Request for Applications: Clinical Trial Awards

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1 Overview Information

1.1 Funder Overview

The ALS Association is the largest philanthropic funder of ALS research worldwide. Our goal is to make ALS livable for everyone, everywhere, until we can cure it. To achieve this goal, our Research Program focuses on finding new treatments and cures, optimizing current treatments and care, and preventing or delaying the harms of ALS. Thanks to the ALS Ice Bucket Challenge and the generous support of our donors, we have been able to dramatically accelerate the fight against ALS by funding cutting-edge

research across the translational pipeline from basic science to clinical trials in addition to research in other important areas, such as assistive technology, natural history, tool development, prevention, fellowship training, and infrastructure. Our efforts have led to the development and approval of new ALS treatments, discovery of new ALS genes, creation of new global research collaborations, and many more promising and significant advances in ALS research.

As a funder in a disease without a cure, we believe that the more researchers collaborate and share information, the faster they will arrive at effective treatments and a cure. With this in mind, we value collaboration as an important tool to increase efficiency, prevent duplication, and promote innovation. We also encourage open access publications, pre-registered protocols, and open data sharing whenever possible. Both collaboration and open sharing 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 or phase 2a) clinical trials of novel or repositioned therapeutics for ALS (either disease-modifying or symptomatic)

1.3 Key Dates

Request for Applications Open: April 12, 2023
Letter of Intent Due: May 17, 2023, 5 p.m. US EDT
Full Proposal Due (by invitation only): August 2, 2023, 5 p.m. US EDT
Anticipated Award Decision: October 2023
Anticipated Earliest Start Date: November 2023

Our expectation is that contracting will be completed within 60 days of the 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 at https://www.als.org/Grants-Policy-Statement.

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 repositioned approaches for ALS. Both disease-modifying and symptomatic treatments are in scope. 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 or phase 2a) interventional 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 and studies assessing 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 of ALS-linked genetic mutations.
- **Therapeutic approaches**: Novel or repositioned approaches for ALS (either disease-modifying or symptomatic), including small molecules, genetic therapies, stem cell approaches, peptides, antibodies, and antisense oligonucleotides.

2.1.3 Trials Not Supported Under This Funding Opportunity

The following are **not appropriate** for this funding opportunity, and applications focusing on these topics will be administratively withdrawn.

- Non-pharmacological interventions
- Surgical interventions
- Observational studies or natural history studies

2.1.4 Requirements

- The therapeutic should have completed or be in the process of completing Investigational New Drug (IND)-enabling studies by the time the full proposal is due.
- IND (or similar regulatory authority) approval is required for the CTA Program, meaning that at the time of award, the applicant:
    - Has an approved IND application or similar (if outside the US) in hand
    - Has submitted an IND (or similar) application and approval is pending
    - Has filed a new IND (or similar) application within 3 months of the project start date
    - **Please note:** Evidence of any correspondence, meeting minutes, etc. with regulatory authorities will need to be submitted at the full proposal stage.
- Successful applications will:
    - Provide a strong and compelling preclinical data package providing the rationale for the proposed treatment moving to the clinical stage
    - Provide a clear plan, including “go/no-go” decision milestones for moving the approach through the essential stages of clinical 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 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. Applicants can propose a two-year or three-year project.

2.2.5 Payments Provided

- For a two-year project:
  - Year 1: $500,000
  - Year 2: $500,000
- For a three-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.
- Postdoctoral 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 proposal stage. Specific roles and responsibilities for each collaborator should be clearly articulated.
    - If the collaboration is multi-organizational, participating organizations will ensure the success of the collaboration by resolving any 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 the 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, which includes:
    - **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. Also indicate if this is a novel therapy or repurposed/repositioned approach from another disease. In addition, 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. If you are using a novel endpoint, please describe any engagement with FDA's Rare Disease Endpoint Advancement Pilot Program.
    - **Trial population**: Briefly describe the intended study population, including numbers in each recruitment cohort/arm and a description for each cohort/arm.

    - **Trial therapeutic dosage**: Please specify dosage, the route, and dosage form. Also briefly indicate how dosing was determined and what pharmacokinetic, pharmacodynamic and/or bioavailability data supports dosage choice.
- Biosketch of principal investigator
- Signature page

2.4.2 Review Criteria for Letter of Intent

- **Fit**: The letter of intent should allow reviewers to assess whether there is a good match between the Association's mission, the intent of the funding program, and the proposed trial.
- **Relevance and 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 or mid-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 proposal. Reviewer comments from the letter of intent review phase will not be provided to the applicant.

2.4.3 Content of Full Proposal

If/when an applicant's letter of intent is accepted, instructions for submitting a full proposal will be provided.

2.4.4 Review Criteria for Full Proposal

- **Impact/contribution to ALS**: How the approach fits with current ALS treatments in development and the potential for the proposed trial to make an important contribution to the ALS therapeutic development landscape
- **Target/pathway and preclinical data package**: Rationale for testing the therapeutic against the given target/pathway biology and the strength of the preclinical package (e.g., 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, analysis plans including go/no-go milestones, and plans for disseminating study results
- **Study sites and team**: Appropriateness of qualifications of the principal investigator, key personnel, and collaborators/consultants to perform the proposed research project and expertise and track record of trial sites in conducting ALS trials
- **Intellectual property/patent landscape**: Impact on future development/commercialization of the therapeutic

2.4.5 Peer Review and Selection Process

- All full proposals are peer reviewed by an ad hoc Scientific Review Committee constituted by the Association.
- The Scientific Review Committee's priority scores are forwarded only to the Association's Board of Trustees, which has the sole authority for approving the funding of research grants.
- For applications selected for funding, the Association will send the reviewer comments to the principal investigator. To the extent practical and within the scope of the budget, the Association recommends that the principal investigator integrates 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 application materials (letters of intent and full proposals) 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 are available at https://docs.proposalcentral.com/RegUser.pdf.
- Application materials must be prepared according to Proposal Central's instructions, which can be found at https://docs.proposalcentral.com/CreateApp.pdf.
- Upon receipt, application materials will be evaluated for completeness and compliance with application instructions. Application materials that are incomplete and/or non-compliant will not be reviewed.

2.5.2 Funding Restrictions

Association awards are subject to the terms and conditions described in the Grants Policy Statement and the award Agreement.

- Awards will be limited to $1,000,000 total costs for the entire two- or three-year period of performance.
- Indirect costs are limited to 10% of total direct costs.
- The Association will contract with the lead principal investigator's organization with all funds going to a single organization. The principal investigator will be responsible for budgetary and scientific oversight and management of all trial sites. The principal investigator will also be responsible for subcontracting with secondary sites, drug manufacturers, etc.
- If awarded the grant, the 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 the 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 Association grant is described in the Grants Policy Statement.

2.5.3 Administrative and National Policy Requirements

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

- **Human subject requirements**: The Association requires its grantees to establish appropriate policies and procedures to ensure the protection of human subjects participating in the research it supports.
    - **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).

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 Association, will include the negotiated terms and conditions of the award between the 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 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 Association's 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 Association's approval at least 30 days 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 Association's acceptance of the report(s).
- The Association's issuance of the next award payment, when applicable, serves as confirmation that the information provided has been reviewed and approved by the 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 research program and welcome the opportunity to answer questions from potential applicants. Submit all correspondence to ResearchGrants@als.org.