2024 GRANT APPLICATION GUIDELINES

Application deadline: December 20, 2024 at 11:59 pm (ET)

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Grant Application Instructions

ABOUT EMILY'S ENTOURAGE:

Emily's Entourage (EE) is an innovative 501(c)3 foundation that accelerates research for new treatments and a cure for individuals with cystic fibrosis (CF)—a fatal genetic disease primarily affecting the lungs and digestive system—that do not benefit from currently available CFTR modulator therapies. Since 2011, EE has awarded millions of dollars in research grants, securing over $52.3 million in follow-on funding; launched a CF gene therapy company that is now in a clinical trial; developed a patient database and clinical trial matchmaking program to accelerate clinical trial recruitment; and led worldwide efforts to drive high-impact research and drug development. The organization has been featured in national media, including *The New York Times*, STAT, CNN, *People*, and more.

KEY OBJECTIVES:

Mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene cause cystic fibrosis (CF). Throughout the past ten years, incredible progress has been made with the approvals of CFTR-modulator therapies to benefit approximately 90% of individuals with CF. The final 10% of the CF community that does not benefit from currently available CFTR modulators due to genetically ineligible mutations are left without effective treatments. In addition, there is also a significant portion of the CF community that despite having mutations that are genetically eligible from CFTR modulators are unable to benefit due to side effects from or a suboptimal response to CFTR modulators.

EE has spearheaded efforts to prioritize and drive research for all individuals with CF who do not benefit from current CFTR modulators. EE's ongoing commitment to accelerate research and drug development is designed to provide a sustained and robust pipeline of novel therapeutics for people with CF for whom there are no therapeutic options currently available.

EE has identified critical high-need areas with the potential to speed therapeutic development for those that do not benefit from CFTR modulators and remove barriers and limitations that are holding back the advancement of such therapies. EE's grant program aims to provide essential seed funding to researchers pursuing innovative strategies in five major research areas to

advance CF treatment. The following five major research areas are currently supported by the program.

1. Nucleotide based therapies

Gene editing tools can provide new gene therapy strategies to achieve permanent correction such as Zinc Finger Nucleases (ZFNs), transcription activator-like effector nucleases (TALEN), and CRISPR gene editing (base and prime). Base editing offers a means to repair rare CFTR mutations. Solutions to limit or eliminate bystander effects, identifying the appropriate airway cell types for targeting and thus optimal delivery technologies, will be crucial for further development of DNA repair or full gene replacement in the context of CF. Full gene replacement, gene editing and repair, RNA, and other nucleotide based therapies are within the scope of this RFP.

2. Viral and non-viral gene delivery technologies

Given the recent advances in novel encapsulation techniques and formulations with carrier particles and customized chemical modifications of nanoparticles, EE is focusing funding efforts to derisk non-viral delivery platforms for genetic therapies. Additionally, EE is focusing on advancing the development of novel viral vectors for gene delivery.

3. Treatment and prevention of Staphylococcus aureus and other clinically important pathogens that present an unmet need in people with CF

Given the role that multidrug resistant (MDR) bacterial pathogens play on the health outcomes of people with CF, EE is exploring new ways to advance research into new therapies and vaccines that could target pathogens such as MRSA, Nontuberculous mycobacteria (NTM), as well as additional pathogens of interest that present a significant unmet need in the CF community. These may include novel antimicrobials with new mechanisms of action, novel aerosol formulations of antibiotics already in use, as well as novel targets for vaccinations. Antifungals are also within the scope of this RFP.

4. Drug repurposing

Drug repurposing could potentially provide novel therapeutic options for individuals with CF. Drug repurposing is a strategy to identify new indications for approved or investigational drugs that are outside the scope of the original medical indication. Exploiting a systems biology approach will allow EE to identify molecular features, such as phenotypes associated with

complex and heterogeneous diseases, which share common disease-causing features with CF and would otherwise remain unknown.

5. Promising early-stage research.
EE is at an inflection point in the research and development of novel therapeutics for CF with many therapeutics entering or poised to enter clinical trials in the near future. EE is eager to fund early-stage research that is looking to tackle CFTR mutations with a completely novel and fresh approach.

GRANT PROGRAM OVERVIEW:
Investigators are expected to have a good track record of peer reviewed publications and extramural funding. Awards are set at **$100,000 per annum** (direct costs) and, typically, funding will last for a **total of two years**. Awards are associated with additional indirect costs set at 10% such that total payments per annum will be $110,000. Funding will be allocated at 6 month intervals with payments of $50,000 released by EE, subject to sufficient progress being accomplished. Acceptance of funding requires submission of PROGRESS REPORTS that will be used to assess research progression. Continued financial support is contingent upon satisfactory completion of proposed research objectives delineated in the 'MILESTONES' section of GRANT APPLICATIONS. The first PROGRESS REPORT will be requested after 5 months of funding, and thereafter at 6 month intervals. Acceptance of funding will require execution of the EMILY'S ENTOURAGE GRANT CONTRACT by an authorized representative of the grantee institution.

APPLICANT ELIGIBILITY CRITERIA:
Applicants must have:

- Faculty appointment at an academic institution
- PhD, MD, or DO
- There are no restrictions on citizenship or geography
- No funding from other sources for the project for which they are applying to EE
- Track record of publication and funding
- Multiple PIs are encouraged to collaborate and apply

EVALUATION CRITERIA:

Competitive proposals will demonstrate:

- Potential to have a major scientific impact in the field of CF
- Innovation
- Objectives that will enable therapeutic advances
- Feasibility (for instance in the form of preliminary data, or research conducted in the Principal Investigator's laboratory)
- Milestones that are clearly and logically delineated

REVIEW PROCESS:

- Applications will be reviewed internally and by external reviewers prior to consideration by members of the EE Scientific and Leadership Team
- Following preliminary review, additional information may be requested from applicants
- Applicants that move to the final stage will be invited to a video presentation, before a final funding decision is made.

KEY DATES:

- 2024 global call for proposals opens on November 1, 2024 and closes on December 20, 2024 at 11:59 pm (ET).
- Applicants will be notified by the end of January 2025 if they are selected to move to the next round of reviews.
- Applicants will be invited to respond to reviewer comments.
- Funding decision will be made by April 1, 2025 with project start dates by May 1, 2025.

APPLICATION INSTRUCTIONS:

Provision of the following components is required to complete the GRANT APPLICATION process. All components should be compiled and submitted as a single pdf. In addition, the IMPACT STATEMENT and LAY ABSTRACT (described below) should be provided as a single .docx document. Finalized grant packages should be returned on or before the closing date to Chandra Ghose PhD, CSO, Emily's Entourage (chandra@emilysentourage.org).

*SPECIFIC AIMS***:** *(Page limit: one page)*

Please provide a project title and include an overview of the proposed research project with proposed objectives, and rationale for the studies described. Also include explicit details of each SPECIFIC AIM that will be addressed to achieve the proposed project goals.

*RESEARCH PLAN**:** (Page limit: 2 pages)*
The *RESEARCH PLAN* should detail information related to the project including:

- *SIGNIFICANCE* – describe the relevant background for the current research plan
- *INNOVATION* – discuss how the proposed research challenges or advances current knowledge, or introduces novel concepts, approaches or technology
- *APPROACH* – detail methodologies to address the proposed research objectives

It is strongly recommended that the *APPROACH* section includes any pertinent preliminary data Any cited literature in the GRANT APPLICATION should be included in additional pages using a numbered format.

In terms of institutional compliance, the *RESEARCH PLAN* should explicitly state, as appropriate, that the proposed research requires use of animals and / or human subjects. As necessary, an IACUC approval letter or note if approval is pending, and / or an IRB approval letter or note if approval is pending, should be included in an *APPENDIX*. Otherwise, please note in the *RESEARCH PLAN* that IACUC and / or IRB approval are not required.

MILESTONES: (Page limit: 1 page)
Provide a schematic representation and written description of the proposed project progression based on 6 month intervals. As stated above, continued financial support is contingent on submission of PROGRESS REPORTS and satisfactory completion of proposed research objectives specifically detailed in the MILESTONES section. In the event that MILESTONES are not robust, quantifiable and described in sufficient detail, EE may request resubmission of a revised MILESTONES section prior to making a funding decision. EE reserves the right to terminate funding if there is a lack of adequate scientific progress during any funded time period. The described MILESTONES will play a key role in the assessment of project progression.

BUDGET: (Page limit: 1 page)
Please submit a budget and justification using this Excel spreadsheet (save as a pdf for submission) for each of the two years of funding. Indirect costs are set at 10%, which will be included in addition to the $100,000 annual award (total award $110,000 per year). The budget justification should explicitly state that overlapping funds do not support the proposed studies.

*IMPACT STATEMENT**:** (Page limit: half page)*
Describe how the proposed research will lead to new or improved therapeutic approaches for people with CF that do not benefit from existing CFTR modulators or address an unmet need in the CF therapeutic landscape, particularly for the population without highly effective modulator therapies.

*LAY ABSTRACT: (*Page limit: half page provided on the same page as the IMPACT STATEMENT)
Summarize the research project in a manner that the layperson could appreciate. As described in the **EMILY'S ENTOURAGE GRANT CONTRACT**, information provided in the LAY ABSTRACT will be used and potentially published via formats such as the EE website or social media accounts, at the discretion of EE.

NIH BIOSKETCH(ES):
Please provide an NIH format Biosketch for Principal Investigator(s) associated with the application. In the RESEARCH SUPPORT section, please include all current and pending grant applications, and include an explicit statement that current funding does not directly overlap with funding for the proposed research to be supported by EE.

APPENDIX:
A brief appendix is allowed for information pertinent to the GRANT APPLICATION, including accepted but not yet published manuscripts, additional supplementary experimental results, and similar information. In addition, IACUC and / or IRB approval, and all other pertinent material, should be included in the APPENDIX. The following may be added to the Appendix -

RESOURCE SHARING:

In the event that a resource is generated that could enable development of novel CF therapies for individuals with CF that do not benefit from CFTR modulators (for instance, cell lines, murine models, etc.), information should be forwarded to chandra@emilysentourage.org for inclusion on the EE resource webpage: https://www.emilysentourage.org/research-resources/

COLLABORATORS AND/OR CONSULTANTS:
Include any appropriate letter from all individuals confirming their involvement in the proposed project.

FORMATTING INSTRUCTIONS:

- All pages of the application should include a header with the name of the Principal Investigator at the top right hand corner, and a footer with a page number in the center of the page
- Application formatting should follow NIH guidelines using 11pt Arial font with a minimum of 0.5" margins
- Any tables or figures should be embedded in the body of the Application and not included in the APPENDIX