CURE CITIZENS UNITED FOR RESEARCH IN EPILEPSY

REQUEST FOR PROPOSALS

CURE CATALYST AWARD

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

CURE: 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.

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PRIORITY AREAS

CURE funds research that has the potential to truly transform and save lives. The purpose of this funding opportunity is to stimulate and accelerate discovery and development of new, transformative therapies for epilepsy, moving promising, well-supported preclinical and/or clinical research closer to clinical application. The award is intended to support nimble development of data necessary to attract larger commercialization funding opportunities and is not intended to replace those opportunities. Projects based on novel biological pathways and/or highly differentiated therapeutic approaches which are likely to have a high probability of success transitioning to clinical development are strongly encouraged. The award is not intended to fund basic research on the mechanisms underlying epilepsy.

Projects supported by this award mechanism should advance research to clinical trial readiness through development of biomarkers, optimization of new entities based on entities with established proof-of-concept including pharmacokinetics/pharmacodynamics, safety profiles and/or improved formulations, as well as studies that advance preclinical findings to pilot clinical trials. Prospective pilot clinical trials where limited testing of a novel intervention is needed to inform the next step in the translational research may be considered. Priority areas include:

- Innovative approaches that can prevent, modify and/or arrest the development of acquired epilepsy.
- Development of novel approaches to prevent onset or halt the progression of severe pediatric epilepsies.
- New, effective treatments for the >30% of the epilepsy population who are pharmaco-resistant.

ELIGIBILITY REQUIREMENTS

This award is available to independent researchers at or above the level of Assistant Professor (or equivalent) at universities and non-academic research institutions, including small biotechnology companies, that seek to develop new interventions for epilepsy. International applicants are welcome. Postdoctoral fellows may not apply for this award. All materials must be submitted in English.

AWARD TIMELINE

Activity	Key Dates
Open call for Letters of Intent	Monday, June 1, 2020
Letter of Intent deadline	Monday, July 6, 2020, 9 PM ET
Full proposal invitations	Thursday, August 13, 2020
Full proposals due	Thursday, September 17, 2020, 9 PM ET
Awardee notification	Late-December 2020
Anticipated award start date	March 2021

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BUDGET

Funding requests must be itemized and based on specific, milestone-based scientific aims. Requests may be made for up to a maximum of $250,000 paid over 2 years. Awards of lesser amounts and shorter duration that will accomplish key milestones needed for clinical advancement are strongly encouraged. CURE reserves the right to fund only select specific aims or stage funding of proposals based on 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 cost, and travel to an epilepsy-related conference only if the PI is presenting his/her CURE-funded research. **Indirect costs are not supported.**

LETTER OF INTENT INSTRUCTIONS (2-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 (2) 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 outcomes based on go/no-go criteria. Include a brief description of the proposed research plan and how it aligns with CURE's mission which seeks to push research on a cure for epilepsy forward by leaps rather than by incremental steps (1 ½-page maximum).

2) **Future Directions:** Describe what next steps will be taken once the goals of your proposed project have been achieved (1/2-page maximum, including spaces). This must include clear steps to critical next stages in the development process such as scale-up, engagement of a patient cohort and a potential funding plan.

A few points to note:

- Lower scores will be given to proposals that are not milestone-based with stated go/no-go criteria that are achievable within a 2-year timeframe.
- Graphs and charts do not count towards 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.

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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.

PROPOSALCENTRAL 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 & 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.
5) *Institution & Contacts:* Information should auto-populate from applicant's profile.
6) *Co-Principal Investigator/Collaborators:* Please enter information for any co-investigators or collaborators, if applicable.
7) *Keywords:* Select at least 3 keywords from the list that best describe the specific focus of your research proposal.
8) *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.
9) *Attach LOI:* Once the LOI is finalized, attach it by uploading the PDF into this section of proposalCENTRAL.
10) Biosketch for PI: Applicants may use NIH biosketch format if preferred over the provided template. ***Please include a statement that clearly describes your interaction(s) with an epilepsy-related patient community and how your proposed work will benefit them.***
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:* Hit "submit" after your application has been successfully validated.

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, e.g., improved selectivity, specificity or pharmacokinetics of a new entity based on established proof-of-concept of an existing entity, improved safety or formulation, validation of a biomarker that will enable clinical testing, etc. Each specific aim is considered a unique milestone and should be defined by clear go/no-go criteria, and each must be aligned to a specific, milestone-based budget.

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

Preliminary Data: Provide any preliminary data including but not limited to the following: potency, selectivity, sensitivity, oral bioavailability, pharmacokinetics, efficacy against stated specific endpoints or outcome measures and/or preliminary safety/toxicology data that are available at the time of submission.

Research and Development Plan: Describe the specific experiments that will be done to address each specific scientific milestone including details of research design, methods and endpoints in sufficient detail for scientific peer review. Specifically:

- Describe the experimental paradigm including specific endpoints that will differentiate the new entity or therapeutic approach from existing approaches. Provide a justification for those endpoints and describe how data will be collected and statistically analyzed. As appropriate, provide key assay metrics that help establish go/no-go decision criteria, for example measures of assay sensitivity, specificity and reproducibility. Include a power analysis to demonstrate that sample size is appropriate.
- Articulate expected outcomes with outcome metric(s) and clear go/no-go criteria, how results will be interpreted and note potential pitfalls.
- Describe key collaborations and expertise that will help ensure appropriate advancement of the work.
- Regardless of the stage of work, applicants must present a plan that describes availability of and access to a suitable patient population that would support meaningful progression of the work. Access to patients may be enabled through patient advocacy groups, specific clinical consortia, inpatient populations, etc.

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- If human subjects will be used, describe the plan for recruitment over the course of the study as well as inclusion/exclusion criteria and the process for seeking informed consent. Identify all study risks and safety measures that will be utilized to minimize risk to human subjects and study personnel.
- Applicants must clearly describe the steps that will be taken to advance the intervention/ approach into the next stage of development including potential funding mechanisms following conclusion of the work proposed in this award. Strong consideration will be granted to applicants who can provide specific regulatory milestones, e.g., submission of an application to the FDA for obtaining Investigational New Drug (IND) approval and a feasible plan for achieving milestones.
- If aspects of the project have been reviewed by another funding agency but not funded because of articulated gaps in the research plan, applicants are encouraged to submit prior review summary statements and describe how the revised proposed plan will address those gaps.

Statement of Relevance to CURE's Mission: Include one paragraph detailing how the proposed research addresses CURE's goal of curing epilepsy through transformative, clinically translatable research and/or clinical research.

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, application to clinically relevant steps of translational research and potential to be transformative.

*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

- Type font: 12-point.
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- 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 PROPOSALCENTRAL

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 & Instructions:* Access a copy of these guidelines and download a biosketch template if you have not already completed one.

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.

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

6) *Co-Principal Investigators/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:* Answer the questions in each box according to the instructions below:
   a. Lay Summary: The lay summary will be reviewed by a member of CURE's Lay Review Council. Please take special care to describe the proposed work and its potential to contribute to the development of a transformative therapy in language appropriate for a nonscientific 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 a new, transformative treatment or prevention that improves the lives of those with or at risk for epilepsy. 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.

8) *Budget Period Detail:* Provide a detailed budget that is itemized and aligned with the scientific milestones identified in the proposal. Each specific aim is considered a milestone. The maximum budget for this award is $250,000 USD over 2 years. Include an itemized list of how funds will be used for each specific aim within the proposal, e.g., salary, fringe benefits, supplies, animals, disposables, vendor costs (if work will be sourced to a third party), travel. 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 2 investigators (the PI and Co-PI). Limited equipment purchases that are required to complete goals will be considered but must be clearly justified. **Please note that indirect costs and institutional overhead are not provided.** All expenses must be converted to U.S. dollars (USD).

9) *Budget Summary and Justification:* Review the summarized budget to make sure 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.

10) *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.

11) *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.

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

   b. Facilities/Institutional Assurances (do not exceed ½ 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. ***Please include a statement that clearly describes your interaction(s) with an epilepsy-related patient community and how your proposed work will benefit them.***

   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. Informed consent form: If a clinical trial is included as part of the research plan, the applicant conducting the trial must provide a copy of the informed consent form used to enroll subjects.

   g. Timeline for execution of the studies: in a simple graphic, depict the timeline for accomplishing each specific aim and milestone.

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

13) *ORCID ID*: CURE now requires an ORCID ID with all full proposal submissions. If your ORCID ID

is not already provided on this page, enter an ORCID 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 & Instructions.

14) *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.

15) *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.

16) *Submit:* Please **make sure to hit 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.