CYSTIC FIBROSIS FOUNDATION

For application technical support, please contact ewarnke@cff.org

Program Name: 2023 Clinical Postdoctoral Research Fellowship Award

Brief Program Overview/Description: Clinical postdoctoral research fellowships are offered for support of postdoctoral research training related to CF. These awards are intended to enable research training in new research areas and methods to advance the scientific knowledge of the applicant and to collect data to enable their transition into an impactful research career. Research projects proposed through this program should be clinical in focus. ***Applicants seeking to submit proposals focused on basic science topics such as the restoration of CFTR protein function or mechanisms of disease progression should apply through the Path to a Cure Postdoctoral Research Fellowship Award Program or Postdoctoral Research Program.***

Funding Amount: Awards may be approved for up to a two (2) year period. Funding of up to $75,000 in the first year, and up to $76,000 in the second year may be requested. Indirect costs are not allowable.

Eligibility:

- Candidates must be U.S. citizens, permanent residents, or non-residents working in a U.S.-based laboratory.
- Postdoctoral applicants engaged in or planning CF-related research are eligible. Preference will be given to recent graduates and those just beginning their research careers and those with a clear commitment to CF research.
- The proposed research project should be clinical in nature in order to be eligible for this mechanism.
- Applicants can apply for this fellowship anytime during their postdoctoral period. However, funding levels are based on the year when the award is made, not the year of the applicant's fellowship.
- Additional eligibility requirements can be found in **Section IV**. below.

Key Dates:

Published	September 21, 2023
Application Deadline	December 6, 2023
Committee Review Date	February/March 2024
Notification to Applicants	March 2024
Earliest Project Start Date	April 1, 2024

Table of Contents:

I. About the Cystic Fibrosis Foundation

The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with CF the opportunity to lead long, fulfilling lives by funding research and drug development, partnering with the CF community, and advancing high-quality, specialized care.

To achieve this mission, various types of grants and awards are offered to support meritorious research in CF.

Diversity, Equity, and Inclusion

Cystic fibrosis affects people of different racial and ethnic backgrounds. Diversity, equity, and inclusion (DEI) are core to our ability to make a meaningful difference in the lives of all people with CF. Improving the representation of people of color within the CF community – including those in the CF research workforce – and addressing health disparities that exist within these groups is critical to the Foundation's mission of serving all people with CF. Making clinical trial design and engagement more inclusive of people of color with CF will be critical for improving treatment options and health outcomes for these groups; Black and Hispanic people with CF account for nearly 40 percent of individuals with rare mutations that are not candidates for available treatments addressing the underlying cause of the disease. As PIs prepare application materials, we strongly encourage the consideration of how to support inclusion of diverse participants, including plans for building trust with community members and ensure adequate recruitment of people from diverse backgrounds.

II. Program and Award Overview

Clinical postdoctoral research fellowships are offered for support of postdoctoral research training related to CF. These awards are intended to enable research training in new research areas and methods to advance the scientific knowledge of the applicant and to collect data to enable their transition into an impactful research career. Research projects proposed through this program should be clinical in focus.

Postdoctoral fellows applying to this program are expected to be using clinical samples, data, or interacting with patients. We strongly encourage applicants from programs in physiology, physical therapy, biostatistics, nutrition, registered nursing, social work, social and behavioral science, or similar programs to consider applying.

Applicants seeking to submit proposals focused on basic science topics such as the restoration of CFTR protein function or mechanisms of disease progression should apply through the Path to a Cure Postdoctoral Research Fellowship Award Program or Postdoctoral Research Program.

III. Funding Amounts

Awards may be approved for up to a two (2) year period. Funding of up to $75,000 in the first year, and up to $76,000 in the second year may be requested. Indirect costs are not allowable.

Funding levels:

Fellowship Year	Stipend (salary + fringe)	Travel	Research	Total
First-year Fellowship	$66,000	$1,500	$7,500	$75,000
Second-year Fellowship	$67,000	$1,500	$7,500	$76,000

***Note: funding cannot be moved between budget categories.**

IV. Eligibility

- Candidates must be U.S. citizens, permanent residents, or non-residents working in a U.S.-based laboratory.
- Postdoctoral applicants engaged in or planning CF-related research are eligible. Preference will be given to recent graduates and those just beginning their research careers and those with a clear commitment to CF research.
- Applicants can apply for this fellowship anytime during their postdoctoral period. However, funding levels are based on the year when the award is made, not the year of the applicant's fellowship.
- Candidates who are clinical fellows should apply to the CFF Clinical Fellowship programs. Please refer to the Policies and Guidelines of the Clinical Fellowship programs on the CFF website at www.cff.org.
- Fellowships are awarded on the basis of individual and institutional merit. Awards are not transferable to other individuals or institutions unless previously approved by the CFF Program Officer (PO).
- Applications should focus on one or more of the research areas of interest outlined in Section VI below.
- Fellowships are intended to support mentored training to enable awardees to be competitive for independent, faculty positions. For awardees who obtain a faculty position before the end of their 2-year, please contact the CFF PO to determine if part of your award may be eligible to be converted to a P&F for the remainder of the funding period.
- Applicants may have clinical (or similar) commitments but should be able to provide an institutional commitment to research time. Ideally, this will be a commitment to >50% research time. For applicants who cannot make that large of a research commitment, please reach out to the PO to discuss appropriate options.

V. Mentorship Requirements

- Each fellow must have a Mentor who will be responsible for the fellow's training and research activities.
- The Mentor(s) must be able to provide the mentorship needed to guide the project if awarded.
- The Mentor(s) must be at the institution where the applicant will be carrying out the work for the project.

VI. Goals of Research Currently of Interest to CFF/Priority Areas

Proposed research must be relevant to the CFF's mission and to the health and well-being of people with CF. Applicants are encouraged, but not required, to address a research priority outlined below, and in further detail on https://www.cff.org/key-research-priorities-applicants . All applications are reviewed and scored based on the individual, training program, scientific merit, and relevance to the CFF mission.

Research Priorities:

- Treat the underlying cause of CF for all people with the disease and drive progress toward a cure. In particular, research related to **evaluating genetic-based therapies** that may have clinical impact for people with CF, developing therapies that address the **underlying cause of CF for individuals with nonsense and rare mutations**, and **improving and better understanding cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies**. *Note: projects focused on the mechanistic aspects of therapy development are not appropriate for this program and should be submitted to either the Postdoctoral Research Fellowship Award Program or Path to a Cure Postdoctoral Research Fellowship Award Program.*
- Understand the basis of and advance new and improved treatments to address the many complications of CF, including:
    - Mental health;
    - Infections affecting people with CF;
    - Inflammation, impaired airway hydration, and mucus clearance;

- Serious complications of CF outside the lungs, such as GI complications (including in the liver, the pancreas, and the impact of nutritional deficiencies), endocrine system dysfunction (including CF related diabetes and CF bone disease);
- Sinus disease;
- Lung transplant and advanced lung disease;
- Sexual and reproductive health – applicants with an existing hypothesis and interest in research in this space are encouraged to connect with the Sexual Health, Reproduction, and Gender Research (SHARING) Working Group for additional mentoring.

- Improve understanding of system-level and societal barriers to optimal CF care and explore opportunities to minimize their effects, including racial disparities and socioeconomic barriers to equitable care.
- Characterize the best CF care and treatment regimens to provide optimal, individualized care as the CF treatment landscape evolves.
- Ensure that the CF care model adapts to meet the future needs of people with CF across their lifespan. This includes considerations for the aging CF population and the increasing utilization of remote care.

Note: Applicants seeking to submit proposals focused on topics that are non-clinically related should apply through either the Path to a Cure Postdoctoral Research Fellowship Award Program (https://www.cff.org/path-cure-academic-programs) or the general Postdoctoral Research Fellowship Award mechanism (https://www.cff.org/postdoctoral-research-fellowship-award).

VII. Review and Award

All applications are evaluated by an external review committee, whose recommendations are reviewed by the Medical Advisory Council (MAC) and/or the Board of Trustees. Funding of awards is based on the priority score awarded to each application and the recommendations of the committee. Funding decisions are based on the relevance of the proposed study to the goals of the Foundation, alignment with specific research priorities, and enhancing the existing CFF project portfolio. All awards are subject to compliance with applicable regulations and CFF policies and are contingent upon the availability of CFF funds.

In addition to scientific merit and relevance to the CFF mission, applications will be evaluated in the following areas:

Applicant	Mentor(s)	Environment	Training & Research Development Plan
• Commitment to, or intent to pursue, a research career related to CF • Potential to develop an independent research career related to CF • Research accomplishments	• Established expertise in CF-related clinical research or related research areas of high priority to CFF • Commitment of the primary Mentor for the duration of the applicant's development and research plan • Track record of the Mentor training individuals for in the relevant field	• Quality (breadth and depth) of faculty in basic and/or clinical sciences related to CF at applicant institution • Quality of institution's CF research and training programs • Demonstrated interaction between basic and clinical investigators • Institution's commitment and ability to provide opportunities and facilities necessary for	• Feasibility and impact of the proposed plan • Didactic course work required by the applicant (if indicated) • Scientific and technical merit of the proposed research • Ability of the proposed plan to develop research skills of the applicant needed for independence • Relationship to applicant's career development

		research career development related to CF	

Applications will be reviewed and scored by the committee. CFF may withdraw applications receiving low scores, and/or those deemed nonresponsive to the program announcement before the review meeting. In these cases, CFF will notify applicants if their application has been withdrawn without discussion. Applications that have not been funded in two review cycles will not be accepted for further consideration by CFF. In order to resubmit unfunded applications during future application cycles, applicants must indicate that it is a resubmission and address reviewer critiques.

Chief causes for assigning low priority scores to applications during review include the following:

- Insufficient information or documentation
- Inadequate statement of hypothesis, experimental design or methods
- Failure of the applicant to demonstrate awareness of and plans for coping with key problems and pitfalls associated with the proposed research
- Insufficient or improper controls
- Failure of the applicant to describe potential relevance of the proposed study to issues in CF
- Failure of the applicant to document the necessary skills or training to accomplish the goals of the proposal
- Failure of the applicant to meet all of the criteria described in the policy statement for a given award

VIII. Submission Information

Application deadline: Wednesday, December 6, 2023, by 5:00 PM (Eastern)

Submit online through http://awards.cff.org
(Refer to Section X of these guidelines for specific submission instructions)

An application will be considered incomplete if it fails to comply with the instructions, or if the submitted material is insufficient to permit adequate review. CFF reviews applications electronically, and only documents submitted online at http://awards.cff.org will be reviewed.

General Timeline:

Application Deadline	December 6, 2023
Committee Review Date	February/March 2024
Notification to Applicants	March 2024
Earliest Project Start Date	April 1, 2024

*We strongly encourage all applicants pre-register their profile, institution, contacts, and title of their application at least two weeks prior to the application deadline. This will help to ensure the CFF Grants & Contracts Management and Administration (GCMA) Office is able to assist all applicant with any potential system-related queries prior to the Application Deadline.

IX. Letter of Intent Guidelines

Not applicable to this RFA

X. Full Application Guidelines

Applications must be submitted online at https://awards.cff.org

Documents should be typed using:

- Font: Times New Roman 12 or Arial 11
- Margins: No less than a half inch on each side

Note: *When all the documents have been uploaded to awards.cff.org, the system will compile them into a single PDF file. You may preview this file by selecting "Application Full Print", as well as exporting the compiled PDF file.*

To login, please visit: https://awards.cff.org

For all first-time applicants in the new Grants Management System, we ask that you pre-register to create a username and password for "http://awards.cff.org" and complete a profile prior to submitting an application. ***Please note:*** Applicants should register their profile using the "Domestic Institution" or "International Institution" options to ensure that your profile aligns properly with the institution where the project will be conducted. We also request that as you begin your application, you enter the title of your project, if available. If you are registered and cannot remember your password, click on the **"Forgot Password?"** link below the **"Login"** fields.

Once logged in, the award opportunities, including this Request for Applications (RFA), will be listed in the **Funding Opportunities** tab on the opening screen.

Locate the listing for the "**2023 Clinical Postdoctoral Research Fellowship Award**" program. Click on the "Apply" button in the column on the far right to open the application form.

Applicants may stop at any point but must click the **"Save"** button at the bottom of each page *before exiting* in order to save their progress. When you wish to return to your draft application, please do not go through the "Funding Opportunities" tab. Instead, go to the "**My Applications**" tab in the right corner of the main page. When you are in the "**My Applications**" tab you will be able to find all your draft applications by clicking on the "Draft Applications" module.

The following sections are displayed as tabs across the application screen. Click on each section and follow the directions. Click "**Save**" as you complete each section.

GENERAL

Enter the title of your project, enter the project start and end dates, select the number of periods being requested, and complete the organizational assurances indications (i.e., IRB, IACUC, and/or IBC/rDNA approval letter and status at the time of submitting the application) in this section.
***Please ensure that you review and comply with the below Organizational Assurances and Certifications as cited at the end of this section on page 11.**

CONTACT PROFILE

If a profile was completed upon registration, the fields in this section will already be populated with the information entered in your Professional Profile. If you need to make any changes, you may update your profile in this section. Once updated you must "**Save and Validate**" prior to returning to continue your submission.

INSTITUTION

If a profile was completed upon registration, the Applicant's/Principal investigator's institution will be preloaded as the Lead Institution. Domestic applicants must verify their institution by entering the Employer Identification Number (EIN) or Tax Identification Number (TIN) to search the system for the correct institution. **Please be sure to use the dash formatting when entering your EIN/TIN (XX-XXXXXXX).**

If the EIN/TIN is not located, you may add the legal institution. Please also confirm if the project site is the same as the legal institution.

Verification of Applicant Institution's Tax Status (upload as PDF documents):
The CFF GCMA Office must have a copy of the applicant institution's current W-9 and 501I3 letter, or other documentation verifying its Federal tax status and will not issue Award Letters to Awardees if these documents are not received and on file.

- Applicants from for-profit organizations must submit a copy of the applicant institution's W-9 and IRS documentation verifying the organization's Federal tax status. Awards are not issued prior to having these documents on file with the CFF GCMA Office.

International Applicants (if applicable):
Not applicable

CONTACTS

Please note: The INSTITUTION tab must be completed prior to adding internal contacts to ensure that the contacts are properly associated with the applicant institution.

Complete the required contact fields by searching by name for existing contacts at your institution for each role. If the desired institutional contact is not available in the system, you may select "**Add Internal Contact**" to create a basic contact profile in order to add the individual to your application.

Additional contacts not associated with the applicant institution may also be added. These contacts are considered additional contributors involved in the proposed research plan. These may include consultants, collaborators, or subcontractors. In order to add contacts external to the applicant institution, please select the appropriate "Add Subcontractors" or "Add Consultants/Collaborators" button(s) and add the contacts in the table, then click "Save".

REFERENCES

Letters of Support and/or Reference are weighted heavily in the review. At least four (4) letters are required as follows:

- **The Mentor(s) for this award –** A Letter of Support from the Mentor(s) should clearly identify the merits of the applicant and must include a description of CF-specific and other training the applicant will receive while working under the Mentor's direction (i.e. seminars, new techniques, professional development, etc.).
- **Additional referees** – Letters of Reference from at least three (3) other individuals familiar with the applicant's scientific interests and abilities (with no more than two [2] from the same institution) should attest to the candidate's academic qualifications, motivation, and research potential.

Letters of Reference must be submitted prior to submission of the application. To invite Referees, go to the "**REFERENCES**" tab of the online application, then select the blue button to open a pop-up window in order to add the referees in the table. You must click "Invite" in order to trigger the e-mail to the referee. The referee(s) will be sent an e-mail asking them to Accept or Decline the invitation to submit a letter of reference and will be provided instructions to submit the letter. **The applicant will be alerted if a referee Declines the invitation; please make sure to check this tab regularly to see the status of the references.** The applicant should inform Referees to submit the letters at least one (1) week prior to the application deadline. This helps to ensure that the letters have been uploaded before the application is submitted. Once the application has been submitted, no documents can be added.

Letters uploaded to http://awards.cff.org should not be password protected or otherwise encrypted. Such encryption will cause errors in assembling a single-print PDF of the application. The applicant should inform the individuals writing letters to not include password protection on their documents.

ABSTRACTS/RELEVANCE

In the space provided online for abstracts, provide a statement of no more than 2,000 characters (including spaces) explaining the subject of the research proposal and its relationship to CF. Two different abstracts are required, as follows:

- **Lay Abstract**: This statement will be used to inform the non-scientific departments of CFF and the general public of the nature of this work. Applicants should not include any confidential or proprietary information, including intellectual property, in the lay abstract.
- **Scientific Abstract**: This statement will be used to inform the scientific community.
- **Summary of Relevance to CFF mission**: All applications are reviewed and scored not only on scientific merit but also on relevance to CFF's mission:

  The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with CF the opportunity to lead long, fulfilling lives by funding research and drug development, partnering with the CF community, and advancing high-quality, specialized care.

  Provide a statement of no more than 3,000 characters (including spaces) summarizing the relevance of the proposed research to the health and well-being of CF patients, for a scientific audience who may or may not have a background in the subspecialty of the proposed research.

BUDGET

Select the "**Edit Budget**" button under Application Budget, to enter and begin completion of the application's budget detail for each year of funding being requested. Postdoctoral Research Fellowships funded through this RFA are for a maximum of two (2) years. The total budget request cannot exceed $75,000 for Year 1 and $76,000 for Year 2 (please refer to the funding table in Section III above). Indirect costs are not allowed.

Salaries & Benefits - List the names, positions, and percent effort of all professional and non-professional personnel involved in the project, **whether or not salaries are requested**. For each individual, be sure to complete all fields on the Budget Detail in full on the template provided. In accordance with National Institutes of Health (NIH) policy, salary requests may not use an institutional base salary in excess of the current federal salary cap of **$212,100**. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all funding agencies and foundations.

Travel - Describe the purpose of any travel being requested. Please note: For North American applicants, expenses for travel outside the North American Continent, including travel to Hawaii, Puerto Rico, and other U.S. territories are not allowable expenses without prior written approval from the CFF GCMA Office. **Travel expenses may not exceed $1,500 per person per year**. Registration fees associated with conferences are in addition to this allowance should be listed under "Other Expenses". Applicants are encouraged to attend the North American CF Conference each year to present their work.

Consumable Supplies - Itemize supplies e.g. glassware, chemicals, animals, in separate categories and give the estimated cost of each category. If animals are involved, state the number, unit purchase cost, and unit care cost.

Other Expenses - Itemize other expenses by major categories, such as duplication costs, publication costs, minor equipment (under $5,000), conference registration fees, etc. Requests for computer hardware maybe considered if the need is well justified and the Trainee's Mentor agrees to share the costs.

Budget Detail – Indirect Costs

Indirect costs are not allowable

FULL APPLICATION UPLOADS

Download the available templates applicable to the project, upload the completed templates to the corresponding attachment types within this section. Templates available for download include:

- Budget Justification
- Research Plan
- Training Plan
- Biographical Sketches for Key Personnel
- Other Support
- Facilities Available
- Mentor's Results of Past and Current CFF/CFFT Support
- Critique Response (if resubmission)
- Data Safety Monitoring Plan
- CFF Patient Registry Data Request Application (if applicable)
- CFF Biorepository Clinical Specimen Confirmation Letter (if applicable)

BUDGET JUSTIFICATION

Describe costs listed in the Budget Detail. Use major categories, such as Salary & Benefits, Consultant Costs, Major Equipment, etc. Justify all items and make sure amounts and figures listed in the narrative are consistent with those listed in the Budget Detail. ***Budget Justification uploads should be provided individually for each year of funding support being requested. These can be uploaded as a single PDF or separate PDF uploads for each year.***

RESEARCH PLAN

Page limit: **Seven (7)** single-sided pages, not including the Literature Cited. Applications exceeding this page limit will not be reviewed. Type the PI's name in the space available in the header of the document. The template available will track page numbers at the bottom.

- Include sufficient information to permit effective review without reference to previous applications. Information should be presented in a clear and concise manner, while being specific and informative.
- Key figures and legends must be included in the Research Plan and should be of sufficient quality and size to be evaluated by the reviewer. If uploaded as Appendices, they will NOT be reviewed.
- If the application is a resubmission of an earlier one, revisions must be clearly indicated by a change in font, bolded or underlined. **CFF will not review resubmissions that have not been revised.**

    a. **Hypothesis and Specific Aims:** State concisely and realistically the intent of the proposed research and the hypothesis to be tested. The specific aims should be relevant to the mission of the Cystic Fibrosis Foundation. Do not exceed one page.
    b. **Background and Significance**: Briefly describe the background. Critically evaluate existing knowledge and specifically identify the gaps that the project is intended to fill. Concisely state the importance and rationale of this research by relating the specific aims to longer-term objectives. This section should also show the potential importance of the proposed work to CF, in particular those areas listed as areas of special interest to CFF. In addition, describe the relationship of the proposed work to your long-term career goals. Preference will be given to applicants who express an interest in a long-term career in CF-related research.
    c. **Preliminary Results**: If applicable, provide a detailed discussion of any preliminary results.
    d. **Experimental Design and Methods**: Provide a detailed discussion of the experimental design and methods to be used to accomplish the specific aims. Describe the protocols, including methods for new techniques, and explain potential advantages over existing methodologies. Discuss the

data expected to be obtained and the means by which data will be analyzed and interpreted. Discuss potential pitfalls and/or limitations of the proposed procedures and alternative approaches to achieve aims.

If clinical samples are included in the Research Plan, provide details of the methods for patient selection. Point out any procedures, situation or materials that may be hazardous to personnel or patients and the precautions to be exercised. Please discuss (if applicable): primary and secondary outcome measures; study sample inclusion and exclusion criteria; subject enrollment including age range; sex distribution; randomization scheme; description of experimental procedures and schedule including a study timeline; drugs and dosage; measures of compliance; follow-up schedule including a study timeline for full project up to two years; efficacy and safety evaluation, and data monitoring and quality control.

Clearly describe the statistical methodologies, including software, to be used for each aim of the proposed study. Clearly describe analytic strategies for each endpoint or outcome measure being collected. Describe any potential confounders or demographic variables that will be considered during analysis. Provide discussion on how the statistical methods are appropriate for the proposed sample size. Provide a rationale for the number of participants who will be studied. If a full power calculation is provided, the sample size and statistical power calculations should contain sufficient detail, including assumptions made, such that a reviewer can readily duplicate the sample size. A discussion of how missing data will be handled should be included. Any planned interim analyses should also be described.

e. Literature Cited: References should be numbered in the sequence that they appear in the text at the end of the Research Plan. Each citation must include the names of all authors, title, the name of the journal or book, volume number, page number and year of publication (titles are optional).

TRAINING PLAN

The applicant, in conjunction with the Mentor(s), should develop a personalized training plan that outlines skills and techniques that will be learned during this fellowship period as well as CF-specific training and mentorship that will be available to the applicant. The training plan should also include a description of seminars and conferences the applicant will attend. Applicants are encouraged to attend NACFC and submit an abstract each year of their award. This plan should also address the applicant's long-term career goals and include training and professional development activities that will facilitate the applicant's transition to an impactful research career. Do not exceed four (4) pages.

BIOGRAPHICAL SKETCH(ES) OF KEY PERSONNEL

Complete and upload an NIH Biographical Sketch for all the Applicant/Principal Investigator and the Mentor(s). Do not exceed five (5) pages per person.

OTHER SUPPORT

Complete and upload an NIH Biographical Sketch for all the Applicant/Principal Investigator and the Mentor(s). There is no page limitation. Information on other support assists CFF in the identification and resolution of potential sources of overlap. Scientific and budgetary overlap should be minimized. Commitment of an individual's effort greater than 100 percent, is <u>not</u> permitted. If an applicant has a current source of funding (i.e. training grant or other fellowship) that will be relinquished if this award is received, please note that in the Other Support document.

FACILITIES AVAILABLE

Describe the facilities and equipment available at the applicant's institution that will be used for this project, such as laboratory, clinical, animal, computer, office, etc. Provide any additional information about the environment, including any support services available that will be utilized. Describe their pertinent capabilities, proximity and anticipated extent of use. If facilities or equipment at a consultant's or collaborative site will be used, they should be identified and clearly described. There is no page limit. Use continuation pages, if necessary.

MENTOR'S RESULTS OF PAST AND CURRENT CFF/CFFT SUPPORT
Mentor(s) are requested to Identify the results of past and current CFF/CFFT support (e.g., subsequent funding from other sources, journal articles, and invited presentations) and the CFF/CFFT grant/award from which they resulted for the past three to five years. Please note that the following information must be included with each research project identified:

- CFF/CFFT Award Number
- Principal Investigator (PI)
- CFF/CFFT Project Title
- Applicant's Title on Project
- Project Start/End Dates
- Total CFF/CFFT Award Amount
- Results of Support

CRITIQUE RESPONSE (if resubmission)
If the application is a resubmission of a previously declined application, please provide a point-by-point response to the prior reviews. There is no page limit to your responses, but please be concise and succinct.

DATA SAFETY MONITORING PLAN (template available for download, upload if applicable)
In compliance with Federal regulations, all applicants must submit a general description of the Data Safety Monitoring Plan (DSMP) for any proposed study that places human subjects at more than minimal risk. A DSMP helps to ensure subject safety, as well the validity and integrity of the data. Furthermore, a DSMP allows for the monitoring of study data to assess whether or not an early termination is necessary for safety or efficacy reasons.

The extent of monitoring required for a study is dependent on the level of risk involved for the subjects, as well as the size and complexity of the study. Large, multi-center CFF-funded interventional clinical trials may be required to utilize a Data Safety and Monitoring Board (DSMB). In addition, because its members are CF clinicians and clinical trial experts, CFF strongly encourages and may require that investigators utilize the CFF DSMB for any other interventional CF clinical trial that meets one or more of the following criteria:

- Multi-center;
- Randomized;
- Conducted in an emergency setting;
- Use high-risk interventions, such as gene therapy, gene transfer, or bronchoscopy; or Include particularly vulnerable study populations, such as pediatric patients.

Note: On the available template, please check whether a DSMP is required and upload the template regardless of the response.

Address the following areas in the DSMP:

Assessment of Risk – Describe the level of risk the proposed research presents to subject participants and provide a detailed justification for the level of risk. Discuss who will monitor the study.

Level of Risk

- Minimal Risk
  - Study poses no more risk than expected in daily life (blood draw, physical exam, etc.)
  - Observational studies
  - Survey or questionnaire studies
- Low Risk
  - Post-marketing study Phase IV drug or device, as defined by FDA
- Moderate Risk
  - Substantial risk (>5%) of a Serious Adverse Event (SAE) originating from the underlying condition of the enrolled subject
  - Phase I or II study with available safety data in humans
- High Risk
  - Involves an intervention or invasive procedure with substantial risk
  - Involves the use of a new chemical or drug for which there is little or no toxicology data in humans
  - A gene therapy study or research involving recombinant DNA or RNA molecules (gene transfer)
  - Involves vulnerable populations (pediatric, pregnant, etc.)

Anticipated Adverse Events and Grading Scale – Describe anticipated adverse events (AEs), including expected frequency and the grading scale to be used. Discuss plans for addressing AEs.

Reporting of AEs – Detail the plan for reporting AEs, including who shall be notified in the event an AE should occur.

Safety Monitoring Plan – Describe all tests, evaluations, and exclusion criteria that will be implemented to ensure and monitor the safety of human subjects. Discuss stopping rules for the study subjects or for the overall study if necessary.

Safety Reviews – Describe the process for monitoring and reviewing subject safety data, including the frequency of such reviews. Include details as to who will perform the monitoring and plans for reporting. If utilizing the CFF DSMB, provide the frequency of meetings, the reporting requirements, including AEs and SAEs, and the procedure for interim reporting as necessary. If this information is not available at the time of submission of the application, note that CFF will not release awarded payments until it is provided.

Registrations for Investigator-Initiated Clinical Trials:

- Clinicaltrials.gov (United States): Applicants are required to register all non-exempt human subject studies in the ClinicalTrials.gov database to ensure information is freely available on CFF-funded trials within the community. The registration should be no later than twenty-one (21) days after the first subject is enrolled. CFF requires copies of documentation confirming this registration, when applicable.
- EudraCT Registration (European Union): For interventional clinical trials with medicinal products conducted in the European Union, the Institution must provide documentation to CFF confirming registration of the clinical trial when applicable

CFF Patient Registry Data Request (download available, upload if applicable)
Researchers who wish to request Registry data for their proposed clinical research study must complete and submit the "Application for CFFPR Data and Confidentiality Agreement" application to datarequests@cff.org prior to submitting their full application to CFF. The formal application for CFF Patient Registry Data Requests can be found at https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/Patient-Registry-Data-Requests/

Note: *The application must be submitted using the online system available from the link above and the email from the system indicating receipt of the application must be uploaded to the submission. Funding is contingent upon approval to access registry data.*

CFF Biorepository Clinical Specimen Confirmation Letter (if applicable)
To request clinical samples from the CFF Biorepository to use in the proposed study, please follow the following steps:

1. Visit https://www.cff.org/researchers/cf-foundation-biorepository#biobanked-samples-available to identify potential sample fit and download request form.
2. Submit fully completed clinical specimen inquiry form to ezagnit@cff.org at least 6 weeks prior to the Full Application deadline.
3. Two letters will be provided:
   - You will receive documentation confirming receipt of your request and that the sample request is feasible from the Sr. Clinical Research Development Specialist. ***This does not confirm access to the requested samples.***
   - A letter documenting available sample counts and other pertinent biorepository details, and confirming access to samples pending CFF funding will be provided by the Sr. Clinical Research Development Specialist for submission with the Full Application. ***Applications without this documentation may have funding held OR may be downgraded during review due to lack of CFF Biorepository support.***

   Late requests may not be processed in time for submission of materials with the application.

Note: *Applicants must upload the confirmation letter provided by the CFF Sr. Clinical Research Development Specialist to the application. Funding is contingent upon approval and availability to access clinical specimens.*

APPENDICES (IF APPLICABLE)
Appendices are restricted to the following two (2) categories:

- Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable.
- Up to three (3) reprints of the applicant's work relating to the general area of research in the proposal may be uploaded in PDF format.

***Organization Assurances & Certifications**
CFF requires, as applicable, that all U.S.-based awardees obtain Institutional Review Board (IRB) approvals for human subject research, Institutional Biosafety Committee (IBC) approval for recombinant or synthetic nucleic acid research, and Institutional Animal Care and Use Committee (IACUC) approval for animal research, (see additional information regarding these approvals below). Copies of these approvals, if available at the time the application is submitted, must be uploaded with the application as appendices. CFF will not release payments to awardee institutions until these documents are received and on file with the CFF GCMA Office.

Awardees based outside of the U.S. must comply with the applicable equivalent regulations in their respective countries and provide copies of approvals as soon as they are available. CFF will not release payments until these documents are received and on file with the CFF GCMA Office.

Research Involving Human Subjects: CFF policy pertaining to the protection of individuals as research subjects requires that for each proposal awarded, the awardee institution certify in writing that an Institutional Review Board (IRB) has reviewed and approved the procedures for the use of human subjects, or human organs, tissues and body fluids, in the proposed research, in accordance with the

Department of Health and Human Services policies found at https://www.hhs.gov/ohrp/regulations-and-policy/index.html. In the event the IRB has determined a study is exempt, documentation demonstrating the exempt status must also be submitted to the CFF GCMA Office.

Research Involving Recombinant or Synthetic Nucleic Acid Molecules: All research involving recombinant or synthetic nucleic acid and human gene transfer studies supported by CFF must meet the requirements contained in the document *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (updated April 2019*). This publication and announcements of modifications and changes to the NIH Guidelines are available from the Office of Science and Policy, National Institutes of Health, 6705 Rockledge Drive, Ste 750, MSC 7985, Bethesda, MD, 20892-7985 or online at https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf.

Research Involving Animals: Applications submitted to CFF involving the use of animals must meet the guidelines of the National Institutes of Health found at https://grants.nih.gov/grants/olaw/olaw.htm, which require that all proposed studies be reviewed and approved by an Institutional Animal Care and Use Committee (IACUC). In addition, CFF awardee institutions and laboratories must be accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and/or have other verifiable assurances that the institution and laboratory meet appropriate standards.

Validation and Submission

Prior to selecting "**Sign & Submit to AIO**", please complete a thorough review of the entire application. The "**Sign & Submit to AIO**" button will trigger validation on all required fields and identify any upload errors or incomplete fields. Upon selecting Sign & Submit to AIO, the ability to edit the application will be locked pending review and approval by your AIO.

After selecting **Sign & Submit to AIO**, the applicant will receive an email asking them to sign the application Face Page electronically using Adobe Sign. Once signed by the PI, the Face Page will then be routed to the AIO contact that is listed on the application for review and signature.

To ensure the application is fully signed and submitted ahead of the Application Deadline for this program, please be sure to complete the application, and begin the Sign & Submit to AIO process in advance of the 5:00 PM EST deadline. The status of your application will display "Submitted" once fully signed, to indicate that your application has been received by CFF.

XI. Other Information

Not applicable to this RFA

XII. Contact Information

For technical support and program/content information:
Primary CFF GCMA Office contact Erik Warnke ewarnke@cff.org or 301-841-2614
Secondary CFF GCMA Office contact grants@cff.org or 301-841-2614

For scientific questions:
Elizabeth Yu, Ph.D. at eyu@cff.org