CYSTIC FIBROSIS FOUNDATION

**For application technical support, please contact arussell@cff.org**

**Program Name:** 2023 Therapeutics Development Award (TDA) with Letter of Intent (LOI)

**Brief Program Overview/Description:** In an effort to stimulate development of new pharmaceutical products for CF patients, CFF developed the "Therapeutics Development Award" Program. The purpose of this program is to provide funds to companies that will develop commercial products to benefit individuals with CF. Structured as a matching award program, funds will be awarded only if they are matched by the recipient.

**Funding Amount:** This is generally a two-part program, and funding is determined by which phase the project will pursue. Component (Phase) I –Preclinical Development and/or Component (Phase) II – Clinical. Funding for Component I is for up to $600,000 over no more than a three- (3-) year period while Component II is in the range of $3,000,000 to $5,000,000 over no more than a three- (3-) year period. Additional details are provided below in Section III.

**Eligibility:**

- Both U.S.-based and non-U.S. based (i.e., international) companies engaged in research and development are welcome to apply.
- Awards will be made for preclinical and initial clinical development activities (all therapeutic areas relevant to CF).
- In special circumstances CFF support may be used for API manufacture or other chemistry, manufacturing and controls activities, clinical trials involving healthy human subjects, support of senior company personnel engaged in administrative roles or Phase III multi-center clinical trials. Typically, these activities are viewed as the responsibility of the sponsor and may be recognized as matching funds.
- *Additional eligibility requirements can be found in Section IV below.*

**Key Dates:**

| | |
|---|---|
| Published | February 24, 2023 |
| LOI Submission Deadline | Rolling |
| LOI Applicant Notified | Ad-hoc basis |
| Full Application Deadline | Rolling |
| Review | Ad-hoc basis |
| Full Application Notification | Ad-hoc basis |
| Project Start Date | As agreed upon |

**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.

## II. Program and Award Overview

In an effort to stimulate development of new pharmaceutical products for the benefit of persons with CF, CFF developed the "Therapeutics Development Award" Program. The purpose of this program is to provide funds to companies for the development of commercial products to benefit individuals with CF. Structured as a matching award program, funds awarded are expected to be matched by the recipient.

With pressure on biotechnology companies to assure a return on investment to their shareholders, funds to initiate new exploratory research projects are limited. Funding currently available to companies is typically committed to products in the late stage of development. There has been a recent explosion in knowledge about CF; and a goal of the TDA award program is to provide funds that will spur companies to explore the feasibility of new therapeutic approaches to CF care.

The widespread scope of this program is meant to assure new product candidates are adequately explored. This funding mechanism is intended to support activities ranging from pre-clinical testing and clinical examination of a potential product's initial safety and efficacy. Once safety and proof of concept is demonstrated, CFF expects TDA awardees to obtain other financial support necessary to conduct pivotal Phase III clinical trials necessary for regulatory approval.

### Two-Part Application Program

CFF requires that investigators who seek support through TDA applications submit a Letter of Intent (LOI) in advance of a full funding application. Applicants may be able to by-pass the LOI after discussions with the Program team and with prior approval from the CFF Grants & Contracts Management and Administration (GCMA) office.

The CFF also sponsors a second funding mechanism, Path to a Cure (found here: https://www.cff.org/Research/Researcher-Resources/Awards-and-Grants/Research-Awards/Industry-Funding-Opportunities/), the Foundation's ambitious research program to support development of treatments for the underlying cause of the disease and, ultimately, a cure for every person with CF.

**Note:** If your application falls under the area of focus related to Path to a Cure, those applications should be initiated through the PTAC program which focuses on two core strategies to address the underlying cause of CF:

- Restoring CFTR protein when none exists, including for people with CF who have nonsense mutations
- Fixing or replacing the underlying genetic mutation to address the root cause of CF through gene replacement/transfer, gene editing approaches, or stem cell therapy

## III. Funding Amounts

Applicants may apply for funding based on the phase of the proposed research, as follows:

**Component I –Preclinical Development Phase:** The objective of this phase is to establish the technical merit and feasibility of a new therapeutic intervention. Qualifying activities may include medicinal chemistry efforts to improve drug-like properties and preliminary compound testing for pharmacokinetics and bioavailability, as well as specificity and determination of mechanism of action.

When a lead compound has already been identified, funding may be used for animal studies, toxicology, pharmacokinetics, and studies determining a potential new agent's method of delivery. Funding is for up to

$600,000 over no more than a three- (3-) year period. If you have questions regarding the proposal budget, please reach out to the program team members listed at the end of the guidelines.

**Component II – Clinical Phase:** The objective of this phase is to provide support for the continuation of pre-clinical studies and clinical assessment of new interventions, including safety and dose determination studies in CF patients. In special circumstances funding may be provided for chemistry manufacturing and controls (CMC) related activities or studies in healthy human subjects. The decision to allocate CFF resources to such activities is solely at the discretion of CFF. Funding may be in the range of $3,000,000 to $5,000,000 over no more than a three- (3-) year period.

**Funding Approach**

While not required, TDA funding components may be applied for and funded sequentially. For example, an application for Component I may examine the scientific potential of new products whereas applications for Component II may involve support for the continuation of Component I developments and/or clinical studies in people with CF.

Payments are milestone-dependent and will be issued after CFF approval of accomplishment of each milestone (with third party supporting documentation as needed).

## IV. Eligibility

- Both U.S.-based and non-U.S. based (i.e. international) companies engaged in research and development are welcome to apply.
- Awards will be made for preclinical and initial clinical development activities (all therapeutic areas relevant to CF).
- In special circumstances CFF support may be used for API manufacture or other chemistry, manufacturing and controls activities, clinical trials involving healthy human subjects, support of senior company personnel engaged in administrative roles or Phase III multi-center clinical trials. However, these activities are generally viewed as the responsibility of the sponsor and may be recognized as matching funds.
- All projects should be conducted in consultation with a CF-identified investigator representing a CFF-accredited Center, CF-supported Therapeutic Development Center, other funded mechanism by the CFF, or other funding agencies, and subject to approval by CFF.
- Approved awards will be subject to monitoring by a Project Advisory Group (PAG), whose membership is approved by CFF. If applicable, the PAG will determine overall performance of the project. If applicable, the PAG will report to CFF on a periodic basis not less than once every three (3) months. Continued support may also depend on the PAG's approval of project milestones.
- **Milestones**: Each application must contain milestones that are objective achievements demonstrating forward progress for the therapeutic approach and the appropriate timetable for completion of each. Continued funding for the project will be, in part, based upon milestone attainment.
- **Payback**: If a TDA leads to the marketing of a new intervention, CFF will receive reimbursement for its support. Terms will be negotiated prior to finalizing the award, and will typically include reimbursement, plus a multiple following successful regulatory marketing approval, and/or a percentage of net sales. Equity in the company may also be a consideration. CFF may also require certain rights to take the product forward in the event the awardee elects not to advance the product.

## V. Mentorship Requirements

*Not applicable to this RFA*

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

**<u>Areas of Encouragement</u>**

Extensive survey input from the CF community (people with CF, family members, caregivers and key opinion leaders) have identified key research Areas of Encouragement that are most important to them. The areas

selected by the CF community are listed below. Note that the degree of prioritization may change based on the size and scope of the CFF portfolio in a particular area. Applications may address any topic area advancing CF care, or treatment. However, applications addressing the following areas are particularly encouraged:

- Gastrointestinal symptoms (including, but not limited to, GERD, DIOS, and pancreatitis)
- CF-related Diabetes
- Respiratory microorganism treatment against microbes of particular interest to people with CF
- Inflammation
- Mucociliary clearance
- CF-related Liver Disease (including cirrhosis and non-cirrhosis, gall stones, hepatic steatosis, and other clinical manifestations of portal hypertension)
- Diet and Nutrition

## VII. Review and Award

Applications will be evaluated based on the following:

- The soundness and technical merit of the proposed approach
- The qualifications of the Principal Investigator (PI), supporting staff and CF collaborators
- The relative importance of the proposed intervention to CF care
- The size and scope of the existing CFF portfolio in a particular area
- The potential of the proposed research for commercial application
- The appropriateness of the budget requested
- The adequacy and suitability of the facilities and research environment
- The adequacy of milestones to assess overall performance of the project. If deemed appropriate after discussion with the applicant, an application for a large award may be reduced in scope to a lesser award, (e.g., to obtain necessary preliminary data to support increased funding). The GCMA office will reach out with directions on how to revise an application should revisions be required.

CFF will notify applicants once a funding decision has been made [with a goal of within four (4) months after receiving a full funding application]. Applications received in October or later are unlikely to obtain approval within the same calendar year. All successful awardees will be required to execute an agreement specifying the Terms & Conditions of an award before funds are made available.

## VIII. Submission Information

**A Letter of Intent (LOI) must be submitted and approved prior to submitting a Full Application**

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:**

| | |
|---|---|
| LOI Submission Deadline | Rolling |
| LOI Applicant Notified | Ad-hoc basis |
| Full Application Deadline | Rolling |
| Review | Ad-hoc basis |
| Full Application Notification | Ad-hoc basis |
| Project Start Date | As agreed upon |

## IX. Letter of Intent Guidelines

**LOIs Submission Deadline: Rolling**

Submit online through http://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

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. If you need to update your GMS profile, please reach out to the GCMA office (grants@cff.org) for assistance. 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 Therapeutic Development Award (TDA) 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.

**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. 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 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 CFF 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):
Applicants whose institution is not a United States based-entity are required to provide additional information and complete a CFF International Institution Form. The completion of this form also includes submission of additional documentation.

## 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 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 "**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 (Period 1, 2, 3). Applications for Component I Preclinical Development Phase) cannot exceed $600,000 over a three (3) year period (direct costs only); applications for Component II (Clinical Phase) may request between $3,000,000 to $5,000,000 over no more than a three (3) year period (direct costs only). All Therapeutics Development Awards are awarded for a maximum of three (3) years. **Total FTE costs may not exceed $300,000 per person per year**. CFF will not provide funds for travel of employees of applicant institution; however, travel of key personnel to CF-related scientific meetings can be considered as matching funds.
***Note:*** *Matching funds are required for this program, however, at the LOI stage, the budget should reflect funds requested from CFF only (not any company matching funds). If invited to submit a full application, the budget will need to include the company matching funds.*

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 Sketches for Key Personnel
- Opportunity Summary Form

**BIOGRAPHICAL SKETCH(ES) OF KEY PERSONNEL (NIH 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.

**OPPORTUNITY SUMMARY FORM**

Complete a brief summary of your potential CF opportunity using the provided template. There is a five-page limit to your summary; please do not exceed the limit.

**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.

## X. Full Application Guidelines

**Full Application Deadline: Rolling**

Full applications for support of these projects will **only** be accepted if the applicant has an **approved** Letter of Intent (LOI) on file with CFF or has been invited to bypass the LOI stage. Notifications of LOI approval are sent via email from the CFF GCMA office. Once an applicant has been notified that the LOI was approved, applicants can access and complete the full application by logging in at https://awards.cff.org.

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.*

Your draft Full 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 at the bottom of each page *before exiting* 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.

**Please note**: Only select the "**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.

**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. 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 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 CFF 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):
Applicants whose institution is not a United States based-entity are required to provide additional information and complete a CFF International Institution Form. The completion of this form also includes submission of additional documentation.

**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 contact is not available in the system, you may select "**Add Contact**" to create a basic contact profile to add the individual to your application. You may add any additional relevant contacts within this section. Roles and access for each role is specified within the online application portal.

**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 staff of CFF and the general public as to 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. Applications for Component I (Preclinical Development Phase) cannot exceed $600,000 over a three- (3-) year period (direct costs only); applications for Component II (Clinical Phase) may request between $3,000,000 to $5,000,000 over no more than a three- (3-) year period (direct costs only). All Therapeutics Development Awards are awarded for a maximum of three (3) years. ***Note:*** *Matching funds are required and should be indicated in the Total Costs of the Project.* CFF will not provide funds for travel of employees of applicant institution; however, travel of key personnel to CF-related scientific meetings can be considered as matching funds.

**The following budget categories are offered under this program:**
**Salaries & Benefits** – For this program CFF allows FTE costs (**requested from the CFF portion of the budget), of up to $300,000 per person per year, inclusive of fringe**. List the names and positions of all professional and non-professional personnel involved in the project, whether or not salaries are requested. Indicate the percent effort on the project for all personnel. For each individual, be sure to complete all fields on the Budget Detail in full on the template provided.

For academic subcontracts, if applicable, please see subcontractor section below.

**Consultant Expenses** - Give the name and institutional affiliation of any consultant who has agreed to serve in this capacity, including statisticians and physicians in connection with patient research costs if they are not listed under personnel. Under budget justification, briefly describe services to be performed, the number of days, rate of compensation, per diem and any other associated costs.

**Patient Research Expenses** – Funds may be requested for patient research costs specifically related to the proposed research and not considered routine care. The basis for estimating funds requested in this category should 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 or 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)).

**Consumable Supplies** – Itemize supplies e.g. disposables, reagents, 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, Data Safety Monitoring Plan (DSMP) related-expenses (if applicable), computer charges, equipment maintenance, etc. Justify all items.

**Subcontractor 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 subcontracts with academic institutions, indirect costs of up to 12% may be requested. Fringe rates may be included in calculation of total salary requested. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all funding agencies and foundations. For subcontracts with for-profit organizations, indirect costs are not allowable.

**Budget Detail – Indirect Costs**

Indirect costs are not allowable.

**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:

- Budget Justification
- Research Plan
- Biographical Sketch(es) of Key Personnel
- Data Safety Monitoring Plan (if applicable)
- Facilities Available
- International Institution Form (if applicable)
- Critique Response (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(s).

**RESEARCH PLAN**

*Page limit*: **Thirty (30)** single-sided pages, 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.

- Each Component (if applicable) must be clearly identified within the Research Plan.
- Applications with a Clinical Phase must include a Data Safety Monitoring Plan (DSMP). For additional details, please see the information provided below.
- Include sufficient information to permit effective review without reference to previous applications. Information should be presented in a clear, concise manner, while being specific and informative.

a. **Hypothesis, Specific Aims and Milestones Outline:** State concisely and realistically the intent of the proposed research and the hypothesis to be tested. Milestones must be outlined and a timetable for the completion, based upon the requested period of support, must be provided.
b. **Significance:** Briefly describe the background of the present proposal. Critically evaluate existing knowledge and specifically identify the gaps which the project is intended to fill. Specifically, discuss the unmet need the therapeutic intends to fill and its projected impact on CF patient survival, pulmonary exacerbations (duration and/or frequency and CF patient quality of life in the context of existing and emerging CF therapies). 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 the development of new therapies for CF patients.
c. **Experimental Design, Methods and Milestones:** Describe the protocols, including methods for new techniques, and explain potential advantages over existing methodologies as they apply to each milestone attained. Discuss the data expected to be obtained and the means by which data will be analyzed and interpreted. If clinical studies are involved, provide details of the methods for patient selection and care. 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. Applications will be reviewed and evaluated based upon the experimental design and methods used to achieve the milestones outlined above (item a). All applications will be reviewed based upon the appropriateness of the milestones, the timetable for the completion of milestones, and the approaches outlined to achieve milestones to achieve the development of new therapies for CF patients.
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 by letter(s) of intent signed by collaborating individual(s). In addition to letters of collaboration, curricula vitae must also be provided. If clinical material required by this award is to be

furnished by other individuals, include a statement from these individuals agreeing to their participation. All applications must include the name, biosketch, and a letter of support from a CF-identified investigator representing a CFF-accredited Center, CF-supported Therapeutic Development Center, or other funded mechanism by the CFF.

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).

**BIOGRAPHICAL SKETCH(ES) OF KEY PERSONNEL**

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.

**DATA SAFETY MONITORING PLAN**

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 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.*

**<u>Address the following areas in the DSMP:</u>**

**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.

<u>Level of Risk</u>

- 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.
- For interventional clinical trials with medicinal products conducted in the other parts of the world, e.g., Australia, the Institution must provide documentation to CFF confirming registration of the clinical trial in the appropriate database when applicable.

**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.

**INTERNATIONAL INSTITUTION FORM (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.

**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.

**APPENDICES**
Appendices are restricted to the following categories:
- Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable
- Up to four (4) reprints of the applicant's work relating to the general area of research in the proposal
- Letters of reference, support, and/or collaboration, including a letter of support from a CF-identified investigator representing a CFF-accredited Center, CF-supported Therapeutic Development Center, or other funded mechanism by CFF
- Other materials pertinent to the proposal, not already described. Please upload only the most relevant documents, as excessive materials may not 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 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.

## XI. Other Information

*Not applicable to this RFA*

## XII. Contact Information

**For technical support with the online application:**
CFF GCMA Office contact Aimee Lee Russell arussell@cff.org or 301-841-2614

**For program/content information**:
Lindsey Beaman lbeaman@cff.org or 240-200-3780
Maria Wang mwang@cff.org or 240-200-3777