Request for Applications: Clinical Trial Awards

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Revised November 30, 2023

1 Overview Information

1.1 Funder Overview

The ALS Association is the largest philanthropic funder of ALS research in the world. We are working to make ALS a livable disease – by optimizing current treatments and care and preventing or delaying the harms of ALS – while urgently searching for new treatments and a cure. Thanks to the ALS Ice Bucket Challenge and the generous support of our donors, we have dramatically accelerated 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, quality of care, tool development, prevention, workforce development, and research infrastructure. Our efforts have led to the development and approval of new ALS treatments, the discovery of new ALS-linked genes, the creation of new global research collaborations, and many more promising and significant advances in ALS research.

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 2 or 3 years to support early- to mid-stage (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: December 5, 2023
Letter of Intent Due: January 25, 2024, 5 p.m. US ET
Full Proposal Due (by invitation only): April 12, 2024, 5 p.m. US ET
Anticipated Award Decision: June 2024
Anticipated Earliest Start Date: July 2024

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 details on the policies described in this document, please consult our Grants Policy Statement, which is available at www.als.org/Grants-Policy-Statement.

2 Full Announcement

2.1 Funding Opportunity Description

2.1.1 Award Overview

There is an urgent need for new and improved therapies for ALS, as there is still no cure. Clinical trials are the most reliable – and ultimately the fastest – way to translate promising laboratory science into new and better ways to treat and care for people living with ALS. The ALS Association's Clinical Trial Awards seek to de-risk clinical programs of novel or repositioned approaches for ALS by providing up to $1,000,000 in total funding over 2 or 3 years to support early- to mid-stage trials (phase 1 or phase 2a). These awards are open to industry and academic investigators, and both disease-modifying and symptomatic treatments are in scope.

Successful applicants will provide strong preclinical data supporting the biological rationale for the proposed treatment and a clear plan for clinical development. Biomarker-driven clinical trials, along with other methods for increasing the probability that trials definitively answer relevant scientific questions, are strongly encouraged. Long-term development plans should describe essential "go/no-go" decision milestones and a plan to attract follow-on funding if results are positive.

2.1.2 Type of Clinical Trials Supported

To be eligible for this funding opportunity, proposed studies should:

- Be 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 and multiple ascending dose studies to assess safety / tolerability.
    - Studies assessing brain penetration or target engagement in healthy subjects and/or people living with ALS.
- Test novel or repositioned approaches for ALS (either disease-modifying or symptomatic), including:
    - Small molecules
    - Antisense oligonucleotides and other genetic therapies
    - Stem cell approaches
    - Peptides
    - Antibodies
- Include people living with genetic or sporadic forms of ALS, healthy subjects, and/or asymptomatic carriers of ALS-linked genetic mutations.

To review the topics of previously funded projects, please visit our website.

2.1.3 Trials Not Supported by 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
- Natural history studies

2.1.4 Additional Considerations

- 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 projects selected for funding, meaning at the time of the award, the applicant should either:
    - Have an approved IND application (or similar if outside the U.S.) in hand,
    - Have submitted an IND application (or similar) and have approval pending, or
    - Commit to filing a new IND application (or similar) within 3 months of the project start date.
    - *Please note: Records of any correspondence, meeting minutes, etc. with regulatory authorities should be submitted at the full proposal stage.*
- Successful applications will:
    - Include 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.).
- If selected for funding, the Association encourages posting the trial on www.clinicaltrials.gov.

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 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 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 3 years. Applicants can propose a 2-year or 3-year project.

2.2.5 Payment Distribution

- 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 (PI).
- Postdoctoral fellows are not eligible to apply as a PI.

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.
- The applicant organization must be the organization that controls the intellectual property under development, except in situations where a generic medication is being repurposed for ALS. Please consult with Association staff if you need clarification.

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.
- If a collaboration is proposed, letters confirming / supporting the collaboration **are required** at the full proposal stage.
  - Collaborative applications must identify a lead organization.
  - Specific roles and responsibilities for each collaborator should be clearly articulated.
  - One individual is required to serve as the PI.
- 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

The application process has two phases: a letter of intent followed by a full proposal (submitted by invitation only).

2.4.1 Letter of Intent

2.4.1.1 Content

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

- Administrative Information
  - Descriptive Title of Proposed Project
  - PI's Name and Contact Information
  - Names of Other Key Personnel
  - Participating Institution(s)
- Project Information (approximately **3 pages total**, see ProposalCentral for character limits for specific sections)
  - Scientific Abstract
  - Target Biology
  - Therapeutic Summary
  - Trial Design
  - Development and Commercialization Plan
- Attachments
  - PI Biosketch
  - Resubmission Statement (if relevant)

2.4.1.2 Review Criteria for Letter of Intent

Review of the letter of intent emphasizes fit, target and therapeutic, and business plan as described in more detail below.

2.4.2 Full Proposal

2.4.2.1 Content

If/when an applicant's letter of intent is accepted, further instructions for submitting a full proposal will be provided. In summary, the full proposal will include:

- Webform
  - Administrative Information
  - Lay Abstract
  - Scientific Abstract
- Research Plan (**14 pages total**, not including references)
  - Scientific Abstract (copied from webform)
  - Project Roadmap

    - Target Biology
    - Therapeutic Summary
    - Clinical Trial Narrative
    - Biomarker Methods
    - Patient Engagement, Recruitment, and Retention
    - Trial Team and Study Governance
    - Business Plan
    - References
- Budget
    - Planned Expenditures (table)
    - Budget Justification
- Attachments
    - Therapeutic Candidate Fact Sheet
    - PI Biosketch
    - Biosketches for Co-PIs and Collaborators
    - Investigator's Brochure (optional)
    - Letters of Collaboration (if relevant)
    - Regulatory Authorities Correspondence (if relevant)
    - W-9 or Other Relevant Tax Information

2.4.2.2 Review Criteria

- **Fit**: Is there a good match between the Association's mission, the intent of the funding program, and the proposed project?
- **Potential impact:** If the trial and larger development plan were successful, would the results be an important / impactful contribution to ALS research, or would they be incremental? Is this approach unique within ALS drug development?
- **Target and therapeutic:** What is the rationale linking the target / pathway to ALS? Is there sufficient data to support the development of the proposed therapeutic against this target? What is the rationale supporting the use of this therapeutic approach generally and this candidate therapeutic specifically? Do the preclinical data on pharmacology, efficacy, PK/PD, safety/toxicology, etc. justify moving the therapeutic to the proposed clinical stage? If the therapeutic has been tested in the clinic before, are there adequate safety, PK, and target engagement data to support further clinical development of this drug?
- **Trial design**: Based on the clinical outcome measures, trial period, trial population, inclusion/exclusion criteria, dose selection, sample size, biomarker strategy, statistical approaches, and schedule of activities outlined in the application, what are the strengths and weaknesses of the proposed trial? Is it likely that this trial will answer an important question about viability of this therapeutic specifically and/or this therapeutic approach generally? Is the design of the trial adequately developed and appropriate to achieve the proposed aims? Is the trial appropriately pre-registered?

- **Trial team and study governance**: Are the qualifications of the PI, key personnel, and collaborators/consultants appropriate to perform the proposed trial? Is the leadership and governance of the trial clearly described? Is there sufficient rationale provided for the selected trial sites? Should additional expertise (e.g., ALS trialist, statistician) or trial sites be added?
- **Patient experience**: What are the strengths or weaknesses of the patient engagement, recruitment, and retention strategies?
- **Business plan**: Is there a clear path forward for this drug development program? If the proposed trial is funded and successful, will it provide a clear go/no go decision to move forward into larger clinical trials? Are there partnership models or funding partners described that increase confidence in the feasibility and viability of this program moving forward to commercialization? Are there any concerns around the IP and competitive landscape?
- **Budget**: Is the budget justified based on the proposed trial? Are there any items in the budget that are inappropriate for funding?

2.4.3 Peer Review and Selection Process

- Letters of intent will be either 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 phase are not provided to applicants.
- Full proposals are peer reviewed by an ad hoc Scientific Review Committee of independent external experts. These reviewers are **not** the same individuals as reviewers of the letters of intent.
- Reviewers of full proposals do not have access to the letter of intent. Only information submitted as part of the full proposal will be reviewed.
- For full proposals, the Scientific Review Committee's priority scores will be forwarded only to the Association's Board of Trustees, which has the sole authority for approving the funding of research grants. Reviewer comments from the full proposal phase will be provided to applicants.
- For applications selected for funding, the Association recommends that the PI integrate any recommendations suggested by the reviewers to the extent practical and within the scope of the budget to further optimize the project and outcomes.
- Application status notifications and other award-related correspondence will come from ResearchGrants@als.org. Applicants are advised to add this address to their safe sender list to ensure notifications are not directed to their spam folder. Applicants can also check the status of their application materials (i.e., letter of intent or full proposal) in ProposalCentral (proposalcentral.com).

2.5 Application and Submission Information

2.5.1 Format of Application Submission

- All application materials must be submitted through our online grants management platform, ProposalCentral (proposalcentral.com).

- To find this funding opportunity on ProposalCentral, navigate to the Grant Opportunities tab (proposalcentral.com/GrantOpportunities.asp) and search for Grant Maker: The ALS Association.
- Instructions on how to register as a new user of ProposalCentral are available at docs.proposalcentral.com/RegUser.pdf.
- Application materials must be prepared according to ProposalCentral's instructions, which can be found at 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

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

- Awards will be limited to $1,000,000 total costs for the entire 2- or 3-year period of performance.
- Indirect costs are limited to 10% of total direct costs.
- Salary, wages, and fringe benefits of personnel other than the PI are allowed.
- Salary, wages, and fringe benefits of the PI are allowed only when indirect costs are waived.
- Direct salary for individuals should not exceed the salary limitation for Executive Level II of the Federal Executive pay scale (grants.nih.gov/grants/policy/salcap_summary.htm).
- Economy travel up to $3,000 per year to attend scientific conferences is allowed.
- Moveable equipment costs should not exceed 20% of the annual budget.
- Computer hardware and software costs up to $2,000 per year are allowed.
- Recurring annual cost-of-living / inflationary increases up to 3% for personnel and consumable supplies are allowed.
- All funds must be expended within the approved period of support.
- Unexpended funds remaining at the end of the project must be returned to the Association.

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 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), PI, 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.
- All funds will go to a single organization. The PI will be responsible for budgetary and scientific oversight and management of all trial sites. The PI will also be responsible for subcontracting with secondary sites, drug manufacturers, etc.

2.6.2 Administrative Requirements

- The grantee is expected to utilize the Association's funds in direct support of the research project and expend funds in accordance with 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 Association's Request for Applications 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 the 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. Please direct all correspondence to ResearchGrants@als.org.