



2016 DRUG DISCOVERY INITIATIVE AWARDS INTRODUCTION AND GUIDELINES

Founded in 1978 as the National Neurofibromatosis Foundation, the Children's Tumor Foundation is a non-profit organization committed to identifying effective drug therapies for neurofibromatosis type 1 (NF1), neurofibromatosis type 2 (NF2) and schwannomatosis, and to improving the lives of those living with these disorders. NF is one of the most common of the rare diseases, affecting 1:3,000 individuals (around 100,000 persons in the US; and over 2 million worldwide). Since its inception, Children's Tumor Foundation has committed over \$35 million to research grants and initiatives, supporting scientists around the world to conduct groundbreaking NF research.

NF causes a range of brain and nerve tumors (benign and malignant), bone abnormalities, learning disabilities, pain, vascular complications and other manifestations. 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 there is currently no effective therapy. The signaling pathways affected in NF are common to many other tumor disorders and many existing drugs developed for these disorders could be effective in NF.

The Drug Discovery Initiative Awards program supports early stage testing of candidate drug therapies for the treatment of neurofibromatosis (NF): NF1, NF2 and schwannomatosis. These Awards have yielded over \$5M in follow-on funding from the federal government and other sources, as well as multiple industry collaborations and publications. DDI Awards is a catalyst program that has helped to fuel the drug pipeline with promising leads.

DDI Awards represent a critical early-stage doorway into the NF preclinical pipeline. The program will support projects that may have no preliminary data but which do have a sound rationale for testing candidate therapeutics in NF cell or mouse models. The goal for these projects is to go on and secure larger grants from federal or private sources to continue progress. To keep momentum, the Foundation has placed particular emphasis on rapid review of DDI applications. In most cases funded applicants receive funding within 8-10 weeks of the application deadline.

The program in 2016 is as follows:

Up to \$40,000* DDI *in vitro* Awards: to fund cell-based preclinical drug testing studies
Up to \$85,000* DDI *in vivo* Awards: to fund animal-based preclinical drug testing studies

DDI Awards require only a brief application. If Award yields promising data, awardees may apply for subsequent funding to continue the research.

DDI Advanced Awards are no longer being offered.

*Total includes 10% indirect costs.

Indirect costs MUST NOT exceed 10% of the total award. Indirect costs are those overhead administrative and facility costs which are not readily identifiable with the project, but are nevertheless necessary for general operation. Examples of indirect costs include the salary and related benefits of individuals of administrative personnel, office supplies, rent, depreciation and utilities.

The new CTF Discovery Toolbox is an online list of tools for NF drug discovery - mouse models, cell lines, candidate drugs, etc. for investigators to share resources and establish collaborations. It is expected that, unless legally prevented from doing so, DDI Awardees will make tools developed under their DDI award available through the CTF Discovery Toolbox. CTF also strongly encourages researchers to voluntarily submit tools that are created outside the scope of their funding from CTF. To improve the use and sharing of such tools, we introduced a new regulation that will make it more transparent and easier to access to any researcher: we added an upfront agreement to CTF standard conditions for the transfer of the tools, as outlined in the MTA available for download in the application. Investigators who will decide to make their tools available in the toolbox will be notified by CTF if the tool is requested, and CTF will coordinate the final agreement between the two parties. For full details about the new Toolbox, content and use regulations, visit: <http://www.ctf.org/Network/Drug-Discovery-Toolbox.html>

ADDF-ACCESS

A more streamlined and efficient path to clinical development can be accomplished by partnering with contract research organizations (CROs). The Children's Tumor Foundation is pleased to partner with **ADDF-ACCESS** to offer applicants free access to an online marketplace of CROs and a network of expert consultants and collaborators who focus on drug discovery and development. ADDF ACCESS also provides educational resources and guidance on the process of selecting and managing a CRO contract. If the applicant determines that partnering with a CRO will benefit their application, they can choose a CRO at the following site: <https://addfaccess.ondeckbiotech.com/>

Where appropriate for applicants, a CRO may be identified for work proposed in the work plan. CTF will evaluate and approve potential CROs, or suggest a different option. If the applicant does not identify a CRO, CTF may suggest a CRO during the review process or at the 6 month progress report, and may require an amendment to the DDI application. The additional cost of work done by the CRO will be paid by CTF. Results generated by the CRO will belong to the applicant only and be treated by CTF as if they had been generated by the applicant

Choosing a CRO (optional)

The applicant can identify their CRO partner at the following points:

1. The applicant may decide to insert a CRO at the time of proposal. CTF will evaluate and approve it or suggest a different option. A letter of commitment including a quote for service fees should be included at time of application.
2. If the applicant does not identify a potential CRO, CTF might suggest a specific piece of work to be added and suggest a potential CRO during the review process. Both parties have to agree for approval.
3. At the 6-month progress report, a CRO partnership can be proposed by the applicant or by CTF. Both parties have to agree for approval. The additional cost of work done by the CRO will be paid by CTF. Results generated by the CRO will belong to the applicant only and be treated by CTF as if they had been generated by the applicant

APPLICATION GUIDELINES

The DDI Award Application must come from the individual who will oversee the drug screening experiments. Collaborators, e.g. those providing therapeutics, can be listed as subcontractors and receive part of the funding, but the grant will be administered through the institution of the principal investigator as defined above.

Applicant Eligibility:

- Applicant should have an MD, PhD or equivalent and have full access to, or identified collaborators with, all required resources including all *in vivo* and *in vitro* models
- There are no citizenship requirements for this program. Applications are welcomed from all qualified individuals worldwide
- As the program offers only seed funding, it is anticipated applicants already have established, in their laboratory, or have direct access to, any additional resources needed to complete the proposed research
- Applications are welcomed from both the academic and private sectors. Partnerships between the two are actively encouraged. If applicants are partnering with a CRO, a quote for service fees should be included in the application. These fees, once approved, will be paid for by CTF and are in addition to the DDI award amounts.

SPECIAL NOTE FOR FEDERAL EMPLOYEES (e.g. NIH intramural researchers)

For all of our funding awards, the Children's Tumor Foundation requires the CTF Patent Policy (in the attachment section) to be signed by all awardees and recipient institutions. The Children's Tumor Foundation has been advised that the National Institutes of Health are prohibited by congressionally enacted federal law from accepting the terms of the CTF Patent Policy. As a result, depending on the project being funded, the patent policy may be waived for federal employees (such as NIH intramural researchers). Federal employees wishing to apply for a grant are thus invited to inquire with CTF prior to submitting their grant proposal to discuss their project. Any information given will be treated confidentially

APPLICATION PREPARATION

Applications received after the deadline will NOT be reviewed. The Foundation will not check or correct formatting errors. Applicants should retain electronic copies of submitted materials.

A critical goal of DDI Awards is to offer rapid review and funding. Pending signature of Award acceptance materials, you may receive funding as early as 8-10 weeks after the submission deadline.

ATTACHMENTS

Applicant must provide the following documents (where applicable) during the online submission:

1. List of literature cited
2. Appropriate institutional review board and/or animal care and use committee approval forms
3. Letters of commitment from individuals who will be providing therapeutics or other resources required for the screen (if applicable)
4. Letter of intent from CROs including a quote for services (if applicable)
5. Signed patent policy
6. Approved CTF MTA agreement for the sharing of resources through the CTF Discovery Toolbox
7. Abstract pages and award amounts from all other grant-based sources of support (current or pending) held/applied for by the principal investigator
8. Institutional Certification: all signatures requested MUST be provided
9. Budget Justification: provide breakdown of intended use of funds requested
10. Research Plan: provide attachment with maximum THREE pages total, plus 1 page describing the partnership with a CRO if included
11. Refusal for CTF Discovery Toolbox sharing: copy of Acts or agreements that legally prevent the sharing of my tools within the CTF Discovery Toolbox (if applicable)

DDI Awards Timeframe and Funding It is anticipated that the timeframe of DDI Award studies is one year. *In vitro* DDI Awards are up to \$40,000 and *in vivo* DDI Awards up to \$85,000. *In vitro* Awards will be disbursed in full at the commencement of the Award period. *In vivo* Awards will be disbursed 50% at the commencement of the Award period; and 50% after receipt and review of the 6-month Progress Report.

Applying for Consecutive DDI Awards

If an *in vitro* Awardee generates promising data, s/he may apply for an *in vivo* Award to continue the research. If you intend to do this please contact Dr. Salvatore La Rosa, Vice President of R&D, at slarosa@ctf.org. To ensure momentum, make sure you contact us in time to be able to apply for the next DDI Award deadline.

DDI Awards Reporting

Awardees are expected to submit brief Progress Reports at 6- and 12-months after the study commences. In addition, once funding has concluded the Foundation may follow up with periodic DDI Awardee Surveys; these are important tools helping us to track the ongoing impact of the DDI Awards program. Templates for Progress and Expenditure Reports are available online at the following address:

<http://www.ctf.org/Research/Report-Templates-for-Researchers.html>

REVIEW GUIDELINES

Review Process

DDI Award applications are reviewed by a DDI Review Committee members of which are drawn from the Children's Tumor Foundation Research Advisory Board. Review will consider:

- a) Drug & screening model selection rationale
- b) Preliminary data:
 - If an *in vivo* screen is proposed, is there sufficient *in vitro* data or other preliminary findings to support advancing to the animal model?
 - For an *in vitro* screen, is there sufficient data to support the use of this system to identify new promising compounds?
- c) Feasibility of proposed study
- d) Is applicant qualified?
- e) Are all required resources available?
- f) Is a CRO necessary? If so, has an appropriate CRO been chosen and a quote included in the application?
Reviewers will consider the opportunity to suggest the applicant to collaborate with a CRO for a particular piece of work to be added to the application.
This has to be agreed between the applicant and CTF. Results generated by the CRO will belong to the applicant only.

Based on an assessment of these merits, the DDI Review Committee will select and recommend applications for funding. Recommendations will then be considered by the Foundation's Board of Directors (BOD), which will make the final determination on those applications that will be funded. **No funding decision will be final until approval by the BOD.**

TERMS OF AWARD

Applicant Notification

Applicants will be notified as soon as possible as to the outcome of the review, the target timeframe being no later than 8-10 weeks of application submission. All applicants, both funded and not funded, will be provided with a Summary Statement of feedback highlighting the key comments of the reviewers.

DDI Award Activation and Payment

Payment will be activated as soon as the Awardee and Institution officials sign the following documents:

1. Acceptance of Award: Accepting the Children's Tumor Foundation Terms of Award (*see below*).
2. Patent Policy (*see below*)

Award Cancellation or Early Termination

In the event an award is cancelled or terminated, the award amount will be prorated on the basis of the number of months it was in effect. A final financial report of award expenditures and a refund of any monies unexpended during the period of the award must be submitted to Children's Tumor Foundation within 60 days after cancellation or termination. **Note:** Failure to provide Progress Reports and Expenditure Reports by the required dates will result in a suspension of the award until the materials are received.

Patent Policy Relating to Foundation Funded Research

Prior to activation of Children's Tumor Foundation funding awards, the awardee's institution must sign the Children's Tumor Foundation Patent Policy (*see Attachment section*). We strongly recommend agreeing and signing the Patent Policy at the time of application submission in order to speed up the process of award assignment. If your institution is not able to agree to the terms of the Patent Policy as they stand, please contact the foundation as soon as possible at grants@ctf.org. The Patent Policy is intended to ensure that any inventions or patented technologies arising from research supported by the Children's Tumor Foundation are commercialized where possible. Children's Tumor Foundation anticipates recouping some revenues arising from commercialized technologies it has supported, that is in proportion to the contribution made by the funding initially provided by the Children's Tumor Foundation.

Submitting your Tools to the CTF Discovery Toolbox

In receiving this award, it is anticipated that you will be willing to submit research tools being used in the award - mice, cell lines, etc. - to the CTF Discovery Toolbox. Listing your tools in the Toolbox makes other researchers aware of tools available for NF research, and could provide an opportunity for you to identify future collaborators. For complete information on the CTF Discovery Toolbox please visit our website, <http://www.ctf.org/Network/Drug-Discovery-Toolbox.html> or contact the Foundation by email at grants@ctf.org.

It is however requested that you submit any tool created or developed under this award to the CTF Discovery toolbox. CTF will only make exceptions for those who are legally prevented from doing so.

In the event that tools are shared via the Toolbox, your institution must agree to transfer such tools to any party at CTF's request and under the conditions of the CTF MTA (*see Attachment section*).

Public Notification of Awards Funded

Once the Award has been accepted, the Children's Tumor Foundation will advertise online and in other Foundation public documentation the Principal Investigators/Institutions and title of applications that have received funding through DDI.

DDI Award Reporting

Progress Reports must be submitted to the Foundation at 6 months and 12 months after the commencement of DDI Award funding. A template for these reports and reminders to submit the reports will be available online at <http://www.ctf.org/Research/Report-Templates-for-Researchers.html>. Acknowledging that these reports will contain details of unpublished work, they will not be made public by the Foundation. However high-level outcomes from these reports (e.g. successful hit *in vivo/in vitro*; tumor type represented by assay; etc.) will be used in summary reports on DDI to the Foundation's Board of Directors, donors, etc.

Financial Reporting

A financial statement must be provided to Children's Tumor Foundation itemizing expenditures for the DDI Award at the completion of funding. This report is due within 60 days after the end of the anticipated 12-month period during which the DDI award will be used. An Expenditure Report template will be available at <http://www.ctf.org/Research/Report-Templates-for-Researchers.html>. Financial reports should be signed both by the awardee and by the responsible institutional financial officer. Any unexpended and uncommitted funds in the possession of the awardee at the end of the award period shall be returned to the Foundation within 60 days of the end of the award. In addition to the above, interim accounting may be requested by the Children's Tumor Foundation.

Publicity

No awardee shall release for publication, other than through the usual professional or scientific journals, the results of his work without notifying the Foundation of his/her intention to do so and furnishing a copy of the material intended for release. All announcements to any media of public information pertaining to an awardee and/or work to be done or accomplished under a Children's Tumor Foundation award must have the approval of the awardee, the awardee's institution, and the Foundation.

Status of Personnel Compensated Under an Award

The awardee shall be considered an employee of the awardee's institution, and not of the Foundation.

Status of personnel

The awardee shall be considered to be an employee of the awardee's institution, and not of the Foundation.

Extended leaves of absence

Should the awardee need to take a leave of absence for over a month (i.e. maternity/paternity leave, illness, etc.), the Foundation must be informed of the date of departure and expected date of return.

Award Status Change or Transfer of Institutions

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

Follow-on Funding

As a condition of this award, grantees are required to provide the Children's Tumor Foundation any information about the research funded in this award as it pertains to follow-on funding, collaborations, publications, etc. This information will be requested annually via our online system for a period of 5 years following the end of the award period. These continuing communications with grantees will allow us to more easily measure the impact of our research funding.

Publications or Exhibits of an Awardee

The Foundation should be notified at the time of public disclosures by the awardee based on their work supported by a Foundation. This includes when a paper is published in a scientific or medical journal, or when a presentation (e.g. poster, slide presentation) is made before a professional scientific or medical organization. All such publications or presentations based on work supported by the Foundation must credit in acknowledgements support from Children's Tumor Foundation. The Foundation requests that the awardee submits to the Foundation an electronic (PDF or Word) copy of the paper, abstract with slide presentation, or copy of the poster materials. This material should be forwarded to the Foundation - if possible once accepted for publication or presentation, and certainly, immediately following publication or presentation, together with the name of the publication or the organization accepting it, and the time and place of the meeting. Information should be sent to grants@ctf.org. This information shall be considered confidential by the Foundation until publicly presented or published by the awardee. The Foundation will coordinate with the awardee in promoting the presentation or publication on the Children's Tumor Foundation website (www.ctf.org) or in other Foundation communications to its constituents (E-NewsBlast, NF NewsLetter, website, etc.)