Request for Applications:
The Lawrence and Isabel Barnett Drug Development Program

Table of Contents

Revised 31 October 2023

1 Overview

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: The Lawrence and Isabel Barnett Drug Development Program

Award: $500,000 in total funding over 2 years to support the preclinical assessment of novel or repurposed therapeutics for ALS

1.3 Key Dates

Request for Applications Open: November 7, 2023
Letter of Intent Due Date: December 18, 2023, 5 p.m. US ET
Full Proposal Due Date (by invitation only): March 7, 2024, 5 p.m. US ET
Anticipated Award Decision: May 2024
Anticipated Earliest Start Date: June 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 Program Overview

There is an urgent need for new and improved therapies for ALS, as there is still no cure. The Lawrence and Isabel Barnett Drug Development Program seeks to accelerate the availability of new, effective ALS treatments by supporting the preclinical assessment of novel therapies or repositioned treatment approaches in preparation for clinical testing. These 2-year awards with a maximum budget of $500,000 are open to both industry and academic investigators. Applicants should have a development candidate in hand as this funding opportunity aims to support programs that have a high probability of entering the clinic within 3 years.

Successful applications will include strong and compelling data supporting the biological rationale for the proposed treatment and a clear plan for moving it through the essential stages of development, including essential "go/no-go" decision milestones. Applications should thoroughly describe what is known about pharmacokinetic and pharmacodynamic (PK/PD) relationships, including plans to address any gaps in this understanding. Studies can be performed by a contract research organization in collaboration with the principal investigator (PI).

2.1.2 Topics of Interest

Both novel programs and repurposing of approved or clinically safe therapies from other disease indications are appropriate for this funding opportunity. We are especially interested in:

- *In vivo* efficacy testing of therapeutic candidates (pharmacological treatments, biological therapies, or gene therapies) in models of ALS.
- Studies focused on pharmacokinetics, pharmacodynamics, preclinical toxicology/safety (ADME/Tox), dose-range finding, and target engagement.
- Other Investigational New Drug (IND)-enabling studies.

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

2.1.3 Topics 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.

- Early drug discovery studies involving high-throughput screening, hit-to-lead, and lead optimization
- Clinical trials

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 $500,000 (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 2 years.

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 PI.
- Postdoctoral fellows are not eligible to apply as a PI.
    - Junior postdoctoral fellows are encouraged to consider the Association's Milton Safenowitz Postdoctoral Fellowship instead.

2.3.2 Eligible Organizations

- U.S. and non-U.S. biotechnology/pharmaceutical companies or other publicly or privately held for-profit entities.
- 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.
- The applicant organization must be the organization that controls the intellectual property under development. For example, if an academic lab has out-licensed the relevant intellectual property to a commercial partner, then the commercial partner must be the applicant organization, even if the work will be completed by the academic lab. Please consult with Association staff if you need clarification.

2.3.3 Collaborations

- The preclinical drug development process often requires resources beyond those available at a single organization. Therefore, applications are open to investigators participating in synergistic collaborations focused on testing and developing lead candidates for the treatment of ALS.
- If a collaboration is proposed, letters confirming / supporting the collaboration **are required** at the full proposal 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.
- **Collaborative applications must identify a lead organization, which must be the entity that controls the intellectual property under development.**

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 the following:

- Administrative Information
  - Descriptive Title of Proposed Project
  - PI's Name and Contact Information
  - Names of Other Key Personnel
  - Participating Institution(s)
- Project Information (approximately **2.5 pages total**, see ProposalCentral for character limits for specific sections)
  - Scientific Abstract
  - Target Biology
  - Therapeutic Summary
  - Specific Aims
- Attachments
  - PI Biosketch
  - Resubmission Statement (if relevant)

2.4.1.2 Review Criteria

Review of the letter of intent emphasizes fit, potential impact, and the target / therapeutic, as described in more detail in section 2.4.2.2 Review Criteria for Full Proposal.

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 Summary (2,000 characters maximum)
  - Scientific Abstract (2,000 characters maximum)
- Research Plan (**10 pages total**, not including references)
  - Scientific Abstract (copied from webform)
  - Project Roadmap, including Specific Aims and Timeline
  - Target Biology
  - Therapeutic Summary
  - Preliminary Data
  - Experimental Plan
  - Commercialization Plan
  - Team and Environment
  - References
- Budget
  - Planned Expenditures (table)
  - Budget Justification (5,000 characters maximum)
- Attachments
  - Lead Candidate Fact Sheet
  - PI Biosketch
  - Biosketches for Co-PIs and Collaborators
  - Letters of Collaboration (if relevant)
  - Resubmission Statement (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 project 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 / 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?
- **Scientific merit**: What are the strengths and weaknesses of the proposed project? Do the preliminary data justify further development of this candidate therapeutic? Is the design of the project adequately developed and appropriate for the aims of the study? Have potential problem areas been acknowledged and alternative tactics been considered? Are the milestones and timelines feasible? Are the go / no-go decision points clear and used to inform future development of the therapeutic?
- **Research team / environment**: Are the qualifications of the PI, key personnel, and collaborators / consultants appropriate to perform the proposed project and planned downstream development activities? Does the environment in which the work will be done contribute to the probability of success? Will the proposed collaborative arrangements help get the work done?
- **Commercialization plan**: If the proposed project is funded, how will it impact future development of this therapeutic? Is this plan sufficiently logical and detailed? Is the long-term development and commercialization plan for this therapeutic backed by sufficient financial and business resources (or credible plans to obtain those resources)? Are there any specific intellectual property / patent issues that may impede development of the therapeutic?
- **Budget**: Is the budget justified based on the proposed project? 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 Submissions

- 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 $500,000 in total costs for the entire 2-year period of performance.
- 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).
- Indirect costs are limited to 10% of total direct costs.

- 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 animal welfare, 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 Association requires its grantees to establish appropriate policies and procedures to ensure the humane care and use of animals used in the research it supports.
- 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.

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.