasibility, scientific merit, and alignment with the mission of this program to advance knowledge and tools targeted to a rare epilepsy syndrome.

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*The 10-page limit of the Proposal Narrative is inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and other relevant information needed to judge the proposal.

FORMATTING GUIDELINES

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- Type density: No more than 15 characters per inch (including spaces). For proportional spacing, the average for any representative section of text should not exceed either 15 characters per inch or 114 characters per line.
- Spacing: Single-spaced between lines of text, no more than five lines of type within a vertical inch.
- Margins: Minimum of 0.5-inch top, bottom, right, and 1-inch left.

FULL PROPOSAL INSTRUCTIONS FOR PROPOSAL CENTRAL

Full proposals must be submitted through proposalCENTRAL (https://proposalcentral.altum.com). To access your application, log in to proposalCENTRAL and go to the Manage Proposals tab. Below are instructions for each section of the online application:

1) *Title Page:* Enter proposal title (maximum 150 characters, including spaces).

2) *Download Templates and Instructions:* Access a copy of these guidelines and download a biosketch template if you have not already completed one. Instructions on completing your ORCID are also provided in this section.

3) *Enable Other Users to Access this Proposal:* Use this optional section to grant access to co-investigators or collaborators, so they may review or enter information into the application.

4) *Applicant/PI:* This section should auto-populate from the professional profile. Double check that the information is complete and correct. If it is not, click *Edit Professional Profile* to update the information. Indicate whether you are an early career or established investigator. An early career investigator must have a mentor to advise on development and execution of the research project and an articulated mentorship plan. CURE Epilepsy now requires an ORCID iD with all full proposal submissions. If your ORCID iD is not already provided on this page, enter your identifier in your Professional Profile by clicking *Edit Professional Profile*. Detailed instructions may be accessed in Step 2 of the on-line application – Download Templates and Instructions.

5) *Institution and Contacts:* Information should auto-populate from your profile.

6) *Co-Principal Investigator (Co-PI)/Collaborators:* Enter contact information for co-PIs and/or collaborators. Typically, Co-PIs are co-funded by the grant whereas collaborators are not.

7) *Abstract and Keywords:* Answer the questions in each box according to the instructions below:
   a. Lay Summary: The lay summary will be reviewed by members of the rare epilepsy community who would benefit from this research. Please take special care to describe the proposed work and its potential to contribute to the advancement of research in language appropriate for a non-scientific audience. Include the following:
      i. *Project Goals:* Bulleted list of goal(s) for the project.
      ii. *Aims:* Bulleted list of how those goals will be tested.
      iii. *Deliverables:* Bulleted list of tangible deliverables to result from this work, if successful.
      iv. *Impact:* Briefly explain how the work, if successful, will contribute to advancement of knowledge and/or research tools for a specific rare epilepsy(ies). In this section, you may also explain the next steps in your research plan once the goals of your proposed project have been achieved.
   b. Scientific Summary: Please provide a brief (250 word) scientific abstract of your project.
   c. Keywords: Please select at least three and no more than seven keywords that are appropriate to the proposed project. The keywords will be used to align proposals with appropriate scientific peer reviewers.

8) *Specific Aims and Milestones*: Each specific aim should have a clearly defined outcome or milestone. For example, a specific aim screening a compound library in an organoid model might have a milestone such as: Test X number of compounds at _ different concentrations in _ organoid models derived from __ patients. For each aim and associated milestone enter a short and long description.

9) *Aims and Milestones Schedule:* Enter budget, start date and end date for each specific aim and associated milestone. Each specific aim should be associated with only one milestone. Do not enter multiple milestones per specific aim. The dates for different milestones can overlap.

10) *Budget Period Detail:* The maximum budget for this award is $100,000 U.S. Dollars (USD) over one year. Provide a detailed budget that is itemized and aligned with the specific aims and milestones identified in the proposal. Enter proposed start and end date for Period 1. Enter funds for personnel costs using template provided. For each personnel item entered, indicate the milestone(s) that will be associated with that item. Click *Save* to save changes. The system will automatically calculate the total for the section. Next, enter non-personnel costs for each category listed e.g., materials, supplies,

travel, disposables, publication fees, etc., using the template provided. Vendor costs (if work will be sourced to a third party) can be included in the 'Other Expenses' category. Leave the category blank if no expenses exist for that category. For each item entered, indicate the milestone that will be associated with that item. Please note that there is a travel cap of $1,500 USD for international applicants and $1,000 USD for U.S. applicants per year, which can be budgeted for a maximum of two investigators (the PI and Co-PI). Limited equipment purchases that are required to complete goals will be considered but must be clearly justified in the next section. Repeat steps above for Period 2. The 'copy Period 1 Forward' tab allows you to copy expenses entered in Period 1 into Period 2 and then edit as needed. **Please note that indirect costs and institutional overhead are not provided. Funds cannot be used to cover institutional expenses such as network charges, computer maintenance and services, insurance dues, or other miscellaneous expenses not directly related to performing the project.** All expenses must be converted to U.S. Dollars (USD).

11) *Budget Summary and Justification:* Review the summarized budget to ensure that details have been entered correctly. Provide a budget justification that clearly details how and where the funds will be used and why these expenditures are critical to the success of the proposed research.

12) *Current and Pending Support:* Enter all current and pending support for all PIs on the proposal. Please indicate if there is any overlap with the proposed work.

13) *Organization Assurances:* Answer the questions regarding use of human subjects, animals, recombinant DNA, and the possession of a Schedule 1 license should the work involve Schedule 1 substances.

14) *Proposal Narrative and Other Attachments:* Upload the following documents:
    a. Proposal Narrative.

    b. Facilities/Institutional Assurances (do not exceed one-half page): Provide a description of facilities available at the institution(s) where the work will be performed. If an institution does not have an official assurance document, please provide, in writing, assurances from the department chairperson or practice colleagues confirming the applicant's time, facilities, and future position, if research is funded. Please submit facilities/institutional assurances for each PI.

    c. Biosketch for PI: Applicants may use NIH biosketch format if preferred over the provided template.
        i. ***Please include a statement that clearly articulates the specific rare epilepsy(ies) that your work targets. Also describe your interaction(s) with a rare epilepsy-related patient community and how your proposed work will benefit them.***
        ii. *Optional: Applicants are encouraged to provide statements regarding their commitment*

to fostering diversity, equity, and inclusion in their research environment (100 words).

iii. *Optional: Applicants may include a one-half page section describing any life events or circumstances that contributed to delays or gaps in their career trajectory. This may include information that may not otherwise be apparent to reviewers and can help provide context as they evaluate your professional trajectory and achievements. Examples include but are not limited to: being a member of a community underrepresented in biomedical research, having experienced a life event that impacted career trajectory (such as parenthood, family, or medical leave), COVID-19 pandemic-related effects, having a learning or other disability, coming from a low-income family, and being the first in your family to go to college.*

d. Co-Investigator Biosketch: Upload biosketch for each co-investigator, if applicable.

e. Collaborator Letters of Support: Upload letters from collaborators indicating their support of the proposed work, if applicable.

f. Statement from mentor: A clearly articulated mentorship plan must be submitted for early career investigators.

g. Informed consent form: If applicable, provide a copy of the informed consent form for the proposed study.

h. Signed signature pages: Upload signed signature pages, which are generated in Step 15 of the application.

15) *Validate:* The system will check for required components that have not been completed. You will not be able to submit until all required components are completed.

16) *Signature Pages:* Click *Print Signature Page* to obtain a PDF of the document that needs to be signed by you (the submitting PI) and an institutional representative. After signatures have been collected, scan and upload to Section 13.

Submit: Please **make sure to Click *Submit*** once your application has been validated by the system.

Inquiries: Questions regarding these guidelines are welcome and should be directed to the Research Team at Research@CUREepilepsy.org or 312-255-1801.