Funding Opportunity: Clinical Trial Awards

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Revised 10 March 2022

1 Overview Information

1.1 Funder Overview

The mission of the ALS Association is to discover treatments and a cure for ALS, and to serve, advocate for, and empower people affected by ALS to live their lives to the fullest. Our Research Program contributes to this mission by funding cutting edge research across the translational pipeline from basic science to clinical trials. The Association is the largest private funder of ALS research worldwide, and our efforts have led to some of the most promising and significant advances in ALS research.

The ALS Association, as a funder in a disease without a cure, believes that the more researchers collaborate and share information, the faster they will arrive at effective treatments and a cure. With

this in mind, the Association encourages open access publications, pre-registered protocols, and open data sharing whenever possible. The Association also values collaboration whenever possible to encourage partnerships to prevent duplication and promote innovation. Both open sharing and collaboration will be positively evaluated in submitted applications.

1.2 Funding Opportunity in Brief

Title: Clinical Trial Awards

Award: $1,000,000 in total funding over two or three years to support early to mid-phase (phase 1, phase 2a) clinical trials of novel or repositioned therapeutics for ALS.

1.3 Key Dates

Request for Applications Open: March 18, 2022
Letter of Intent Due Date: April 21, 2022, 5 p.m. US ET
Full Application Due Date (by invite only): July 7, 2022, 5 p.m. US ET
Anticipated Award Decision: August 2022
Anticipated Earliest Start Date: September 2022

Our expectation is that contracting is completed within 60 days of award offer. If not, we reserve the right to rescind the award offer and redirect the funds to other projects.

1.4 Grants Policy Statement

For more detail on all policies described in this document, please consult our Grants Policy Statement, available here.

2 Full Text of the Announcement

2.1 Funding Opportunity Description

2.1.1 Overview

There is an urgent need for new and improved therapies for ALS, as there is still no cure. The Clinical Trial Awards (CTA) Program is open to industry and academic investigators proposing to clinically test novel or repositioning approaches for ALS. The CTA program seeks to de-risk clinical programs by supporting clinical trials with clear go/no-go criteria that, if positive, will attract follow-on funding and enable further development (such as participation in The Healey ALS platform trial).

2.1.2 Scope/Type of Clinical Trials Supported

- Clinical Stage: Early to mid-phase (phase 1, phase 2a) clinical trials exploring safety or biomarkers to justify larger phase 2b or phase 3 studies. This includes single ascending dose (and multiple ascending dose) studies to assess safety/tolerability; brain penetration, or target engagement in healthy subjects and/or people living with ALS.

- Trial population: Can include genetic or sporadic forms of ALS, healthy subjects, and / or asymptomatic carriers.
- Therapeutic approaches: Small molecule, genetic therapies, stem-cell approaches, peptides, antibodies, antisense oligonucleotides, and others.
- The following are **not appropriate** for this funding opportunity:
    - Non-pharmacological or surgical interventions
    - Observational trials or natural history studies

2.1.3 Requirements

- The therapeutic should have completed or be in the process of completing Investigational New Drug (IND)-enabling studies by the time the full application is due.
- IND (or similar regulatory authority) approval is required for the CTA program.
    - EITHER the applicant should have an approved IND application or similar (if outside of US) in hand.
    - OR an IND (or similar) application has been submitted and approval is pending.
    - OR applicant will need to file a new IND (or similar) application by 3 months from the start of the project date.
    - Evidence of any correspondence, meeting minutes, etc. with the regulatory authorities will need to be submitted at the full-proposal stage.
- Successful applications will
    - Provide strong and compelling preclinical data package providing the rationale for the proposed treatment moving to the clinical stage.
    - Provide a clear plan, including essential "Go/No-Go" decision milestones, for moving the approach through the essential stages of development.
    - Describe what additional funding sources are in hand already or will be pursued to fund the entire trial (e.g. government, private/VC investors, industry partnerships, etc.).

2.2 Award Information

2.2.1 Funding Instrument

- Grant: A support mechanism providing money to an eligible entity to carry out an approved project or activity
- If the funded research contributes to revenue generation, the Association expects to share, proportionally, in that revenue (see Grants Policy Statement for details)

2.2.2 Funds Available and Anticipated Number of Awards

- The number of awards is contingent upon The ALS Association's budget allocation and the submission of a sufficient number of meritorious applications

2.2.3 Award Budget

- Budgets for total costs up to $1,000,000 (inclusive of both direct and indirect costs) may be requested
- Indirect costs are limited to 10% of total direct costs

2.2.4 Award Period of Performance:

- The maximum period of performance is three (3) years. Applicant could propose a 2-year or 3-year project.

2.2.5 Payments Provided

- For a 2-year project – Year 1: $500,000; Year 2: $500,000
- For a 3-year project – Year 1: $500,000; Year 2: $250,000; Year 3: $250,000

2.3 Eligibility

2.3.1 Eligible Individuals

- Individuals with the skills, knowledge, and resources necessary to carry out the proposed research may apply as a principal investigator
- Post-doctoral fellows are not eligible to apply as a principal investigator

2.3.2 Eligible Organizations

- U.S. and non-U.S. public and private non-profit entities, such as universities, colleges, hospitals, laboratories, units of state and local governments and eligible agencies of the federal government
- U.S. and non-U.S. biotechnology/pharmaceutical companies, or other publicly or privately held for-profit entities

2.3.3 Collaborations

- The clinical trial process will likely require resources beyond those available at a single organization. Therefore, applications are open to investigators participating in synergistic collaborations, though one individual is required to serve as the principal investigator.
- If a collaboration is proposed, letters confirming/supporting the collaboration are **required** at the full application stage. Specific roles and responsibilities for each collaborator need to be clearly articulated. If the collaboration is multi-organizational, participating organizations will ensure the success of the collaboration by resolving potential intellectual and material property issues and by removing organizational barriers that might interfere with achieving high levels of cooperation.

2.4 Content and Review of Applications

2.4.1 Content of Letter of Intent

By the date listed in Key Dates above, prospective applicants are required to submit a letter of intent that includes the following information:

- Title and total amount requested
- Name, address, and telephone number of the Principal Investigator
- Name, address, and telephone number of the organization
- Names of other key personnel

- Project Narrative
    - Scientific abstract
    - **Target Biology**: Please describe the biological target, hypothesized mechanism and pathway for the therapeutic and how this biology is significant and relevant to ALS. Please summarize relevant target validation studies including genetic and/or pathological links of the target/pathway to ALS.
    - **Therapeutic Summary**: Describe the lead therapeutic being developed (e.g. compound name), approach (e.g. small molecule, ASO, siRNA, AAV), mode of action/ pharmacology (e.g. agonist, antagonist), proposed route of delivery and how the therapeutic was identified. Please indicate if this a novel therapy or repurposed/repositioned approach from another disease. Please summarize the pre-clinical package (efficacy, PK/PD, safety/tox) that justifies your therapeutic moving to the clinical stage.
    - **Trial Design**: Provide a brief summation of the design of the study, including site numbers, blinding, type of trial design, length of study, treatment course, patient groups, etc
    - **Trial Population**: Briefly describe the intended study population including numbers in each recruitment cohort/arm) and description for each cohort/arm.
    - **Trial Therapeutic Dosage**: Specify dosage, the route and dosage form and briefly indicate how dosing was determined and what pharmacokinetic, pharmacodynamic and/or bioavailability data supports dosage choice
- Biosketch of PI
- Signature page

2.4.2 Review Criteria for Letter of Intent

- **Fit**: The letter of intent should allow the ALS Association staff to assess whether there is a good match between The ALS Association's mission of advancing the field of ALS, the intent of the funding program and the proposed trial.
- **Relevance & Rationale**: The Letter of intent should provide appropriate scientific rationale for the proposed therapeutic to be tested clinically and the relevance of the target/pathway to ALS.
- **Overall Objectives**: The letter of intent should clearly describe the trial objective, design, intended study population and why this particular therapeutic is ready for early-stage clinical trials for ALS.

The letter of intent can either be accepted or declined. If the letter of intent is accepted, the applicant will be invited to submit a full application. Results from the letter of intent review phase will not be provided to the applicant.

2.4.3 Content of Full Application

Application instructions for the full application will be provided when/if the applicant is invited to submit the full application.

2.4.4 Review Criteria for Full Application

- **Impact/contribution to ALS**: Potential for the proposed trial to make an important contribution to ALS therapeutic development landscape and how does the approach fit the current landscape of ALS treatments in development.
- **Target/Pathway and Preclinical data package**: Rationale for testing the therapeutic against the given target/pathway biology and the strength of the preclinical package (efficacy, PK/PD, target engagement, safety/toxicity).
- **Study Design**: Feasibility, timeline and trial methodology including length of trial, treatment course, patient groups, inclusion/exclusion criteria, dosage justification, outcome measures, safety considerations, sample-size considerations, patient recruitment/engagement plans and plans for disseminating study results.
- **Study sites and team**: Qualifications of the PI, key personnel, and collaborators/consultants are appropriate to perform the proposed research project and expertise and track record of trial sites in conducting ALS trials.
- **IP/Patent landscape**: Impact on future development/commercialization of the therapeutic.

2.4.5 Peer Review and Selection Process

- All applications are peer reviewed by an ad hoc Scientific Review Committee constituted by The ALS Association
- The Scientific Review Committee's priority scores are forwarded only to The ALS Association Board of Trustees, which has the sole authority for approving the funding of research grants
- For applications selected for funding, The ALS Association will send the reviewer comments to the PI. To the extent practical and within the scope of the budget, The ALS Association recommends that the PI integrate any recommendations that the reviewers may have suggested to further optimize the project and outcomes.

2.5 Application and Submission Information

2.5.1 Format of Application Submission

- All applications are to be submitted through our online grants management platform, Proposal Central: https://proposalcentral.com/
- To find this funding opportunity on Proposal Central, navigate to the Grant Opportunities tab (https://proposalcentral.com/GrantOpportunities.asp) and search for Grant Maker: The ALS Association
- Instructions on how to register as a new user of Proposal Central: https://docs.proposalcentral.com/RegUser.pdf
- Applications must be prepared according to Proposal Central's instructions: https://docs.proposalcentral.com/CreateApp.pdf
- Upon receipt, applications will be evaluated for completeness and compliance with application instructions. Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed.

2.5.2 Funding Restrictions

The ALS Association awards are subject to the terms and conditions described in The ALS Association Grants Policy Statement (see: Grants Policy Statement) and the award Agreement.

- Awards will be limited $1,000,000 total costs for the entire two-year or three-year period of performance
- Indirect costs are limited to 10% of total direct cost
- The ALS Association will contract with the lead-PI's organization with all the funds going to a single organization. The PI will be responsible for budgetary and scientific oversight and management of all trial sites and will also be responsible for sub-contracting with secondary sites, drug manufacturers, etc.
- If awarded the grant, The ALS Association will work with the awardee to develop a timeline for the planning phase of the study (typically the first 12 weeks post award). Planning phase activities could include finalization of study protocol, IND submission, patient recruitment plans, IRB approval, subcontracts put in place, drug supply plan, and posting the trial on www.clinicaltrials.org.
- The allowability of costs supported under an ALS Association grant is described in the Grants Policy Statement

2.5.3 Administrative and National Policy Requirements

All ALS Association grants include The ALS Association Grants Policy Statement (see: Grants Policy Statement) as part of the Research Grant Agreement. The Grants Policy Statement includes the requirements applicable to animal welfare, human subject protections, data sharing, research resource sharing, publications, etc. All necessary ethical and regulatory approvals must be in place before experiments are initiated.

- **Animal Welfare Requirements:** The ALS Association requires its grantees to establish appropriate policies and procedures to ensure the humane care and use of animals used in research supported by The ALS Association
- **Human Subject Requirements**: The ALS Association requires its grantees to establish appropriate policies and procedures to ensure the protection of human subjects participating in research supported by The ALS Association
    - **Health Insurance Portability and Accountability Act (HIPAA):** Domestic grantees must comply with the requirements of HIPAA
    - **General Data Protection Regulation (E.U. 2016/679):** Foreign grantees must comply with the Regulation E.U. 2016/679, or its amended regulation, of the European Parliament and of the Council of 27 April 2016
- **Intellectual Property**: Grantees shall have the first right, but not the obligation, to prepare, file, prosecute, and maintain all registerable rights in Intellectual Property arising from implementation of the Research Scope of Work at its sole expense.
- **Revenue Sharing**: If the funded research contributes to revenue generation, the Association expects to share, proportionally, in that revenue (see Grants Policy Statement for details).

2.6 Award Administration

2.6.1 Award Agreement and Payment Schedule

- A formal notification in the form of an ALS Association Research Grant Agreement (Agreement) is the authorizing document and will be provided to the applicant organization for successful applicants.
- The Agreement, signed by the applicant's authorized organizational representative (AOR), principal investigator and The ALS Association, will include the negotiated terms and conditions of the award between The ALS Association and the Grantee.
- Milestone driven award payments will be made to the Grantee on an annual or semi-annual basis as outlined within the Agreement.

2.6.2 Administrative Requirements

- The Grantee is expected to utilize The ALS Association funds in direct support of the research project and expend funds in accordance with the established organizational policies and procedures
- Funds charged to The ALS Association award must be for allowable project costs that are determined to be reasonable, allocable, consistently applied and conform to the program guidelines and/or limitations outlined in The ALS Association Funding Opportunity Announcement and the Agreement
- The Grantee is expected to seek The ALS Association's prior approval before making certain types of post-award changes (see Grants Policy Statement)

2.6.3 Reporting Requirements

- The Grantee will be required to submit semi-annual Research Progress Reports and annual Grant Expenditure Reports during the period of an award unless otherwise noted in the Agreement
- Future grant payments are contingent upon the grantee's submission of and The ALS Association's acceptance of the report(s)
- The ALS Association's issuance of the next award payment, when applicable, serves as confirmation that the information provided has been reviewed and approved by The ALS Association
- Final closeout reports (i.e., final research progress and expenditure reports) are due within 90 days following the termination date of the Agreement

2.7 ALS Association Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Submit all correspondence to researchgrants@alsa-national.org.