Part I. Overview Information:

Section 1. Funding Opportunity Title: Clinical Trial Awards (CTA) Program

Section 2. Key Dates:

- Request for Application Open: August 9, 2021
- Letter of Intent Due Date, if applicable: September 3, 2021, 5 p.m. US ET
- Full Applications Invites sent out: September 17, 2021
- Full Application Due Date (by invite only): November 8, 2021, 5 p.m. US ET
- Anticipated Award Decision: December 2021
- Grant Contracting: December 2021/January 2022*

*Note: The start date should be prior to January 31, 2022.

Part 2. Full Text of the Announcement

Section I. Funding Opportunity Description:

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, and if positive, will attract follow-on funding and get it ready for future development (such as The Healey ALS platform trial).

2. **Scope/Type of Clinical Trials supported through CTA program:**

- **Clinical Stage:** Early to mid-phase (phase 1, phase 2a) clinical trials exploring safety or biomarkers to justify larger phase 2b studies including single ascending dose; multiple ascending dose studies to assess safety/tolerability; brain penetration; and target engagement studies in healthy subjects and/or people living with ALS.
- **Trial population:** Can include genetic or sporadic forms of ALS, healthy subjects, as well as asymptomatic carriers.
- **Therapeutic approaches:** Small molecule, genetic therapies, stem-cell approaches, peptides, antibodies, antisense oligonucleotides, and others.
- **Please Note:** Non-pharmacological or surgical interventions are not considered appropriate for this RFA. Observational trials or natural history studies are not considered appropriate for this RFA.

Section II. Award Information:

1. **Funding Instrument:**
   - **Grant:** A support mechanism providing money to an eligible entity to carry out an approved project or activity.

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.

3. **Award Budget:**
   - Budgets for direct and indirect costs up to $1,000,000 per project may be requested.

4. **Award Period of Performance:**
   - The maximum period performance is three (3) years. Applicant could propose a 2-year or a 3-year project.

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

Section III. Eligibility

1. **Eligible Individuals:**
   - Individuals with the skills, knowledge, and resources necessary to carry out the proposed trial may apply as a principal investigator.
   - Post-doctoral fellows are not eligible to apply as a principal investigator.

2. **Eligible applicants:**
   - 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.

Section IV. Application and Submission Information

1. Content and Form of Application Submission
   • It is critical that applicants follow the instruction of the application guide. Applications that are out of compliance with these instructions may be delayed or declined during administrative review.

   • Letter of Intent: By the date listed in Part I Overview Information, prospective applicants are required to submit a letter of intent that includes the following information:
     a. Title and total amount requested.
     b. Name, address, and telephone number of the Principal Investigator
     c. Name, address, and telephone number of the organization.
     d. Names of other key personnel (note: You do not need to have names of the Site PI’s at the LOI stage).
     e. Project Narrative
        ▪ Scientific abstract (no more than 1200 characters).
        ▪ Trial Design (no more than 1800 characters): 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 (no more than 1800 characters): Briefly describe the intended study population including numbers in each recruitment cohort/arm) and description for each cohort/arm.
        ▪ Trial therapeutic dosage (no more than 1800 characters): 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.
        ▪ Target Biology (no more than 1800 characters): 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 (no more than 1800 characters): 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.
     f. Biosketch of PI
     g. Signature page

The Letter of Intent should be submitted per the application instructions at this [link](#). 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.

- **Applications**: Applications/Full proposals will be by invite-only. Instructions will be provided as to the information needed when the Letter of Intent is selected to move to the full-proposal stage. Applicants may expect to receive recommended revisions to their workplan or clinical trial design as part of the review process.

2. **Page Limitations**
   - All page limitations described in the Research Plan instructions must be followed.

3. **Submission Dates and Times**
   - Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date.
   - Organizations must submit applications by accessing the application and instructions here.

4. **Funding Restrictions**
   - The ALS Association awards are subject to the terms and conditions described in The ALS Association Grants Policy Statement (GPS) and the award Agreement. The ALS Association GPS is available here.
   - Awards will be limited $1,000,000 total costs (including no more than 10% for indirects) for either a two-year or a three-year period of performance.
   - 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 planning phase of the study (typically the first 12 weeks post award). Planning phase activities will 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 under Chapter 7. Cost Considerations. See Section 7.5.1 Selected Items of Costs for budget preparation.

5. **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 application has been submitted and approval is pending.
     - OR applicant will need to file a new-IND application by 3 months from the start of the project date.
     - OR 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.
provide 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.).

- Inventions, patents, ownership and sharing of net income from the licensing, sale or transfer of any invention related to an ALS Association grant is subject to the terms outlined in the Grants Policy Statement Section 8.3.3.

6. 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 and developing lead agents 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.

7. Administrative and National Policy Requirements
All ALS Association grants include The ALS Association 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. Below is a summary of some of the requirements outlined in the Grants Policy Statement under Chapter 4 Research-Related and Other Requirements and Chapter 8 Administrative and Other Requirements. Refer to the [Grants Policy Statement](#) for more information.

- **Animal Welfare Requirements:** The ALS Association requires its grantees to establish appropriate policies and procedures to ensure the humane care and use of animals. Domestic grantees also bear the ultimate responsibility for compliance with The Public Health Service (PHS) Policy on Human Care and Use of Laboratory Animals. Foreign grantees also bear the responsibility to comply with applicable laws, regulations, and policies of the jurisdiction in which the research will be conducted, and a commitment to follow the [International Guiding Principles for Biomedical Research Involving Animals](#) developed by the Council for International Organizations of Medical Sciences.

- **Human Subject Requirements:** The ALS Association requires its grantees to establish appropriate policies and procedures to ensure the protection of human subjects used in research supported by The ALS Association. The ALS Association grantee must comply with the Department of Health and Human Services (HHS) regulation Title 45 Code of Federal Regulation Part 46. Clinical research involving investigational drugs and devices or products regulated by the Food and Drug Administration (FDA), must comply with all FDA requirements in 21 CFR Parts 50, 56, 312 and 812.

- **Health Insurance Portability and Accountability Act (HIPAA):** The ALS Association requires its domestic grantees to comply with the requirements of HIPAA to ensure the protection of individually identifiable health information for ensuring confidentiality of patient records.

- **General Data Protection Regulation (E.U. 2016/679):** The ALS Association requires its foreign grantees to comply with the Regulation E.U. 2016/679, or its amended regulation, of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to processing of personal data and on the free movement of such data.

- **Invention, Patents, Ownership and Sharing of Net Income:** The ALS Association allows its grantees to have the first right, but not the obligation, to prepare, file,
prosecute and maintain all registerable rights relating to any Invention at its sole expense, except with respect to any Invention, the rights to which the grantee assigns to The ALS Association per the Research Grant Agreement. Additional information on this subject is provided in the Grants Policy Statement within Section 8.3.3.

8. Other Submission Requirements and Information

- Applications must be submitted electronically following the instruction described in create application guideline. Paper applications will not be accepted.
- 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.

Section V. Application Review Information

1. 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.

2. Review Criteria for Full Applications:

- **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.

3. Peer Review and Selection Process

- All applications are peer reviewed by the Scientific Review Committee constituted by The ALS Association to determine the application’s scientific merit, and relevance to ALS.

- The Scientific Review Committee’s priority scores are forwarded to the Research Committee of The ALS Association Board of Trustees, which has the sole authority for approving the funding of research grants.

4. Anticipated Announcement and Award Dates

- After the peer review of the application is completed and a selection is made of the application, The ALS Association will send the combined review results of the grant proposal. 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.

- See Part I, Section II, for dates of peer review, Scientific Review Committee and earliest start date.
- Contracting with the PI organization will begin after award announcement and should be completed (signed and returned) 4 weeks from award notification. The start date of the project should be no later than January 31, 2022.

Section VI. Award Administration Information

1. Award (Agreement) Notice 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.
   - Award payments will be made to the Grantee on an annual or semi-annual basis as outlined within the Agreement.

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 the Grants Policy Statement Section 8.1.2 Prior Approval Requirements for more information.
   - Requests for prior approval should be submitted via email to researchgrants@alsa-national.org at least 30 days before the proposed change.

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.

Section VII. ALS Association Contacts

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