CYSTIC FIBROSIS FOUNDATION

For application technical support, please contact: aminucci@cff.org

Program Name: 2024 Spring Clinical Pilot and Feasibility Award with LOI

Brief Program Overview/Description: Clinical Pilot and Feasibility Awards are offered to support projects involving human subjects (see 45 CFR§46.102(f)) that will develop and test new hypotheses and/or new methods (or those being applied to the problems of cystic fibrosis for the first time), and to support promising new investigators as they establish themselves in research areas relevant to cystic fibrosis. The intent of these awards is to enable investigators to collect sufficient preliminary data to determine the best strategies and methods for approaching a major question that ultimately will require assessment through a larger-scale research and/or multi-center, collaborative trial.

Funding Amount: Applicants may request funding of up to $80,000 per year, plus an additional twelve (12) percent indirect costs for single-center clinical studies; and up to $150,000 per year, plus twelve (12) percent indirect costs for multi-center clinical studies, for up to two (2) years). *Up to an additional $100,000 may be available via supplemental funding.

***NEW* Supplemental Funding to Address High Priority Areas – Please refer to Section III. Funding Amounts below for detailed information regarding Remote Collection and Health Equity Supplements.**

Eligibility:

- United States residents and applicants from outside the United States are welcome to apply.
- Applicants must be independent investigators. An independent investigator is an individual who is out of fellowship training and whose institution allows them to submit applications for research funding as a Principal Investigator.
- *Additional eligibility requirements can be found in Section IV below.*

Key Dates:	**(Spring 2024 Cycle)**	**(Fall 2024 Cycle)**
Published	August 10, 2023	February 22, 2024
LOI Submission Deadline	September 21, 2023	April 4, 2024
LOI Applicant Notified	December 2023	June 2024
Full Application Deadline	February 13, 2024	August 13, 2024
Committee Review Date	May 2024	October 2024
Notification to Applicants	May 2024	November 2024
Earliest Project Start Date	July 1, 2024	January 1, 2025

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*We highly encourage that you pre-register your profile, institution, contacts, and Title of your Application by this date. This will confirm that your submission at the Application Deadline, is without any system-related issue. It will also allow us to assist you on system-related queries before the Application Deadline. This pre-registration is for new applicants to the system and will only need to be completed once.

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.

CF Foundation Resources

The Cystic Fibrosis Foundation supports the development of a number of helpful tools and resources to assist the research community in accelerating the progress toward new scientific knowledge of and new therapies for cystic fibrosis. For more information on Tools and Resources for the CFF research community, please visit: https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/

CFF Patient Registry Data

The CF Foundation Patient Registry collects information on the health status of people with cystic fibrosis who receive care in CF Foundation-accredited care centers and agree to participate in the Registry. This information is used to create CF care guidelines, assist care teams providing care to individuals with CF, and guide quality improvement initiatives at care centers. Researchers also use the Patient Registry to study CF treatments and outcomes and to design CF clinical trials.

The Cystic Fibrosis Foundation Patient Registry is an invaluable tool for researchers who are interested in conducting studies about people with CF in the United States. About 50,000 individuals have been followed in the Registry, and many have been included for over 20 years. In addition, we recently linked the CF Foundation Patient Registry with the Pediatric Health Information System (PHIS) database. Investigators at PHIS sites can request to use these linked data. Instructions on how to request CFFPR data for your research project is included in the application instructions below.

CFF Biorepository

Cystic fibrosis biological samples are available to qualified researchers to help develop promising new studies that will support CF research and aid in drug development and drug discovery. Biorepository samples come in many different forms: blood, urine, stool, tissue, and other material. These samples are stored under appropriate conditions that ensure they are preserved for future analysis.

Since 2006, the Cystic Fibrosis Foundation has collected and stored samples from a variety of clinical trials. The CF Foundation has developed a database that combines information from these samples with data from CF clinical trials and the CF Foundation Patient Registry to create a unique and specific sample profile. Instructions on how to request CFF Biorepository samples for your research project is included in the application instructions below.

Community Voice

The CF Foundation is committed to ensuring that the CF community's voice is heard in all of our activities. In December 2014, the CF Foundation created Community Voice, formerly known as the CF Adult and Family Advisors group, to serve as a consultative body and partner to the Foundation on various activities. Research Voice, a sub-committee within Community Voice, consists of people with CF and their family members who undergo special training on the basics of clinical research to provide insight and feedback to the research community.

Opportunities to partner with the community occur throughout the stages of a research project. Recently, several CFF funded investigator-initiated clinical research projects have utilized community engagement through

Community Voice to successfully execute and complete their projects. The CF Foundation strongly encourages you to engage people with cystic fibrosis throughout the stages of clinical research. Based on your goals and objectives, the CF Foundation will work with you to determine which mechanisms are most appropriate. To learn more about how community insights can help you optimize your research project, email CommunityVoice@cff.org.

National Resource Centers

Specialized procedures are often needed to measure the outcomes of cystic fibrosis clinical trials. These include both laboratory-based measurements, such as cytology and inflammatory markers, and interpretive outcomes, such as computed tomography and nasal potential difference. For more information about National Resource Centers, please visit: https://www.cff.org/Research/Researcher-Resources/National-Resource-Centers

II. Program and Award Overview

Program Overview

The Foundation's Investigator-initiated Clinical Research Programs aim to provide support for academic clinical research projects that have the potential to make an important contribution to the CF Foundation's mission. Academic clinical research projects may address diagnosis, treatment, management of disease or symptom, or the pathophysiology of CF using clinical (observational or interventional), translational or epidemiologic study approaches.

The CF Foundation funds investigator-initiated clinical research through the Idea Development Award (IDA), the Clinical Pilot and Feasibility Award(CP&FA), the Clinical Research Award (CRA), and the Clinical Research Award Plus (CRA+), and other various targeted funding opportunities that occur throughout the year.

Funding for most investigator-initiated clinical research awards is a two-tier process. The CF Foundation requires CP&FA, CRA, and CRA+ to submit either a Letter of Intent (LOI) or Concept Proposal in advance of a full application. Full applications are accepted on an invite-only basis; however, applicants may be able to by-pass the LOI with prior approval from the Program Officer. The Idea Development Award does not contain a Letter of Intent component.

On average, the Foundation invites about 50% of the investigators to submit full applications and funds roughly 30% of full applications.

Award Overview

Clinical Pilot and Feasibility Awards are offered to support projects involving human subjects (see 45 CFR§46.102(f)) that will develop and test new hypotheses and/or new methods (or those being applied to the problems of cystic fibrosis for the first time), and to support promising new investigators as they establish themselves in research areas relevant to cystic fibrosis. The intent of these awards is to enable investigators to collect sufficient preliminary data to determine the best strategies and methods for approaching a major question that ultimately will require assessment through a larger-scale research and/or multi-center, collaborative trial. Special consideration will be given to those projects that pursue new approaches, study under-researched topics, or investigate more creative avenues of research to address the problems of CF. Applications for continued funding of existing projects, or for long-term support of an investigator, will not be considered.

Note: Preliminary data is not required; however, applicants must provide sufficient background information and rationale to support moving this work into human subjects research.

III. Funding Amount

- Applicants may request funding of up to $80,000 per year, plus an additional twelve (12) percent indirect costs for single-center clinical studies; and up to $150,000 per year, plus twelve (12) percent indirect costs for multi-center clinical studies. *Up to an additional $100,000 may be available via supplemental funding.

***NEW* Supplemental Funding to Address High Priority Areas**

Remote Collection Supplement: Applicants may request an additional $50,000 (plus twelve (12) percent indirect costs) over the entire project period to include an additional aim that leverages the proposed main research study aims that address important gaps in knowledge and improve our understanding of the utility of remote collection of either specimens, endpoints, and/or clinical data to address these gaps in knowledge. This supplement is not intended to support Quality Improvement research in sample collection or patient use of daily therapies.

Health Equity Supplement: Applicants may request an additional $50,000 (plus twelve (12) percent indirect costs) over the entire project period to **EITHER** advance our knowledge of health disparities in cystic fibrosis **OR** enhance the diversity, equity, and inclusion in the biomedical workforce.

- Applicants may request funding of up to $100,000 over the course of the entire project period, plus twelve (12) percent indirect costs to support sub-aims or salary to address high priority areas in remote collection and health equity.
- Awards may be approved for up to a two (2) year period. Funding for Year 2 is contingent upon submission and approval of a renewal progress report and the availability of funds.

Direct costs may be requested for:

- Salaries and Benefits
- Research supplies
- Equipment
- Research-related subject costs
- Consultant costs
- Support for multidisciplinary collaborations, including travel
- Travel costs for scientific/technical meeting(s)
- Tuition (proper justification required prior to approval)

Indirect Costs up to twelve (12) percent may be requested from CFF.

- Applicants may request indirect costs on the first $25,000 of each subcontract for the project period.

Indirect costs may be requested for all expenses except for the following:

- Equipment (items over $5,000 in value)
- Computer software
- Software licenses

If the application is funded:
Per CFF Terms and Conditions, the PI is permitted flexibility in the utilization of funds in the research budget. However, any change to revise an amount that exceeds the percentages listed in the table below or to the fundamental purposes of the Project requires prior written approval from the CFF Grants and Contracts Office.

Award amounts:	**Amount that may be re-budgeted without prior CFF approval:**
Up to three hundred thousand USD ($300,000) per year	Twenty percent (20%) up to a maximum of thirty thousand USD ($30,000)
Greater than three hundred thousand USD ($300,000) per year	Ten percent (10%)

Notwithstanding the above table, prior approval is required for changes in percent effort of key personnel.

IV. Eligibility

- United States residents and applicants from outside the United States are welcome to apply.
- International applicants and institutions are required to submit additional information in accordance with USA Patriot Act and the U.S. Department of Treasury Anti-Terrorist Financing Guidelines (see section VI.10.L below).
- Applicants must be independent investigators. An independent investigator is an individual who is out of fellowship training and whose institution allows them to submit applications for research funding as a Principal Investigator.
- New or established investigators with no previous work in cystic fibrosis research who wish to apply their expertise to a problem in this area.
- Candidates who are clinical fellows should apply to the CFF Clinical Fellowship program for the appropriate year.
- Candidates who are postdoctoral fellows should apply to the CFF Postdoctoral Research Fellowship program.
- Industry-sponsored research projects are not eligible to apply through this program and instead should consider applying to the Therapeutics Development Awards program. For additional information, please contact grants@cff.org.

V. Mentorship Requirements

Not applicable to this RFA

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

The Cystic Fibrosis Foundation regularly assesses its key research priorities to ensure we are on track to accomplish our mission to cure CF and to provide people with CF the opportunity to lead long lives. Applicants are encouraged to align submissions to these priorities to maximize their potential for being funded.

Key research priorities for applicants are outlined in further detail on https://www.cff.org/Research/Researcher-Resources/Awards-and-Grants/Applicant-Resources/Key-Research-Priorities-for-Applicants/

Areas of Encouragement

Areas of Encouragement are research topics that are considered gaps in our knowledge in the detection and monitoring, diagnosis, or treatment of a CF complication. The Areas of Encouragement will be updated on a biennial basis during Guidance, Action, Projection (GAP) Meetings and will be informed by GAP meeting attendees, community surveys, CFF Workshop recommendations, and other areas of focus identified by guidelines committees or CFF/TDN research working groups.

Applicants to the funding opportunities reviewed by the Clinical Research Committee are highly encouraged, but not required, to submit research proposals that address one or more Areas of Encouragement.

Areas of Encouragement

CF-RELATED DIABETES (CFRD): Research related to the screening and treatment of CFRD, including discovery and validation of novel biomarkers, when to initiate treatment, novel treatments, and personalized treatment approaches.

SEXUAL & REPRODUCTIVE HEALTH: Research related to fertility, pregnancy, parenthood, gonadal hormones and contraception, urinary incontinence, and sexual/reproductive health of all genders.

BONE HEALTH: Research related to bone accrual in growing children, factors that impact changes in bone density in adults, biomarkers to monitor changes in bone structure and impacts of CF therapies and other therapies on bone health.

DIET AND NUTRITION: Research related to the impact of diet on bone accrual/maintenance, CFRD risk and disease prevention/progression, metabolic syndrome, and the interplay between nutrition and CF symptoms and other co-morbidities.

GUT HEALTH: Research related to the development of relevant endpoints to study gut motility (e.g., gastroparesis).

LIVER & PANCREAS: Research related to the screening and monitoring for pancreatic and liver disease/complications, approaches to detect and treat non-cirrhotic portal hypertension, and to evaluate advanced liver disease.

IMAGING: Research related to the development or validation of novel imaging modalities to screen and/or monitor for pancreatic, liver, and lung disease/complications or response to therapy.

CANCER: Research related to understanding GI tract cancers, including incidence and natural history of GI cancers in CF and the impacts of modulators, endocrine malfunction, and other CF complications on cancer incidence.

REMOTE MONITORING: Research related to the development and use of remote endpoint or remote monitoring across a broad domain of CF complications/symptoms, including microorganism detection, sleep, diet, exercise, cough monitors, lung function, and other wearables.

EARLY LUNG DISEASE PROGRESSION: Research related to monitoring early lung disease progression for patients on modulator therapy that could lead to a better understanding of early benefits of modulator therapy or to create a decision tool on when to initiate modulator therapy.

ADVANCED LUNG DISEASE: Research related to the monitoring of disease progression, the identification of reversible disease, and understanding risk incurred prior to transplant for poor outcomes in Chronic Lung Allograft Dysfunction (CLAD).

LUNG TRANSPLANT: Research related to understanding the usefulness, safety, and impact of modulator therapy post lung transplant, and the identification of therapies/treatment pathways that reduce CLAD post-transplant.

SINUS DISEASE: Research related to improving our understanding of CF sinus disease, including disease pathophysiology (of sinus disease and as surrogate for the lung), identification of best management practices, and impact of sinus disease management on health outcomes, including quality of life, lung disease outcomes, and transplant outcomes.

NEUROCOGNITIVE FUNCTIONING: Research related to advancing the general understanding of neurocognitive function in CF, including research to understand the impact of modulators on neurocognitive and mental health outcomes.

ANXIETY: Research related to the prevention/interventions for anxiety, including procedural distress/anxiety and medical trauma.

DEPRESSSION: Research related to the prevention/intervention for depression, including resilience (self-care, wellness, etc.), suicide risk, and research related to improved understanding of the relationship between mental health and sustaining daily care (adherence).

SLEEP: Research related to the bi-directional impact of sleep disturbance/disorder on physical and mental health.

PAIN: Research related to the diagnosis and treatment approaches (psychological, pharmacological and wellness) to CF-related pain management

ANTIMICROBIAL MANGEMENT: Research related to the optimization of current antimicrobial therapies (e.g., improve understanding of drug-drug-interactions, treatment approaches, long-term impacts of therapies, antimicrobial stewardship, and eradication) in the current post-modulator population.

MICROORGANISM DETECTION: Research related to improving microorganism detection, including development of novel biomarkers, assays, and/or platforms and studies evaluating best approaches for detection (e.g., home collection of sputum, bronchoalveolar lavage fluid (BALF), etc.) and/or assessments of specimen quality and processing requirements needed for research.

MICROORGANISM RELEVANCE & SURVEILLANCE: Research related to microorganism relevance and surveillance, including improving our knowledge of which species are pathogenic, how surveillance samples/studies may help understand disease heterogeneity (relevance of dental disease, sinus disease, etc.), and potential shifts in pathogens (microbiome shifts vs. pathogenic organisms) in the post-modulator era.

INFLAMMATION: Research related to understanding the role and relevance of inflammation in lung disease presence, severity, and progression; innovative ways to detect and monitor inflammation that reflects lung disease severity and progression; role of biomarkers as outcome measures for future CF clinical trials targeting infection and/or inflammation.

More information regarding the research priorities of the CF Foundation can be found here. For specific questions regarding your proposal and the CFF's research priorities, please contact the Program Officer, Dara Riva (driva@cff.org).

VII. Review and Award

Applications to the Clinical Pilot and Feasibility Award program are reviewed by the Clinical Research Committee (CRC), community representative reviewers, and the CFF.

Applications undergo scientific peer-review by the CRC and receive scores based on innovation, scientific merit, and impact on the CF Foundation's mission. Applications will also be evaluated on their experimental design and methods, rationale, and statistical analysis methodology. Applicants should adequately describe how the hypothesis will be tested, demonstrate adequate power for testing the hypothesis, and clearly define all variables in their statistical analysis section. Applicants are required to consult with a biostatistician prior to submitting their proposals. In addition, applicants are required to include a biostatistician with a minimum of 5% effort on their project.

Community representative reviewers evaluate applications based on study design and feasibility from the perspective of people with CF. They also evaluate the project on its relevance to the CF Foundation's mission and the project's potential to impact those living with CF. Community representative reviewers do not review an application for scientific merit. Reviews from the community representative reviewers are used to inform funding decisions.

Applications will be evaluated on the following criteria:

- The soundness of the project's research design and proposed methodology
- The likelihood the project will inform more definitive studies that address fundamental knowledge gaps within CF Foundation research priorities and Areas of Encouragement, including the potential impact on the advancement of the CFF Mission
- The project's level of innovation related to approach, method, and/or idea
- The qualifications of the candidate, collaborators, and other key personnel

- The quality of grantsmanship, including grant writing, level of description, accuracy, and general organization

Funding of awards is approved by the CFF Board of Directors and is based on the availability of funds, priority score assigned to each application, and recommendations of the CRC, community representative reviewers, and CFF Program Officers. All awards are subject to compliance with applicable regulations and CFF policies.

Chief reasons for assigning low priority scores to applications during review:

- Insufficient information or documentation
- Inadequate statement of hypothesis, inadequate experimental design,
- inadequate analytic methods, or experimental plan that does not address hypothesis
- Failure of the applicant to describe potential relevance of the proposed study to address issues or knowledge gaps in CF
- Failure of the applicant to document the necessary skills, training, or collaborate with individuals with the relevant expertise to accomplish the goals of the proposal
- Failure of the applicant to demonstrate adequate level of support/expertise and appropriate plan for data acquisition, management and statistical analyses
- Failure of the applicant to meet all the criteria described in these guidelines

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

VIII. Submission Information

A Letter of Intent (LOI) must be submitted and approved prior to submitting a Full Application. Applicants may only submit one LOI and one full application per cycle.

Submit online at https://awards.cff.org
(Refer to Section IX and 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 https://awards.cff.org will be reviewed.

Specific requests regarding a deviation from these guidelines must be submitted to the Program Officer Dara Riva (driva@cff.org) for approval prior to submitting their application.

Key Dates:	**(Spring 2024 Cycle)**	**(Fall 2024 Cycle)**
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*We highly encourage that you pre-register your profile, institution, contacts, and Title of your Application by this date. This will confirm that your submission at the Application Deadline, is without any system-related issue.

It will also allow us to assist you on system-related queries before the Application Deadline. This pre-registration is for new applicants to the system and will only need to be completed once.

IX. Letter of Intent Guidelines

LOI Submission Deadline: Thursday, September 21st, 2023 at 5:00 PM (EST)

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

Investigators with a previously approved LOI who did not submit a full application, and/or investigators submitting a revised application may request to bypass the LOI stage. These requests must be e-mailed to grants@cff.org with "**Clinical P&F LOI Bypass Request**" in the subject line. LOI bypasses are granted on a case-by-case basis and the CF Foundation Grants & Contracts Management and Administration (GCMA) Office will send a notification of the final determination.

Applicants whose LOI **was not approved in an earlier submission** may resubmit the LOI with (1) appropriate revisions, and (2) an attachment that provides a point-by-point response to the limitations noted by the reviewers.

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 https://awards.cff.org, the system will compile them into a single PDF file. You may preview this file by selecting "LOI 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 well before the date you plan to submit an application. 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 "**2024 Spring Clinical Pilot and Feasibility Award with LOI**" 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 any additional questions. Also, please 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.

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 pre-loaded as the Lead Institution. Domestic applicants must verify their institution by selecting their Employer Identification Number (EIN) or Tax Identification Number (TIN) that will be pre-loaded based on the institution linked to your CONTACT PROFILE. You may find your EIN by referencing the Institutional W-9 or equivalent documentation. If the EIN/TIN is not located in our system, you have the option to 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 CF Foundation GCMA Office must have a copy of the applicant institution's current W-9 and 501(c)3 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 CF Foundation GCMA Office.
- Non-U.S. applicants must provide a copy of the W-8BEN-E form (required). In addition, a tax equivalency letter should be uploaded, if available. If a tax equivalency letter is not available, applicants must upload a letter stating this documentation is not available.

International Applicants (if applicable):

For international applicants, you will need to answer an eligibility question specifying if you are an independent investigator. If answering yes, CFF may require an additional letter of support to be added to the application to verify eligibility.

Applicants whose institution is not a United States based-entity will be required to provide additional information and complete the CFF International Institution Form as part of the Full Application stage. Refer to **International Institution Form** section on page 23.

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”.

ABSTRACTS/RELEVANCE

In the spaces provided online, 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 “**Open**” button under the Budget tab and complete the relevant budget categories for each year of funding. Fill in the applicable amounts for each year of support requested by completing the online fields (Periods 1 and 2) All Clinical Pilot and Feasibility awards are for a maximum of two years. Please refer to Section III. Funding Amounts for detailed funding allotments.

Please refer to Section III. Funding Amounts for detailed funding allotments

Be sure to click “**Save**” prior to closing the budget window.

LOI UPLOADS

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

- Biographical Sketch(es) of Key Personnel
- Response to Prior LOI Critique (if resubmission)
- LOI Project Description
- Innovation Statement
- Protocol Synopsis (if applicable)
- Remote Collection Supplement (if applicable)
- Health Equity Supplement (if applicable)
- CFF Patient Registry Data Request Application (if applicable)

Biographical Sketch(es) of Key Personnel (NIH template available for download)

CFF defines “key project personnel” as any individual with an advanced degree who will play an instrumental role in the research project. An NIH Biographical Sketch form should be completed for each key project personnel and uploaded as PDF. The maximum length for each biosketch is five (5) pages. Personnel must include a biostatistician with a minimum of 5% effort during the entire project period.

Response to Prior LOI Critique (template available for download, if applicable)

Resubmissions of LOI applications that were previously not approved are required to make a point-by-point response to the limitations noted in the critique of the earlier submission. Maximum three (3) pages

LOI Project Description (template available for download)
Upload a PDF copy of the completed document. Maximum of three (3) pages (not including the literature cited). Components should include:

- **Statement of Hypothesis and Specific Aims**: State concisely and realistically the intent of the proposed research and the hypothesis to be tested. The specific aims should both test this stated hypothesis and be relevant to the mission of the Cystic Fibrosis Foundation.
- **Brief Study Design**: Briefly describe the research design and methods for achieving the specific aims, including justification or rationale for clinical endpoints proposed. Briefly describe the eligibility criteria, recruitment and retention processes, study procedures (including participant and study timeline), and study outcomes and other measures. Include a brief statistical section which focuses on the precision of estimates that will be used to design future studies, potential sources of bias/confounding and handling of missing data.
- **Literature Cited**: References should be numbered in the sequence that they appear in the text. Each citation must include the names of authors, the name of the journal or book, volume number, page number and year of publication (titles are optional).

Innovation Statement (template available for download)
Provide a statement of no more than 1,500 characters that highlights how the proposed study is innovative in study concept, research methods or technology, or adaptations of existing methods or technologies for a non-science audience.

Protocol Synopsis (template available for download, if applicable)
Complete the information required in the available template for each aspect of the study protocol.

Remote Collection Supplement (template available for download, if applicable)
Provide a brief description of no more than 1,500 characters of strategy, methodology and analyses. Provide detail on how data obtained through this aim would address important gaps in knowledge and improve our understanding of the utility of remote collection of either specimens, endpoints, and/or clinical data to address these gaps in knowledge. This supplement is not intended to support Quality Improvement research in sample collection or patient use of daily therapies.

Health Equity Supplement (template available for download, if applicable)
Provide a brief description of no more than 1,500 characters of the work you propose to **EITHER** improve our understanding of health disparities in cystic fibrosis **OR** enhance the diversity, equity, and inclusion in the biomedical workforce. Aims of health equity or disparity research may be related to race, ethnicity, gender, or other demographics understudied or underserved in cystic fibrosis. If the supplement is intended to support a BIPOC member of the study team, a biosketch should be included.

CFF Patient Registry Data Request (if applicable)
CF Foundation Patient Registry. Applicants whose project will include requesting data from the CF Foundation Patient Registry should check the appropriate box. It is not necessary to check the box for single site studies or studies acquiring Registry data from the biorepository. Please note: if the LOI is approved for full submission, the applicant will need to submit the project for review by the Registry / Comparative Effectiveness Research (CER) committee prior to grant submission. Instruction regarding submission for review are located at: https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/Patient-Registry-Data-Requests/

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 clinical specimen inquiry form to ezagnit@cff.org at least six weeks prior to LOI submission. You will receive documentation confirming receipt of your request and that the sample request is feasible from the Sr. Clinical Research Development Specialist. This should be submitted with your LOI.
3. Should you be invited to submit a full application, you must connect with the Sr. Clinical Research Development Specialist and finalize your sample request no less than 6 weeks prior to the Full Application deadline (2 January 2024, 2 July 2024). ***Late requests may not be processed in time for submission of materials to the CRC.***
4. 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.***

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.*

Submission

Prior to selecting "**Sign & Submit**", please complete a thorough review of the entire LOI. The "Sign & Submit" button will trigger validation on all required fields and identify any errors. Only the Principle Investigator will need to sign off on the application at the LOI stage.

X. Full Application Guidelines

Full Application Deadline: Tuesday, February 13, 2024 at 5:00 PM (EST)

A Letter of Intent (LOI) must have been submitted and approved prior to receiving an invitation to proceed with a Full Application

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 https://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

If the LOI submission is approved to proceed to a full application submission, the application will have already been pre-loaded in the system. Log in with your existing credentials to access the application.

Your draft application will by listed under "**My Applications**", then within the "**Draft Applications**" section. Upon locating the draft application, you may select it to begin your submission.

Applicants may stop at any point but must click the **"Save"** button before exiting in order to save their progress.

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.

Please note: Only select the "**Sign & Submit to AIO**" button after the application has been fully completed. This will trigger validation on all required fields and send the application to your Authorized Institutional Official "AIO" for review and signature.

GENERAL

Enter the title of your project, enter the project start and end dates, select the number of periods being requested, and complete any additional questions. Also, please 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 Organizational Assurances and Certifications as cited on page 24.**

CONTACT PROFILE

If a profile was completed during the LOI, 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 pre-loaded as the Lead Institution. Domestic applicants must verify their institution by selecting their Employer Identification Number (EIN) or Tax Identification Number (TIN) that will be pre-loaded based on the institution linked to your CONTACT PROFILE. You may find your EIN by referencing the Institutional W-9 or equivalent documentation. If the EIN/TIN is not located in our system, you have the option to 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 CF Foundation GCMA Office must have a copy of the applicant institution's current W-9 and 501(c)3 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 CF Foundation GCMA Office.
- Non-U.S. applicants must provide a copy of the W-8BEN-E form (required). In addition, a tax equivalency letter should be uploaded, if available. If a tax equivalency letter is not available, applicants must upload a letter stating this documentation is not available.

International Applicants (if applicable):

For international applicants, you will need to answer an eligibility question specifying if you are an independent investigator. If answering yes, CFF may require an additional letter of support to be added to the application to verify eligibility.

Applicants whose institution is not a United States based-entity must complete the CFF International Institution Form. Refer to **International Institution Form** section on page 23.

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.

If added during the LOI, this will be pre-populated but can be changed during the full application. 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

CFF defines "junior investigator" as any individual who has not received a CFF/CFFT Research Grant or NIH equivalent (e.g. R01, R21, R23) as a Principal Investigator AND is within their first five years of their first academic appointment at the level of Assistant Professor or equivalent.

Applicant is NOT considered a junior investigator if they meet one or more of the below criteria:

- More than five years after their first academic appointment at the level of Assistant Professor (or equivalent)
- Has received a CFF/CFFT Research Grant or NIH equivalent (e.g., RO1, R21, R23)
- Has been promoted to Associate Professor or higher

Letters of Reference for junior investigators must be submitted by the following individuals:

- **The Chair of the applicant's department at the applicant Institution** – The letter of reference from the Department Chair should indicate the release of sufficient space and facilities for the work described, as well as guarantee the time commitment of the investigator to the project. If the applicant is currently a fellow, the letter of reference should include confirmation of the pending faculty-level appointment.
- **At least two other individuals** familiar with the applicant's scientific interests and abilities.

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 can choose to hit "Save" or "Invite" at the bottom of the screen. Hitting "Save" will not send an invitation to your references. Once you click "Invite" and close the pop-up window, the referees 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.

***Senior investigators, or those who have received a prior CFF/CFFT Research Grant or NIH equivalent, are not required to submit Letters of Reference; however, if they are new to CF research, Letters of Support and/or Collaboration should be provided and uploaded as Appendices.**

ABSTRACTS/RELEVANCE

In the space provided online, 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. Awards funded through this RFA are for a maximum of two (2) years. All Clinical Pilot and Feasibility awards are for a maximum of two years, and up to $80,000 per year (plus an additional 12% indirect costs). Applicants are required to include a biostatistician with a minimum of 5% effort on their project.
- Services that are part of routine medical care (as defined by the U.S. Department of Health and Human Services) may not be included in the project budget. Whenever possible, the price of services (e.g., X-rays, EKGs, PFTs, etc.) provided by the institution should be negotiated to the lowest possible non-profit price.
- Separate professional fees for interpretation of data (e.g., from X-rays, lab tests, PFTs) may not be included when such interpretation is performed by the named investigator(s), co-investigator(s), or consultants as part of the project, other than in exceptional circumstances. In such cases, justification for these fees must be described in detail in the budget justification template.
- Under most circumstances, hospitalization costs of study subjects cannot be included in this budget.
- If supplements are requested …..

The following budget categories are offered under this program:

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.

Consultant Costs - Give the name and institutional affiliation of any consultant who has agreed to serve in this capacity, including statisticians and physicians in connection with the project if they are not listed under personnel. In the budget justification, briefly describe services to be performed, the number of days, rate of compensation, per diem and any other associated costs. Qualifying consultants are individuals that are generally not employed at the applicant institution and/or are consulting independently to the project.

Travel - Describe the purpose of any CF-relevant travel. Please note: 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 CF Foundation GCMA Office with the exception of travel for speaking engagements at the European Cystic Fibrosis Conference to present data obtained through a CFF funding opportunity. **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".

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.

Major Equipment - List all items of equipment greater than **$5,000** requested and the cost of each item. If funds are requested to purchase equipment that is equivalent to items listed under "Facilities Available", justify the duplication. Justify any item of equipment for which the need may not be obvious.

Other Expenses - Itemize other expenses by major categories, such as duplication costs, publication costs, minor equipment (under $5,000), computer charges, conference registration fees, other research costs (e.g., recruitment flyers, brochures, patient travel cost reimbursement, translation of patient facing materials, and reasonable patient stipends for participation), etc. Justify all items. Tuition costs may be requested for personnel supported through this study but may not exceed **$10,000** per person per year.

Patient Research Costs – Funds may be requested for patient research costs specifically related to the proposed research. The basis for estimating funds requested in this category must be justified and applicants must provide detailed information regarding the proposed costs (e.g., number of procedures, cost per procedure, ancillary costs). The scientific need for patient research costs will be considered in the review. Negotiation of these costs are between the applicant institution and the service provider.

If approved as part of the application, patient research costs are capped at the amount requested in the budget and under no circumstances is CFF responsible for any costs that are later determined non-covered by third party insurers. Applicants and applicant institutions acknowledge that CFF is solely a provider of funding for the research performed under an approved award and not a sponsor of the research as defined by the FDA (21 CFR §312.3(b)).

Subcontractors Summary – If applicable, detailed budgets and budget justifications for each subcontract, including indirects, must be provided for each year of support. Subcontractors are added in the prior section entitled **CONTACTS**. The lead/prime applicant (PI) and/or Grants Officer can initiate/complete the subcontract budget. After adding Subcontractor(s), in order to access the subcontract budget activity, please select the "**BUDGET**" tab of the application and click the "Open" button next to each listed subcontractor. After completing the subcontract budget activity, please select "**Pending PI Acceptance**", as well as "**Submit**" to ensure the subcontractor budget is included as part of the main application budget.

For applications that include a subcontract with a third party, the applicant may request indirect costs on the first $25,000 of each subcontract per project period. Negotiations of subcontracts are between the applicant institution and the subcontractor.

Budget Detail – Indirect Costs

Indirect costs of up to twelve (12) percent may be requested from CFF. Indirect costs may be requested for all expenses except for the following:

- Major equipment (items over $5,000 in value)
- Computer software
- Software licenses

LOI UPLOADS

This section will allow access to the documentation uploaded at the LOI stage.

FULL APPLICATION UPLOADS

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

- Collaboration Detail Template (if applicable)
- Research Plan
- Innovation Statement
- Protocol Synopsis
- Critique Response (LOI or resubmission)
- Statement of Community Engagement (if applicable)
- Remote Collection Supplement (if applicable)
- Health Equity Supplement (if applicable)
- Budget Justification
- Biographical Sketches of Key Personnel
- Other Support
- Facilities Available
- Results of Past and Current CFF/CFFT Support
- Data Safety Monitoring Plan
- CFF Patient Registry Data Request Application (if applicable)
- International Institution Form (if applicable)

Collaboration Detail Template (template available for download, if applicable)
On the provided template please list each collaborator, including their institute and responsibilities or resources they are dedicating to the project.

Research Plan (template available for download)

- At the top of each page, type the PI's name. Each page must be sequentially numbered at the bottom.
- Research Plans are limited to eight (8) single-sided pages, not including the Literature Cited. Applications exceeding this page limit will not be reviewed. Include sufficient information to permit effective review without necessitating reference to previous applications, or the cited literature. Information should be presented in a clear and concise manner, while being specific and informative. One page is to be dedicated to the Aims of the proposal.
- **Key figures and legends must be included in the Research Plan. If uploaded as Appendices, they will NOT be reviewed.**
- If the application is a resubmission of a previously reviewed proposal, revisions should be clearly indicated by a change in font, or bolded or underlined text. CFF will not review resubmissions that have not been revised. Applicant's will only be allowed to revise and resubmit their full application for a specific project one time unless granted permission from the CFF Program Officer. An introduction to the revised application, including point-by-point response to prior reviewer critiques (maximum 3 pages), should be included using the template provided.
    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 test this hypothesis and be relevant to the mission of the Cystic Fibrosis Foundation, as well as gaps in present knowledge. 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, including considerations of strengths/weaknesses or gaps in published research. 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.
    c. **Approach:** Describe in detail the proposed research. This section should address the following areas, but the order of presentation can vary to enhance readability and presentation.
        i. **Preliminary Results:** Discuss preliminary studies, data, and/or experience of the study team pertinent to the proposed research plan. Although preliminary data are not required, inclusion of any preliminary available or studies, or detailed rationale for the proposed work informed by

relevant literature, as well as details related to the relevant experience of the study team can enhance the likelihood of success of the application.

ii. **Experimental Design and Methods:** Provide a detailed discussion of the experimental design and methods to be used to accomplish the specific aims, and to test the stated hypothesis. 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. Describe any strategies to establish and evaluate feasibility and specify how the data generated will be used in the development of a larger study to address gaps in CF knowledge.

iii. **Recruitment and Retention Plan:** Applications should include a discussion of the availability of potential participants for the proposed study and anticipated yield from recruitment and screening efforts. If there is more than one recruitment site, please provide a table showing the expected number and demographics of the population to be recruited at each site and overall. The plan should also include a discussion of experience in recruiting and retaining similar populations, expected challenges to recruitment and retention, and possible contingency plans. Applicants enrolling subjects are strongly encouraged to provide a demographic table of anticipated study participants, including race and ethnicity information. Clearly describe descriptions of the appropriate outreach and activities planned for ensuring a diverse study population including individuals historically underrepresented in research (sex/gender, race, ethnicity, socioeconomic status, etc.). Such a plan should include discussion of recruitment of historically underrepresented in research subjects whose primary language is not English.

iv. **Statistical Analysis and Power:** Pilot and feasibility trials are, by definition, not fully powered to answer a question. The investigator should provide a rationale for the number of participants who will be studied, including how such a sample will be sufficient for supporting the development of a larger trial. If a full power calculation is provided, the sample size and statistical power calculations should contain enough detail, including assumptions made, so that a reviewer can readily duplicate the sample size. Anticipated attrition rate(s) should be reported and considered in sample size planning/justification. A discussion of how missing data will be handled should be included. Any planned interim analyses should also be described. In instances of pilot studies where some parameters are unknown, we will accept your best estimates of the unknown parameters if preliminary data are not available. Identify if you are making estimates from data or from personal estimates.

v. **Limitations and Potential Pitfalls:** Discuss potential difficulties and/or limitations of the proposed procedures and alternative approaches to achieve aims. Point out any procedures, situations or materials that may be hazardous to personnel or patients and the precautions to be exercised.

d. Consultant Arrangements: If the proposed project includes consultant arrangements and/or collaboration with other individuals outside the applicant's group, describe the working relationships and support this description with letter(s) of support signed by collaborating individual(s).

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

Innovation Statement (template available for download)

Provide a statement of no more than 1,500 characters that highlights how the proposed study is innovative in study concept, research methods or technology, or adaptations of existing methods or technologies for a non-science audience.

Protocol Synopsis, Schedule of Events, and Subject Reimbursement (template available for download)

Complete the information required in the available protocol synopsis template for each aspect of the study protocol, if applicable.

Provide a Schedule of Events (SOE) in a form of a table listing the study visit timelines and procedures/events associated with each visit over the entire period of the project. Include information on which study visits must occur in person and which may be done remotely. Provide information related to recruitment incentives or payment for study participation for study subjects, this should include proposed method and timing of disbursement.

Critique Response (template available for download, if applicable)
For new applications: Provide a point-by-point response to the limitations noted in the critiques of the LOI, using the template provided. Maximum three (3) pages

For resubmissions: Provide a point-by-point response to the prior reviews. Beginning in 2018, applicant's will only be allowed to revise and resubmit their full application for a specific project one time unless granted permission from the CFF Program Officer. Maximum three (3) pages

Statement of Community Engagement (template available for download, if applicable)
Provide a statement of no more than 500 characters (including spaces) summarizing the proposed work completed under this planning grant that will involve patient engagement. Specifically, please provide descriptions about what type of support you are requesting from the CFF's Community Partnerships department, including survey develop and dissemination, focus groups, or patient partnership identification. Please provide a timeline on when patient engagement will occur during this planning grant. To learn more about Community Engagement and CFF's Community Voice, visit https://www.cff.org/Research/Researcher-Resources/Community-Input-into-Research/

Remote Collection Supplement (template available for download, if applicable)
Maximum of three (3) pages (not including literature cited)
Provide the significance, innovation, and approach for the proposed aim to advance our knowledge of remote collection of specimens, endpoints, and/or clinical data, and how this will address critical gaps in the main protocol or our knowledge in general. Explain how this aim leverages and extends the work being conducted in the main research proposal. Explain the importance of and critical barriers to progress in remote collection, and how the additional aim may shift current research or clinical practice. Describe any novel approaches, devices, or instrumentation. Describe the overall strategy, methodology, and analyses to be used to accomplish the supplemental aim, as well as proposed data and statistical analysis plans. This supplement is not intended to support Quality Improvement research in sample collection or patient use of daily therapies.

Health Equity Supplement (template available for download, if applicable)
Maximum of three (3) pages (not including literature cited)
Provide the significance, innovation, and approach for the proposed aim to **EITHER** advance our knowledge of health disparities in cystic fibrosis **OR** enhance the diversity, equity, and inclusion in the biomedical workforce.

If proposing an additional research aim, explain how this aim leverages the work being conducted in the main research proposal to additionally address issues of health equity and/or disparities. Explain the importance of the research aim proposed, the overall strategy, methodology, and analyses to be used to accomplish the supplemental aim. Describe the proposed data and statistical analysis plans, and strategies related to recruitment and retention that will additionally address critical issues of equity or disparity.

If the supplement is requested to support and enhance the diversity, equity, and inclusion of the biomedical workforce, provide information on activities, curricula, key personnel, mentorship, and/or trainees to justify the proposed funding request to support an additional BIPOC investigative team member. Provide details related to

how this individual will be contributing to the project and how this work will advance their career. A biosketch for this individual should be included.

Budget Justification (template available for download)
Describe costs listed in the Budget Detail. Use major categories, such as Salaries & 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.

Biographical Sketches for Key Personnel (template available for download)
Complete and upload an NIH Biographical Sketch for all key project personnel, beginning with the Applicant/Principal Investigator. International applicants can upload a biosketch that is equivalent in content to the NIH template provided. (CFF defines "key personnel" as any individual with an advanced degree that will play an instrumental role in the accomplishment of the research project.) Do not exceed five (5) pages per person.

Other Support (template available for download)
Complete and upload the Other Support form for all key project personnel, beginning with the Applicant/Principal Investigator. **Make sure all other support is listed not only CF Foundation funded projects (pending, current, and previous support).** 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 not permitted.

Facilities Available (template available for download)
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.

Results of Past and Current CFF/CFFT Support (template available for download)
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 award from which they resulted for the past five years. Please note that the following information must be included with each research project identified:

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

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 (template available for download, 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:

2. Visit https://www.cff.org/researchers/cf-foundation-biorepository#biobanked-samples-available to identify potential sample fit and download request form.
3. Submit clinical specimen inquiry form to ezagnit@cff.org at least six weeks prior to LOI submission. You will receive documentation confirming receipt of your request and that the sample request is feasible from the Sr. Clinical Research Development Specialist. This should be submitted with your LOI.
4. Should you be invited to submit a full application, you must connect with the Sr. Clinical Research Development Specialist and finalize your sample request no less than 6 weeks prior to the Full Application deadline (2 January 2024, 2 July 2024). ***Late requests may not be processed in time for submission of materials to the CRC.***
5. 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.***

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.*

International Institution Form (template available for download, if applicable)
Applicants whose institution is not a United States based-entity must complete the CFF International Institution Form. The completion of this form also includes submission of the following documentation:

- Institution's mission statement
- If the Institution is a nonprofit organization, provide government-issued documentation of the Institution's nonprofit status, if available, as well as governing documents (such as a Charter, Statute, or By-Laws) detailing the funding and expenditures related to activities outlined in the Mission Statement of the Institution compared to activities outside of the mission of the Institution
- If the Institution is a for-profit organization, provide a complete list of key employees, members of the governing board, and/or other senior management as well as any governing documents (such as an Articles of Association or Organization) detailing the funding and expenditures of the Institution
- A complete and accurate Form W-8 signed by the institutional official within the last three years. While CFF issues grant funding to 501(c)(3) and nonprofit institutions, CFF also issues contract award funding to other kinds of institutions.
- A description of external sources of support, including the names of individuals and organizations providing the Institution with major donations, official awards, private endowments, and/or commercial activities

- Standard Operating Procedure(s) or relevant policy to ensure that all awarded funds, including but not limited to CFF funds, are used in compliance with all applicable U.S. anti-terrorist financing, privacy and asset control statutes, regulations and executive orders, resulting in the Institution neither distributing awarded funds to terrorists nor supporting their networks , organizations, or activities (*If your institution does not have a relevant policy, please provide a statement signed by an institutional official indicating that all award funds, including but not limited to CFF funds, will be used in compliance with applicable U.S. anti-terrorist financing, privacy and asset control statutes, regulations and executive orders, resulting in funds never being used to support terrorist networks, organizations and/or activities. In the alternative, if the institution does not have this policy, CFF can provide an Anti-Terrorism Certification Form to be signed by the institutional official).*

Applicants who have provided these documents within the past one (1) year is not required to resubmit them. However, if any of the above documents have been updated since they were previously submitted, please upload any updated documents. The CF Foundation GCMA Office will contact applicants if documents are outdated or missing.

*Applicants must provide English translations for all non-English documents, including material provided in support of the Research Plan.

Appendices (upload as PDF documents)
Appendices are restricted to the following three (3) categories*:

- Signed Letters of Support and/or Collaboration: A Letter of Collaboration from Co-PIs, if any, should be uploaded and included in the application. Investigators new to CF research are required to consult/collaborate with an established CF investigator/clinician either at their own institution or another. The letter from the collaborator/consultant should be explicit as to how the proposed work is relevant to CF and how he/she will assist the investigator new to CF research.
  Note: Junior investigators must provide such letters by contacting referees via section #6 of the navigation bar.
- Certification of IRB approval, or other applicable organization assurances documents such as IACUC and IBC Approval Letters, if available at the time of application.
- 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.

***No other types of Appendices will be reviewed.**

***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 CF Foundation 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 CF Foundation 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 FacePage electronically using Adobe Sign. Once signed by the PI, the FacePage 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 deadline.

XI. Other Information

Not applicable to this RFA

XII. Contact Information

For technical support and program/content information:
Primary CF Foundation GCMA Office contact Angela Minucci at aminucci@cff.org or 301-841-2614

For scientific questions:
Dara Riva, M.S. at driva@cff.org

XIII. Electronic Application Checklist

LOI Submission Deadline: Thursday, September 21, 2023 at 5:00 PM (EST)
Full Application Deadline: Tuesday, February 13, 2024 at 5:00 PM (EST)

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

LETTER OF INTENT

- ☐ Biographical Sketch(es) of Key Personnel - (upload)
- ☐ Response to Prior LOI Critique (if resubmission) – (upload)
- ☐ Innovation Statement – (upload)
- ☐ LOI Project Description - (upload)
- ☐ Protocol Synopsis – (upload)
- ☐ Remote Collection Supplement – (upload, if applicable)
- ☐ Health Equity Supplement – (upload, if applicable)
- ☐ CFF Patient Registry Data Request (if applicable)
- ☐ CFF Biorepository Clinical Specimen Request Confirmation letter (if applicable)

FULL APPLICATION

Face Page (upload) which includes:

- ☐ Signatures
  - ☐ Principal Investigator (Co-PI's are not required to sign)
  - ☐ The Official authorized to sign on behalf of the Applicant Institution
- ☐ Applicant/PI information - (online)
- ☐ Complete Institution and PI Contact information, including correct mailing address - (online)
- ☐ Organization Assurances (check those that apply online)
  - ☐ Human Subjects Certification - Minimal patient risk only
  - ☐ Research Involving recombinant or synthetic nucleic acid molecules information
  - ☐ Research Involving Animals information

Research Plan, Supporting Documents and Appendix:

- ☐ Abstracts ~ Summary of Relevance ~ Keywords - (complete online)
- ☐ Collaboration Detail (upload, if applicable)
- ☐ Research Plan - (upload)
  - ☐ Hypothesis and Specific Aims
  - ☐ Background and Significance
  - ☐ Preliminary Results
  - ☐ Experimental Design and Methods
  - ☐ Limitations and Potential Pitfalls
  - ☐ Consultants/Collaborative Arrangements
  - ☐ Literature Cited (not included in Research Plan page limitation)
- ☐ Innovation Statement – (upload)
- ☐ Remote Collection Supplement – (upload, if applicable)
- ☐ Health Equity Supplement – (upload, if applicable)
- ☐ Protocol Synopsis – (upload)
- ☐ Critique Response (LOI or resubmission) - (upload, if applicable)
- ☐ Budget Detail for each year and for each subcontract, when applicable - (upload)
- ☐ Budget Justification for each year and for each subcontract, when applicable - (upload)
- ☐ Biographical Sketches of Key Personnel - (upload)
- ☐ Other Support for all key personnel (NIH Format) - (upload)
- ☐ Facilities Available - (upload)
- ☐ Results of Past and Current CFF/CFFT Support – (upload)

- ☐ Letters of Reference for Junior Investigators - (invite referees to submit via https://awards.cff.org – *Note: applicant will not be able to see the letters)*
- ☐ Data Safety Monitoring Plan – (upload, if applicable)
- ☐ CFF Biorepository Clinical Specimen Request Confirmation letter – (upload, if applicable)
- ☐ CFF Patient Registry Data
  - ☐ Application for CFFPR Data and Confidentiality Agreement – (upload, if applicable)
- ☐ Verification of Applicant Institution's Tax Status - (upload)
  - ☐ W-9 (U.S. applicants) or W-8BEN-E (non-U.S. applicants)
  - ☐ 501(c)3, IRS Form 147C or equivalent tax status letter
- ☐ International Institution Form (non-U.S. based entities only) - (upload, if applicable)
  - ☐ Institution's most recent Mission Statement
  - ☐ Institution's Tax Exemption Letter, if institution is not-for-profit
  - ☐ Description of other sources of support
  - ☐ Institution's Standard Operating Procedure(s) or relevant policy to ensure that funds provided are neither distributed to terrorists or their support networks nor used for activities that support terrorism or terrorist organizations
  - ☐ For-profit institutions must submit a complete list of key employees, members of the governing board, and/or other senior management
- ☐ Appendices - (upload as PDF documents, if applicable)
  - ☐ Signed Letter(s) of Support and/or Collaboration
  - ☐ Certification of IRB approval, or other applicable organization assurances documents such as IACUC and IBC Approval Letters, if available at the time of application
  - ☐ Up to three (3) reprints of the applicant's work relating to the general area of research in the proposal