Last Updated February 22, 2024

Request for Applications: Preclinical Hub (PCH) Program Application Guidelines

The Children's Tumor Foundation is one of the world's leading organizations dedicated to funding and driving innovative research that will result in effective treatments for the millions of people worldwide living with neurofibromatosis or schwannomatosis, a group of genetic conditions known as NF that causes tumors to grow on nerves throughout the body. One in every 2,000 people is born with some type of neurofibromatosis or schwannomatosis, which may lead to blindness, deafness, bone abnormalities, disfigurement, learning disabilities, disabling pain, or cancer. NF includes neurofibromatosis type 1 (NF1) and all types of schwannomatosis (SWN), including NF2-related schwannomatosis (NF2-SWN), formerly known as neurofibromatosis type 2.

The progress of NF is unpredictable and often presents a chronic lifelong burden to the affected person. There is a need for drug management but, other than Koselugo (selumetinib) for pediatric NF1 plexiform neurofibromas, there are no effective therapies for the diverse manifestations of NF. The signaling pathways affected in NF are common to many other tumor disorders and many existing drugs developed for these disorders could be repurposed for NF. NF affects all populations equally, and while there is no cure yet, the Children's Tumor Foundation mission of driving research, expanding knowledge, and advancing care for the NF community fosters our vision of one day ending NF. For more information, please visit: ctf.org.

DEI STATEMENT

CTF is committed to fostering, cultivating, and preserving a culture of diversity, equity and inclusion. We embrace and encourage our applicant's differences in backgrounds, experiences, race, color, religious creed, sex, national origin, ancestry, citizenship status, family or marital status, physical, mental and/or intellectual abilities, age, military or veteran status, registered domestic partner or civil union status, gender and gender identity, sexual orientation, political affiliation, and socioeconomic status.

PROGRAM FOCUS

The goal of the Preclinical Hub (PCH) Program is to stimulate NF drug discovery by funding the development of relevant and translational preclinical tools to support drug screening efforts as part of the Preclinical Hub model, which will serve to provide access to NF-focused tools and resources for the purposes of drug development.

Specifically, the aims of the PCH Program are as follows:

Support the generation of clinically-relevant *in vitro* (cell-based) or *in vivo* (whole animal) model systems for NF. Topics of specific interest to CTF will include *in vivo* and *in vitro* models of non-*NF2*-related SWN, cutaneous neurofibromas as well as genetically modified models of NF1-related learning and cognitive deficits or pain in schwannomatosis. Proposals should be aimed at either developing and validating a new model or validating an existing model with clinically-relevant tool compounds.

** In order to be considered as an applicant, it will be imperative to have a letter from the applicant's institution committing to making the developed model available to the wider public through CTF's Preclinical Hub. See the full description below under **"Commitment to share model within the Preclinical Hub"** section.

COMMITMENT TO OPEN SCIENCE AND DATA SHARING

CTF values the open sharing of research outputs and since 2018 has funded the NF Data Portal, a public data repository that stores and shares data generated by multiple collaborative research programs focused on NF diseases (neurofibromatosis and schwannomatosis).

By applying to any CTF grant, applicants agree to the principles of the NF Open Science Initiative (NF-OSI), an open effort focusing on finding NF treatments by sharing data and analysis results with the broader community. Please read more about our commitment to open science and data sharing here.

APPLICANT ELIGIBILITY

- Applicants should have an MD or PhD or an equivalent degree from a recognized US or non-US institution.
- As the PCH program offers only seed funding, applicants are expected to have already established in their laboratory, or have identified collaborators with, all required resources including in vivo and in vitro models.
- There is no citizenship requirement. Applications are welcome from all qualified individuals worldwide.
- Applications are welcome from both academic and private sectors.
- CTF requires all applicants to acquire a personal ORCID ID (https://orcid.org/) and to elect CTF as a trusted partner on ORCID. Once an applicant has granted permission, CTF as the trusted organization will be able to see information that they have set as visible to trusted parties in addition to the information set as visible to everyone. Please visit this ORCID page to learn more about visibility settings and trusted organizations. Since ProposalCentral has developed an extended integration with ORCID to allow seamless data transfer, applicants

are strongly encouraged to keep their ORCID ID record up to date, especially in the Education, Funding and Works (publications) sections.

- Recipients of current PCH grants can plan to submit a new proposal or request an extension of their current study only for a maximum of 2 consecutive cycles.
- New submissions from current or past grantees are welcome at every PCH cycle. Current grantees can request a maximum 1 year extension of their grant following the same guidelines. Existing grants timelines cannot overlap with new grant request timelines. Grant extensions submissions will be reviewed, scored, and recommended for funding together with all the other submissions for that cycle.

AWARD DURATION AND FUNDING

Applications can range from one to three years with the goal of delivering a validated model. It is expected that the time requested will be proportional to the level of model development (i.e. if a cell model is already created and only needs to be validated, a one-year grant should suffice).

- For the development or validation of a cell-based model, funding of up to $75,000 per year will be provided.
- For the development and/or validation of an *in vivo* model, funding of up to $125,000 per year will be provided.

Please note that funding amounts are **INCLUSIVE of up to 10% indirect costs.**

APPLICATION PROCESS

The PCH Program application is a one-stage process wherein applicants submit their full research proposal through ProposalCentral (https://proposalcentral.com/). A Letter of Intent is not required.

Applicants will be asked to provide -

1. **Lay Abstract** - *Entered directly in the application form on ProposalCentral.*
   Maximum of 2500 characters.
2. **Scientific Abstract** - *Entered directly in the application form on ProposalCentral.*
   Maximum of 2500 characters.
3. **Cover Letter** - *To upload on ProposalCentral*.
   The cover letter (1-2 pages, single line spacing, Calibri size 11 font) must include -

a. summary of the proposed work, its correlation to previous work, and anticipated timelines

b. statement confirming that all necessary support and approvals are in place or will be obtained

c. statement about potential conflicts of interest

4. **Research Proposal** - *To upload on ProposalCentral.*
   The Research Proposal (up to FIVE pages excluding citations, single line spacing, Calibri size 11 font) must include -

   a. introduction and aim(s) of proposed research

   b. description of proposed experiments with rationale, preliminary data, and sample characteristics and statistical analyses where necessary.

      NOTE: For studies involving statistical analyses, please provide justification for the method used along with all relevant details. For Neyman-Pearson inference please include a statistical power analysis and estimated effect size. For Bayesian hypothesis testing, please include predictions and corresponding Bayes factor, along with distributions and parameters to be used (if resources are limited, please specify the maximum feasible sample size at which data collection would have to cease).

   c. significance of proposed research, milestones and timelines of research plan, and summary of all resources available.

   d. description of model validation and rationale for any proposed reference compounds

   e. translational relevance of the model system.

5. **Citations** - *To upload on ProposalCentral*

   Must include references to studies from databases such as PubChem and NF Data Portal where available. We will preferably consider studies that cite and build from existing data.

6. **Open Access Research Output** - *Entered directly in the application form.*
   In addition to the requirement of key data sharing described below, CTF values the open sharing of research outputs such as open access articles, open access books, book chapters, and/or monographs, copies of your papers, chapters, monographs, or

other published materials in institutional or disciplinary repositories, preprints, datasets, software/code, materials/reagents, preregistration plans, public disclosure of negative results, and any other outputs, and encourages all its awardees to make all research outputs publicly available.

To evaluate an applicant's willingness to openly share research outputs, we ask applicants to provide representative examples demonstrating how they have made outputs from other projects openly accessible. Please also provide, where possible, the DOI and license terms that facilitate access and reuse of these materials. Please know that not having prior open access research outputs does not exclude your application from receiving a fair review.

7. **Biographical Sketch** - *A NIH biosketch template will be provided in the application form. Applicants can also upload a biosketch generated through SciENcv.*

8. **Budget Justification** - *Budget template will be available in the application form.*

9. **Commitment to submit a Data Sharing Plan** - *CTF template will be available in the application form*
   PCH recipients are required to upload annotated key data generated under their grant in the NF Data Portal, where the data will be embargoed for a maximum of 12 months following project completion. Applicants are not required to identify such key data upon application. However, grant disbursement of successful applications will be contingent on such key data being identified in the Data Sharing Plan described below and to the upload of correctly annotated data. Please see the **Award Activation** section below for more information.

10. **Commitment to share model within the Preclinical Hub**

    Applicant's institution is required to commit to making the model available to the broader public by either:

    i) licensing the model to a CRO of CTF's choice. Such CRO shall be allowed to use the model for commercial purposes, or

    ii) act as a CRO itself by providing fee for service access to any entity requiring testing of compounds in that model.

    A detailed letter of commitment will include:

    - outline of the licensing structure
    - clarity on informed consent obtained if the model involves human tissue

- certification that your institution is able to license the model for commercial purposes.

11. **Patent Policy** - *CTF template will be available in the application form*
    Applicant institutions are strongly recommended to sign the CTF Patent Policy at the time of application submission in order to speed up the process of award activation. Please see the **Award Activation** section below for more information.

REVIEW PROCESS

All applications will be reviewed by the CTF PCH Program Committee, a panel of external reviewers, and patient reviewers where necessary. A statistical review of the experimental protocol will be included for all applications. Reviewers will consider, in order of importance:

1. Impact of proposed research
2. Feasibility of proposed research
3. Transparency/soundness of experimental protocol
4. Alignment of budget
5. Applicant qualifications
6. Clinical translatability of model
7. Open science/data sharing readiness

NOTE:

1. Patient reviewers will review and score only specific sections (lay abstract, significance and impact of research on NF patients) of the application. Patient's score and statistical review score will be integrated into the final application score.
2. Based on reviewer feedback, CTF may request the applicant to revise the application and resubmit for review.
3. Open science/data sharing readiness is considered a plus. Lack of evidence will not be considered as a critical factor for rejecting an application.

The PCH Program Committee will select and recommend applications for funding at the end of the review process. These recommendations will then be evaluated by CTF's Board of Directors (BOD), which will make the final decision on applications to be funded. No funding decision will be final until approved by the BOD.

TERMS OF AWARD

I. Applicant Notification

Applicants will be notified about the decision on their application within 6-8 weeks of application submission. All applicants, both funded and not funded, will be provided with a

summary of the feedback from the review of their application.

II. Award Activation

Applicants whose proposals get selected for funding will be requested to complete and return the following documentation to CTF before their award can be activated –

- **Acceptance of Award** – An award acceptance letter will be emailed requesting information on Awardee, Institution, contact officials, and bank information for electronic transfer of payments, and will include terms relative to the milestone achievements and 12-month embargo period on any data uploaded in the NF data Portal.

- **Data Sharing** – Awardees will be required to complete CTF's Data Sharing Plan and register their project as a new study on the NF Data Portal. For more information about the data-sharing process, please visit this page on the NF Data Portal.

- **Patent Policy*** – Awardee institutions will be required to sign CTF's Patent Policy before the award can be fully activated. We strongly recommend signing the Patent Policy at the time of application submission in order to speed up the process of award activation. If your institution is not able to agree to the terms of the Patent Policy as they stand, please contact us as soon as possible at grants@ctf.org. The Patent Policy is intended to ensure that any inventions or patented technologies arising from CTF-supported research are commercialized where possible. CTF anticipates recouping some revenues arising from commercialized technologies it supported, in proportion to the contribution made by CTF's initial funding. Such funds will be used to support further initiatives at CTF.

***Special Note to Federal Employees (e.g. NIH intramural researchers)**

Since the National Institutes of Health are prohibited by congressionally enacted federal law from accepting the terms of CTF's Patent Policy, the policy may be waived for federal employees, such as NIH intramural researchers, depending on the project being funded. Federal employees wishing to apply for a grant are, therefore, invited to discuss their project with CTF prior to submitting their grant proposal. Any information shared with CTF will be treated confidentially.

III. Status of Awardee

The Awardee will be considered an employee of the awardee's institution and not of CTF.

IV. Extended Leave of Absence

Should the Awardee need to take a leave of absence for more than a month for reasons such as maternity/paternity or illness, CTF must be informed of the date of departure and expected date of return.

V. Award Purpose Change or Transfer

Any fundamental change in the purpose for which the award was originally made must have prior written consent of CTF. An award may not be transferred from one institution to another without prior written authorization from CTF.

VI. Award Cancellation or Early Termination

CTF reserves the right to cancel or prematurely terminate an award if required. In such an event, the award amount will be prorated based on the number of months it was in effect. A final report of expenditures and a refund of any unspent funds must be submitted to CTF within 60 days after cancellation or termination. Failure to provide the final expenditure report by the required date will result in suspension of the award and may impact the applicant's eligibility for future funding opportunities at CTF until all materials are received.

VII. No-Cost Extension

CTF allows Awardees to request a No-Cost Extension (NCE) of the final budget period of their award for up to 1 year beyond its original expiration date. All terms and conditions specified in the original contract will apply during the extension period. Upon notification of approval by the Program Committee, CTF will revise the project end date and provide an acknowledgment to the awardee.

VIII. Other Sources of Support

The Awardee and the sponsoring Institution are responsible for informing CTF of possible conflicts related to duplicate funding of the CTF-funded project. Failure to inform CTF of other sources of support can result in loss of CTF funding and may also impact the applicant's eligibility for future funding opportunities at CTF.

IX. Periodic Reporting

Awardees are required to submit two types of reports periodically through their account on Proposal Central -

- **Progress report**
    - A detailed update on the development of the CTF-funded research must be provided every six months after activation of the award.
- **Expenditure report**
    - An expenditure update vs budget must be provided within 60 days after completion of the award.

- All expenses must be reported in US dollars only.
- Expenditure reports must be signed by the institution's financial officer.
- Any unexpended and uncommitted funds in possession of the awardee at the end of the award period must be returned to CTF within 60 days from the expiration of the award.
- In addition to the above, interim accounting may be requested by CTF.

X. Public Notification of Awards Funded

Once an award is activated, CTF will advertise online and in CTF's other public documentation the recipients of the award together with a lay summary of the proposed research. Please include a photograph of yourself (over 2MB) that we can use in award announcements.

XI. Publicity, Publications, or Exhibits Notification of Awards Funded

The Awardee Institution must notify CTF in advance of any publications, presentations, or announcements pertaining to work done under the Award or Follow-Up Work, whether these are to professional audiences or the public media. For professional publications and presentations, once these have been accepted, Awardee Institution must submit an electronic copy of the paper, abstract, slide presentation or poster to grants@ctf.org with details of publication release or presentation (journal, meeting, time, location). CTF strongly encourages the posting of early manuscripts on preprint servers for fast-acting dissemination of results. All information shall be held as confidential by CTF until the time of public presentation or publication. **The support of CTF must be duly recognized everywhere, and must include the CTF grant number and Digital Object Identifier (DOI).**

For announcements to the public, the public media and/or the press, including a posting to the Internet, pertaining to this Award or any Follow-Up Work (collectively, a "Release"), Awardee Institution agrees to provide a draft of such Release to CTF at media@ctf.org at least one week before such publication of such Release so as to provide CTF the opportunity to suggest edits to the language of the Release, particularly as to CTF's role in the Award, any Follow-Up Work, and neurofibromatosis research. Awardee Institution agrees to consider all such suggestions and include them in the Release if they are accurate. Awardee Institution shall not unreasonably decline to include any edits in a Release.

For the purposes of this Award, the term, "Follow-Up Work" shall mean any research predicated upon or directly related to the research funded by this Award.

XII. Open Access Fee Reimbursement Policy

CTF encourages and enables its awardees to publish in open-access journals, which facilitates more rapid dissemination and broad use of their publications. To do so, we have established an annual fund of **$15,000** that is available on a first-come, first-served basis to current awardees to pay the fees incurred for publishing in open-access journals.

- The publication must be based on CTF-funded research.
- Requests must be submitted during the award period, or within 18 months of the award end date.
- Awardees should submit a written request to grants@ctf.org with 1) a copy of the invoice or receipt for publication fees from the journal, 2) PDF copy of the accepted publication, and 3) an active URL link to the publication.

All requests will be reviewed, and if approved and if there are funds remaining, the publication fees will be duly reimbursed. If not available, authors are encouraged to explore "green open access" as a repository-based open access option within their institution.

XIII. Follow-On Funding

Awardees are required to keep CTF informed about any follow-on funding, collaborations, and publications (posters, papers) generated from the research funded. Such continuing communications will allow CTF to measure the impact of its research funding more easily.

Please email grants@ctf.org if you have any questions. We wish you the very best and look forward to receiving your application!