I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Amyotrophic Lateral Sclerosis Research Program

Pilot Clinical Trial Award

Announcement Type: Initial

Funding Opportunity Number: HT942524ALSRPPCTA

Assistance Listing Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application (Letter of Intent) Submission Deadline:** 5:00 p.m. Eastern time (ET), May 24, 2024
- **Application Submission Deadline:** 11:59 p.m. ET, July 10, 2024
- **End of Application Verification Period:** 5:00 p.m. ET, July 17, 2024
- **Peer Review:** September 2024
- **Programmatic Review:** November 2024

This program announcement must be read in conjunction with the General Application Instructions, version 901. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the "Package" tab, clicking "Preview," and then selecting "Download Instructions."

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II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

The U.S. Army Medical Research Acquisition Activity (USAMRAA) is soliciting applications to the fiscal year 2024 (FY24) Amyotrophic Lateral Sclerosis Research Program (ALSRP) using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC) is the program management agent for this funding opportunity. Congress initiated the ALSRP in 2007 to provide support for research of high potential impact and exceptional scientific merit. Appropriations for the ALSRP from FY07 through FY23 totaled $229.4 million (M). The FY24 appropriation is $40.0M.

II.A.1. FY24 ALSRP Pilot Clinical Trail Award Focus Areas

To meet the intent of the funding opportunity, applications to the FY24 ALSRP Pilot Clinical Trial Award must address one of the following Focus Areas. Applicants will be required to select either:

- **Biomarker-Driven Interventions**: Disease-modifying interventions, with mechanism-specific predictive, efficacy, and/or pharmacodynamic biomarkers.
- **Clinical Care:** Improving aspects of clinical care and symptom management for Amyotrophic Lateral Sclerosis (ALS).

II.B. Award Information

The FY24 ALSRP Pilot Clinical Trial Award supports the rapid implementation of clinical trials with the potential to have a significant impact on the treatment or management of ALS. Projects may range from phase 1 to small-scale phase 2 trials and should aim to de-risk and inform the design of more advanced trials by investigating safety, feasibility, biomarker application, and therapeutic efficacy in relevant patient populations. Clinical trials may be designed to evaluate promising drugs, biologics, or devices with anticipated therapeutic impact that is supported by strong scientific rationale and existing preliminary studies and/or preclinical data. Clinical trials aimed to improve aspects of patient care and ALS symptom management are also applicable to this award mechanism.

Funding from this award mechanism must support a clinical trial. A clinical trial is defined as a research study in which one or more study participants are prospectively assigned to one or more interventions (which may include a placebo or another control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. For more information, a Human Subject Resource Document is provided at https://cdmrp.health.mil/pubs/pdf/Human%20Subjects%20Resource%20Document_DEC2022.pdf. Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other FY24 ALSRP program announcements being offered. ***Studies that do***

not seek to measure safety, effectiveness, and/or efficacy outcome(s) of an intervention are not considered clinical trials.

Projects proposing a therapeutic intervention (drug, biologic, and/or device) must incorporate biomarkers specific to the intervention into the trial design. Applicants must clearly describe a biomarker-driven approach and its potential to de-risk and improve the design of anticipated later-stage trials. For further description, see Attachment 13, Biomarker Statement. Biomarker development and characterization can include target engagement biomarkers, pharmacodynamic biomarkers to measure the biological effect of an investigational therapeutic, and/or predictive/cohort-selective biomarkers that indicate whether a specific therapy will be effective in an individual patient or patient subgroup.

Key aspects of the FY24 ALSRP Pilot Clinical Trial Award mechanism include:

- **Impact:** Potential impact from a pilot clinical trial is not whether an intervention is ready at the conclusion of the trial, but rather if the outcomes will improve and accelerate future larger trials or clinical care and symptom management. Applications submitted to this award can have outcomes that focus on specific subpopulations of ALS patients or potentially even individual patients.

    - Biomarker-Driven Interventions: Therapeutic outcomes should directly and substantially de-risk and inform the design of anticipated later-phase trials of the intervention under investigation.

    - Clinical Care: Improving aspects of clinical care and symptom management should have near-term impact on patients. All interventions must offer significant potential impact for individuals affected by ALS; however, this may include just specific subpopulations or potentially even individual patients.

- **Employing Community Collaborations to Optimize Research Impact Is Required.** Research funded by the FY24 ALSRP Pilot Clinical Trial Award should be responsive to the needs of people with ALS, their families, and/or their care partners. Research teams are therefore required to establish and utilize effective and equitable collaborations and partnerships with Community members to maximize impact potential of the proposed research. These collaborations are expected to facilitate accessible, efficient, and humane clinical trials. Applications to the FY24 ALSRP Pilot Clinical Trial Award must name at least one Community partner (e.g., person with ALS, family member and/or caregiver, representative of a community-based organization) who will provide advice and consultation throughout the planning and implementation of the research project.

  Scientific researchers and Community members will ***collaborate and contribute equitably*** on all aspects of the project, which may include needs assessment, planning, research intervention design, implementation, evaluation, and dissemination. Interactions with other team members should be well integrated and ongoing, not limited to attending seminars and semi-annual meetings. Examples for implementing collaborative research approaches include:

- **Person Living with ALS, Family Member, and/or Caregiver:** The research team includes a person with ALS, their family member, or caregiver (past or present) as a project advisor who will provide advice and consultation throughout the planning and implementation of the research project.

- **Partnership with a Community-Based Organization:** The research team establishes partnerships with at least one Community-based organization that provides advice and consultation throughout the planning and implementation of the research project. Community-based organizations may include advocacy groups, service providers, policymakers, or other formal organizational stakeholders.

- **Community Advisory Board:** A Community advisory board is composed of multiple Community stakeholders and can take many forms, from a board of people with ALS, their family members, or caregivers to a coalition of Community-based organizations or any combination thereof. As with people living with ALS and organizational partners, the Community advisory board provides advice and consultation throughout planning and implementation of the research project.

- **Clinical Trial Start Date and Intervention Availability:** The proposed clinical trial is expected to begin no later than 12 months after the award date or 18 months after the award date for Food and Drug Administration (FDA)-regulated studies. The application should demonstrate the documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate, for the proposed duration of the study.

- **Study Population:** The application should demonstrate the availability of and access to a suitable patient population that will support a meaningful outcome for the study. The application should include a discussion of how accrual goals will be achieved, as well as the strategy for inclusion of women and minorities in the clinical trial appropriate to the objectives of the study.

- **Research Personnel and Environment:** The application should demonstrate the study team's expertise and experience in all aspects of conducting clinical trials, including appropriate statistical analysis, knowledge of FDA processes (if applicable), and data management. The application should include a study coordinator(s) who will guide the clinical protocol through the local Institutional Review Board (IRB) of record and other federal agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual. The application should show strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312), Subpart D, are fulfilled.

- **Statistical Analysis and Data Management Plans:** The application should include a clearly articulated statistical analysis plan, a power analysis reflecting sample size projection that will answer the objectives of the study, and a data management plan that includes use of an appropriate database to safeguard and maintain the integrity of the data. If FDA-regulated, the trial must use a 21 CFR 11-compliant database and appropriate data standards. For more on data standards, see

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM511237.pdf.

- **Transition Plan:** Applications should include a transition plan (including potential funding and resources) showing how the intervention will progress to the next clinical trial phase and/or improve current standards of care after the successful completion of the FY24 ALSRP Pilot Clinical Trial Award.

- **Milestone meeting:** The Principal Investigator (PI) will be required to present an update on progress toward accomplishing the goals of the award at annual, virtual In Progress Review meetings to be held during the period of performance. The PI should ideally include their Community collaboration partner(s) in the meeting. The In Progress Review Meeting will be attended by members of the ALSRP Programmatic Panel, CDMRP staff, the USAMRAA Grants/Contracts Officer, and other stakeholders.

For the purposes of this funding opportunity, Regulatory Agency refers to the FDA or any relevant international regulatory agency unless otherwise noted.

If the proposed clinical trial involves the use of a drug that has not been approved by the relevant Regulatory Agency for the country where the research will be conducted, then submission of an Investigational New Drug (IND) application, or equivalent, that meets all requirements under 21 CFR 312 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the relevant Regulatory Agency if an IND, or equivalent, is not required. If an IND, or equivalent, is required, the regulatory application ***must be submitted to the relevant regulatory agency by the FY24 ALSRP Pilot Clinical Trial Award*** *application submission deadline***.** The IND, or equivalent, should be specific for the product and indication to be tested in the proposed clinical trial. For more information on IND applications specifically, the FDA has provided guidance at https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application.

If the investigational product is a device, then submission of an Investigational Device Exemption (IDE), or equivalent, application that meets all requirements under 21 CFR 812 may be required. It is the responsibility of the applicant to provide evidence if an IDE, or equivalent, is not required. If an IDE, or equivalent, is required, the IDE application, or equivalent, ***must be submitted to the relevant Regulatory Agency by the FY24 ALSRP Pilot Clinical Trial Award*** *application submission deadline***.** The IDE, or equivalent, should be specific for the device and indication to be tested in the proposed clinical trial.

If the clinical trial of an investigational product will be conducted at international sites, evidence that an application to the relevant national regulatory agency of the host country(ies) ***has been submitted by the FY24 ALSRP Pilot Clinical Trial Award*** *application submission deadline* is required.

Applicants are encouraged to deposit biosamples and data in well-curated and broadly available ALS research repositories, such as those listed on the ALSRP web page (https://cdmrp.health.mil/alsrp/resources/ALSRPresources). Other platforms may be used, provided they have an adequate description of repository parameters and mechanisms for broad

access. For more guidance on data sharing, refer to the General Application Instructions, Appendix 2, Section K.

For further information on early-phase clinical trial design and biomarker types, qualifications, and their use in ALS clinical trials, it is recommended that applicants consult the following resources:

- FDA/National Institutes of Health (NIH) Biomarkers, EndpointS, and Other Tools (BEST) Resource (https://www.ncbi.nlm.nih.gov/books/NBK338448/)
- National Institute of Neurological Disorders and Stroke (NINDS) Biomarker Program. https://www.ninds.nih.gov/current-research/focus-tools-topics/focus-biomarkers-research
- FDA Biomarker Qualification Program. https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/biomarker-qualification-program
- FDA Guidance Document – "Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment Guidance for Industry." September 2019. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/amyotrophic-lateral-sclerosis-developing-drugs-treatment-guidance-industry
- Verber NS, Shepheard SR, Sassani M, et al. 2019. Biomarkers in motor neuron disease: A state of the art review. *Frontiers in Neurology* 10:291. https://www.frontiersin.org/articles/10.3389/fneur.2019.00291/full
- van den Berg LH, Sorenson E, Gronseth G, et al. 2019. Revised Airlie House consensus guidelines for design and implementation of ALS clinical trials. *Neurology* 92(14):e1610-e1623. https://n.neurology.org/content/92/14/e1610
- Benatar M, Boylan K, Jeromin A, et al. 2016. ALS biomarkers for therapy development: State of the field and future directions. *Muscle Nerve* 53(2):169-182. https://doi.org/10.1002/mus.24979

CDMRP encourages research on health areas and conditions that affect women uniquely, disproportionately, or differently from men, including studies analyzing sex as a biological variable. Such research should relate anticipated project findings to improvements in women's health outcomes and/or advancing knowledge for women's health.

For the purposes of this funding opportunity, research that meets the definition of a clinical trial is distinct from clinical research. Clinical research encompasses research with human data, human specimens, and/or interaction with human subjects. Clinical research is observational in nature and includes:

(1) Research conducted with human subjects and/or material of human origin such as data, specimens, and cognitive phenomena for which an investigator (or co-investigator) does ***not*** seek to assess the safety, effectiveness, and/or efficacy outcomes of an intervention. Research meeting this definition may include but is not limited to: (a) mechanisms of human disease, (b)

diagnostic or detection studies (e.g., biomarker or imaging), (c) health disparity studies, and (d) development of new technologies.

(2) Epidemiologic and behavioral studies that do ***not*** seek to assess the safety, effectiveness, and/or efficacy outcomes of an intervention.

(3) Outcomes research and health services research that do not fit under the definition of clinical trial.

Excluded from the definition of clinical research are in vitro studies that utilize human data or specimens that cannot be linked to a living individual and meet the requirements for exemption under §46.104(d)(4) of the Common Rule.

Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to register the study in the NIH clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 1, Section B, for further details.

The funding instrument for awards made under the program announcement will be grants (31 USC 6304).

The anticipated direct costs budgeted for the entire period of performance for an FY24 ALSRP PCTA should not exceed **$2M**. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

Awards supported with FY24 funds will be made no later than September 30, 2025.

The CDMRP expects to allot approximately $8M to fund approximately three Pilot Clinical Trial Award applications. Funding of applications received is contingent upon the availability of federal funds for this program, the number of applications received, the quality and merit of the applications as evaluated by peer and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY24 funding opportunity will be funded with FY24 funds, which will expire for use on September 30, 2030.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: Extramural and Intramural organizations are eligible to apply, including foreign or domestic organizations, for-profit and non-profit organizations, and public entities.

Extramural Organization: An eligible non-Department of Defense (DOD) organization. Examples of extramural organizations include academic institutions, biotechnology companies,

foundations, federal government organizations other than the DOD (i.e., intragovernmental organizations), and research institutes.

Intramural DOD Organization: Refers specifically to DOD organizations including DOD laboratories, DOD military treatment facilities, and/or DOD activities embedded within a civilian medical center.

Awards are made to eligible ***organizations***, not to individuals. Refer to the General Application Instructions, Appendix 1, for additional recipient qualification requirements.

II.C.1.b. Principal Investigator

Independent investigators at all career levels may be named by their organization as the PI on the application.

For titles outside of academia that may not be analogous to traditional hierarchies, investigators at or above an independent scientist level may be named by their organization as the PI on the application.

An eligible PI, regardless of ethnicity, nationality, or citizenship status, must be employed by or affiliated with an eligible organization.

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

Organizations must be able to access **.gov** and **.mil** websites to fulfill the financial and technical deliverable requirements of the award and submit invoices for payment.

Refer to Section II.H.2, Administrative Actions, for a list of administrative actions that may be taken if a pre-application or full application does not meet the administrative, eligibility, or ethical requirements defined in this program announcement.

II.D. Application and Submission Information

II.D.1. Location of Application Package

Submission is a two-step process requiring both a ***pre-application*** submitted via the Electronic Biomedical Research Application Portal (eBRAP.org) and a ***full application*** (eBRAP.org or Grants.gov). Depending on the type of submission (i.e., extramural vs. intramural), certain aspects of the submission process will differ.

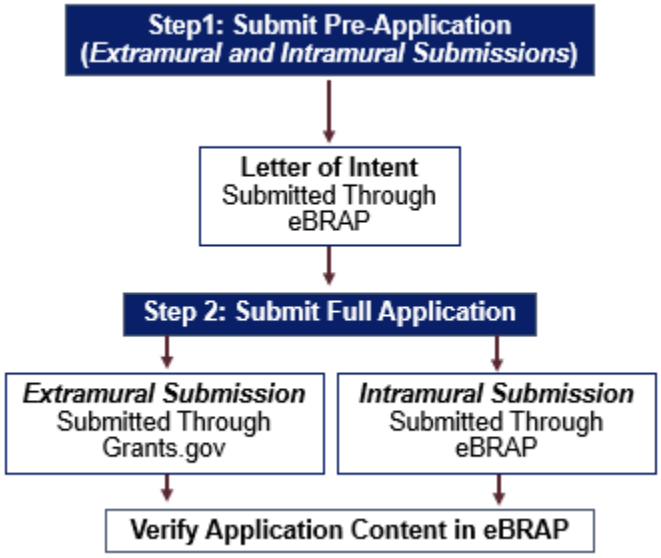
The CDMRP uses two portal systems to accept pre- and full application submissions.

eBRAP (https://ebrap.org) is a secure web-based system that allows PIs and/or organizational representatives from both extra- and intramural organizations to receive communications from

the CDMRP and submit their pre-applications. Additionally, eBRAP allows extramural applicants to view and verify full applications submitted to Grants.gov and allows intramural DOD applicants to submit and verify full applications following their pre-application submission.

Grants.gov (https://grants.gov) is a federal system that must be used by funding agencies to announce extramural grant applications. Full applications for CDMRP funding opportunities can only be submitted to Grants.gov after submission of a pre-application through eBRAP.

Application Submission Workflow



Extramural Submission: An application submitted by an extramural organization for an extramural or intramural PI working within an extramural or intramural organization. For example, a research foundation submitting an application for a DOD employee working within a DOD organization would be considered an extramural submission and should follow instructions specific to extramural submissions. Download application package components for HT942524ALSRPPCTA from Grants.gov (https://grants.gov). Full applications from extramural organizations ***must*** be submitted through Grants.gov.

Intramural Submission: An application submitted by an intramural DOD organization for an investigator employed by that organization. Intramural DOD organizations may submit full applications to either eBRAP or Grants.gov. Download application package components for HT942524ALSRPPCTA from the anticipated submission portal eBRAP (https://ebrap.org) or Grants.gov.

The submission process should be started early to avoid missing deadlines. Regardless of submission type or portal used, all pre- and full application components must be submitted by the deadlines stipulated on the first page of this program announcement. There are no grace periods for deadlines; failure to meet submission deadlines will result in application rejection. ***The***

USAMRAA cannot make allowances/exceptions for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.

II.D.2. Content and Form of the Application Submission

Submitting applications that propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application(s).

Unnecessary duplication of funding, or accepting funding from more than one source for the same research, is prohibited. See CDMRP's full position on research duplication at https://cdmrp.health.mil/funding/researchDup.

Including classified research data within the application and/or proposing research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns, may result in application withdrawal. Refer to the General Application Instructions, Appendix 7, Section B.

FY24 ALSRP Programmatic Panel members should not be involved in any pre-application or full application. For questions related to panel members and pre-applications or applications, refer to Section II.H.2.c, Withdrawal, or contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

II.D.2.a. Step 1: Pre-Application Submission

Regardless of submission type (i.e., extramural or intramural), all pre-application components must be submitted by the PI through eBRAP.

During the pre-application process, eBRAP assigns each submission a unique log number. This unique log number is required during the full application submission process. The eBRAP log number, application title, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent throughout the entire pre-application and full application submission process. Inconsistencies may delay application processing and limit or negate the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application submission deadline.

II.D.2.a.i Pre-Application Components

Pre-application submissions must include the following components (refer to the General Application Instructions, Section III.B, for detailed instructions regarding pre-application submission):

> **Letter of Intent (LOI) (one-page limit):** Provide a brief description of the research to be conducted. State the FY24 PCTA Focus Area and intervention. Include relevant biomarkers, as applicable. Indicate how many study participants will be enrolled. Briefly describe your community collaboration including the names of individuals participating.

LOIs are used for program planning purposes only (e.g., reviewer recruitment) and will not be reviewed during either the peer or programmatic review. ***An invitation to submit a full application is NOT provided after LOI submission. Applicants are encouraged to develop pre-application and full application components concurrently and submit a full application AFTER successful submission of the pre-application.***

II.D.2.b. Step 2: Full Application Submission

II.D.2.b.i. Full Application Submission Type

Extramural Submissions: Full applications from extramural organizations ***must*** be submitted through Grants.gov Workspace. Full applications from extramural organizations, including non-DOD federal organizations, received through eBRAP will be withdrawn. Refer to the General Application Instructions, Section IV, for considerations and detailed instructions regarding extramural full application submission.

Intramural Submissions: Intramural DOD organizations may submit full applications through either eBRAP or Grants.gov. There is no preference from the CDMRP for which submission portal is utilized; submission through one portal or the other does not provide the application any advantage during the review process. Intramural DOD organizations that choose to submit through Grants.gov should follow Extramural Submission instructions. Intramural DOD organizations that are unable to submit through Grants.gov should submit through eBRAP. For the remainder of this program announcement, it will be assumed intramural DOD submissions will proceed through eBRAP. Refer to the General Application Instructions, Section V, for considerations and detailed instructions regarding intramural DOD full application submission.

II.D.2.b.ii. Full Application Submission Components

Each application submission must include the completed full application package for this program announcement. See Section II.H.3 of this program announcement for a checklist of the required application components.

(a) SF424 Research & Related Application for Federal Assistance Form *(Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B, for detailed information.

(b) Attachments:

Each attachment to the full application components must be uploaded as an individual file in the format specified and in accordance with the formatting guidelines listed in the General Application Instructions, Appendix 2.

- **Attachment 1: Project Narrative (15-page limit): Upload as "ProjectNarrative.pdf".** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs (uniform resource locators) that provide additional information that expands the Project Narrative and could confer

an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

Describe the proposed project in detail using the outline below.

The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 5-8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

- **Background and Rationale:** Describe in detail the scientific rationale for the study. Provide a literature review and analysis. Describe the preliminary studies and/or preclinical data that support the development of the proposed clinical trial. Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety and stability (as appropriate) of the intervention. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). This section should establish the relevance of the study and explain the applicability of the proposed findings.

- **Hypothesis or Objective:** Clearly state the purpose and objectives. Include detailed study questions/hypotheses.

- **Clinical Trial Design:**

  - Describe the type of study to be performed (e.g., treatment,), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to show a clear course of action.

  - Identify the intervention and describe the projected results. *Additional details should be provided in Attachment 5, Intervention.*

  - Define the primary and any secondary or interim endpoints/outcome measures, outline why they were chosen, and describe how and when they will be measured. Include a description of appropriate controls. Outline the timing and procedures planned during the follow-up period.

  - Describe and justify the study population and the inclusion and exclusion criteria that will be used to meet the needs of the proposed clinical trial.

  - Briefly outline the methods that will be used for recruitment (e.g., convenience, simple random, stratified random). *Additional details should be provided in Attachment 6, Human Subject Recruitment and Safety Procedures.*

- Define each arm/study group of the proposed trial, if applicable. Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures). Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).

- Outline whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.

- Describe potential problem areas and discuss alternative methods/approaches that may be employed to overcome them. Estimate the potential for subject loss to follow-up, and how such loss will be handled/mitigated.

– **Biomarker Plan (required for Biomarker-Driven Interventions Focus Area only):** ***Briefly*** describe how the proposed biomarker and data analysis is relevant to a specific therapeutic/class of therapeutics or to a specific type of ALS (such as a particular genetic mutation). Reference how qualification criteria described in relevant ALS biomarker literature is being considered. *Additional details of the biomarker effort should be provided in Attachment 13, Biomarker Statement.*

– **Statistical Plan and Data Analysis:**

- Describe the statistical model and data analysis plan with respect to the study objectives.

- Specify the approximate number of study participants to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site.

- Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study and all proposed correlative studies.

- If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study.

- Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.

○ **Attachment 2: Supporting Documentation: Combine and upload as a single file named "Support.pdf".** Start each document on a new page. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested or viewed as

an extension of the Project Narrative will result in the removal of those items or may result in administrative withdrawal of the application.

- **References Cited:** List the references cited (including URLs, if available) in the Project Narrative using a standard reference format.

- **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols.

- **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present government award under which the facilities or equipment items are now accountable. There is no form for this information.

- **Publications and/or Patents:** Include a list of relevant publication URLs and/or patent abstracts. If articles are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.

- **Letters of Organizational Support:** Provide a letter (or letters, if applicable) signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the program announcement, such as those from members of Congress, do not impact application review or funding decisions.

- **Letters of Collaboration *(if applicable)*:** Provide a signed letter from each collaborating individual and/or organization demonstrating that the PI has the support and resources necessary for the proposed work. If an investigator at an intramural DOD organization is named as a collaborator on a full application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural DOD organization authorizing the collaborator's involvement.

- **Letters of Commitment *(if applicable):*** If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating the availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.

- **Data and Research Resources Sharing Plan:** Describe the type of data or research resource to be made publicly available as a result of the proposed work. Describe how data and resources generated during the performance of the project will be shared with the research community. Include the name of the repository(ies) where scientific data and resources arising from the project will be archived, if applicable. If a public repository will not be used for data or resource sharing, provide

justification. Provide a milestone plan for data/results dissemination including when data and resources will be made available to other users, including dissemination activities with a particular focus on feeding back the data to affected communities and/or research participants. Refer to CDMRP's Policy on Data & Resource Sharing located on the eBRAP "Funding Opportunities & Forms" web page https://ebrap.org/eBRAP/public/Program.htm for more information about CDMRP's expectations for making data and research resources publicly available. **Include considerations of existing, publicly available, curated ALS repositories.**

- **Use of DOD/U.S. Department of Veterans Affairs (VA) Resources *(if applicable)*:** Provide a signed letter of support confirming access for the entire period of performance to active-duty military population, VA patients, and/or VA/DOD resources, databases, or research spaces. Describe any required data sharing, memorandum of understanding, or other agreements required to access and publish data.

- **Questionnaires and Other Research Data Collection Instruments, if applicable (no page limit):** The Questionnaires and Other Research Data Collection Instruments attachment should include a copy of the most recent version of questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.

- **Attachment 3: Technical Abstract and Lay abstract (two-page limit): Upload as "TechAbs.pdf".** The technical abstract is used by all reviewers. ***Abstracts of all funded research projects will be posted publicly.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Technical abstracts should be written using the outline below. Clarity and completeness within the space limits are highly important.

  - **Background:** Present the scientific rationale behind the proposed research project.

  - **Clinical Intervention:** State the intervention to be tested.

  - **Objective(s):** State the objective(s) to be reached.

  - **Specific Aims:** State the specific aims of the study.

  - **Study Design:** Describe the study design, including appropriate controls.

  - **Clinical Impact:** Briefly describe how the proposed project will de-risk and improve the design of anticipated later phase trials of the intervention under investigation or will optimize components of established ALS clinical care.

Lay abstracts should be written using the outline below. This should be written in a manner that can readily be understood by readers without an audience in science or medicine at or around the eighth-grade level. Do not duplicate the technical abstract.

- Summarize the objectives and rationale for the proposed research. Explain what the intervention is.
- What population will the research help, and how will it help them?
- What are the potential applications, benefits, and risks of the anticipated outcomes?
- What are the likely contributions of the proposed research project to advancing research, patient care, and/or quality of life

- **Attachment 4: Statement of Work (six-page limit): Upload as "SOW.pdf".** Refer to the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for the suggested SOW format and recommended strategies for assembling the SOW.

  For the Pilot Clinical Trial Award, refer to the "Example: Assembling a Clinical Research and/or Clinical Trial Statement of Work" for guidance on preparing the SOW. Use the "Suggested SOW Format" to develop the SOW for the proposed research. Submit as a PDF.

- **Attachment 5: Intervention (no page limit):** Upload as "Intervention.pdf". The Intervention attachment should include the components listed below.

  - **Description of the Intervention:** Describe the intervention to be tested and describe the particular outcomes. Describe how the intervention addresses the clinical needs and how it compares with currently available interventions and/or standards of care.
    - As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed.
    - Describe measures to ensure consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions).
    - Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits.
    - Other types of interventions should be fully described. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for conduct of the clinical trial.
  - **Study Procedures:** Describe the interaction with the study participant, including the study intervention that they will experience.

- Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience.

- Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures.

- Describe which questionnaires, data collection forms, rating scales, interview guides, or other instruments will be used for the evaluations. For each instrument, state how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable. Provide copies of the instruments in **Attachment 2**.

- Clearly delineate research procedures from routine clinical procedures.

- Discuss how compliance with current Good Laboratory Practice (GLP) guidelines, Good Manufacturing Practice (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.

– **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Good Clinical Practice (GCP) compliance by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

○ **Attachment 6: Human Subject Recruitment and Safety Procedures (no page limit): Upload as "Recruit.pdf".**

– **Study Population:** Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Provide a table of anticipated enrollment counts at each study site.

- Demonstrate that the research team has access to the proposed study population at each site and describe the efforts that will be made to achieve accrual goals.

- Discuss past efforts in recruiting study participants from the target population for previous clinical trials (if applicable).

- Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention.

- Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress.

- Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender. ***For clinical trials proposing to include military personnel, refer to the General Application Instructions, Appendix 1, for more information.***

– **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

– **Women and Minorities in the Study:** Describe the strategy for the inclusion of women and minorities in the clinical trial appropriate to the objectives of the study, including a description of the composition of the proposed study population in terms of sex/gender, race, and ethnicity, and an accompanying rationale for the selection of subjects. Provide an anticipated enrollment table(s) with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. The Public Health Service (PHS) Inclusion Enrollment Report is a three-page fillable PDF form, which can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm.

– **Description of the Recruitment Process:**

- Explain methods for identification of potential study participants (e.g., medical record review, obtaining sampling lists, healthcare provider identification).

- Describe the recruitment process in detail. Address who will identify potential study participants, who will recruit them, and what methods will be used to recruit them.

- If study participants will be compensated for participation in the study, include a detailed description of and justification for the compensation plan.

- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.

– **Description of the Informed Consent Process:** Specifically describe the plan for obtaining informed consent from study participants. P***rovide a draft, in English, of the Informed Consent Form.***

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that study participants' questions will be addressed during the consent process and throughout the trial.

- Include information regarding the timing and location of the consent process.

- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such

as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.

- Address how privacy and time for decision-making will be provided and whether the potential human subject will be allowed to discuss the study with anyone before making a decision.

- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.

- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. ***Note:*** In compliance with 10 USC 980 (https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf), the application must describe a clear intent to benefit for study participants who cannot give their own consent to participate in the proposed clinical trial. If applicable, refer to the General Application Instructions, Appendix 1, for more information.

- ***Assent:*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

– **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. ***Note:*** Some screening procedures may require a separate consent or a two-stage consent process.

– **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the study participant is exposed to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. Consider how the proposed clinical trial might affect the daily lives of the individuals participating in the study. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

– **Risk management and emergency response:**

- Appropriate to the study's level of risk, describe how safety monitoring and reporting to the IRB and FDA/international regulatory agency (if applicable) will be managed and conducted.

- Describe all safety measures to minimize and/or eliminate risks to study participants and personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.

- Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, including who will be responsible for the cost of such care.

- Address any special precautions to be taken by the study participants before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).

- Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for the study participants enrolled in the study.

– **Potential benefits:**

- Describe known and potential benefits of the study to the study participants who will participate in the study.

- Articulate the importance of the knowledge to be gained as a result of the proposed research.

- Discuss why the potential risks to study participants are reasonable in relation to the anticipated benefits to the participants and others that may be expected to result.

○ **Attachment 7: Data Management (no page limit): Upload as "DataManage.pdf".** The Data Management attachment should include the components listed below.

– **Data Management:** Describe the data to be gathered and all methods used for collection, including the following:

- **Data:** The types of data, software, or other materials to be produced.

- **Acquisition and processing:** How the data will be acquired, including the time and location of data acquisition, if scientifically pertinent. If use of existing data resources is proposed, describe the origin of the dataset. Provide an account of the standards to be used for data and metadata format and content. Explain how the data will be processed.

- **Identifiers:** Describe the unique identifiers or specific code system to be used to identify study participants, if applicable.

– **Confidentiality**

- Explain measures taken to protect the privacy of study participants and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.

- Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DOD are eligible to review study records.

- Address requirements for reporting sensitive information to state or local authorities.

– **Data capture, verification, and disposition:**

- Describe how data will be captured and verified, including the quality assurance and quality control measures taken during collection, analysis, and processing.

- Describe where data (both electronic and hard copy) will be stored; who will keep the data; how the data will be stored, if applicable; the file formats and the naming conventions that will be used; the process for locking the database at study completion; and the length of time that data will be stored, along with a justification for the time frame of preservation, which may include considerations related to the balance between the relative value of data preservation and other factors such as the associated cost and administrative burden of data storage.

- Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process.

- For studies requiring Regulatory Agency oversite, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.

– **Data reporting:** Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with a Regulatory Agency, if applicable.

– **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether the results of screening and/or study participation will be shared with study participants subjects or their primary care provider, including results from any screening or diagnostic tests performed as part of the study. In cases of national security or controlled unclassified information concerns, include a statement that the data cannot be made available to

the public (e.g., "This data cannot be cleared for public release in accordance with the requirements in DoD Directive 5230.09.").

- **Laboratory Evaluations**

  - **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.

  - **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of study participants).

  - **Storage:** Describe specimen storage, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the plan to store specimens for future use, including considerations for informed consent and providing study participants with an opportunity to decline participation in the study.

  - **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, the applicable quality standard, and any special precautions that should be taken in handling the samples. Special precautions that should be taken by the study participant before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Attachment 8: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** Answer the following questions and provide supporting documentation as applicable.

  State the product/intervention name. Provide the current status for manufacturing development (e.g., manufacturer's name, GMP-compliant lots available, status of stability testing), non-clinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support phase 1 testing, etc.), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).

  For products/interventions that do not require regulation by the FDA or an international regulatory agency:

  - For investigator-sponsored regulatory exemptions (e.g., IND, IDE) provide evidence of institutional support. Provide evidence that the clinical trial does not require regulation by the regulatory agency. If the clinical trial will be conducted at international sites, provide equivalent information relevant to the host country(ies) regulatory requirements. No further information for this attachment is required.

  For products that require regulation by the FDA and/or an international regulatory agency:

- State whether the product is regulatory agency-approved, -licensed, or -cleared, and marketed in the country the clinical trial will take place in.
    - Describe the overall regulatory strategy and product development plan that will support the planned product indication/label.
    - Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of regulatory agency meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.
- If the product is marketed in the United States, state the product label indication. If the product is marketed in an international country, provide the equivalent information equivalent.
    - State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population.
    - Indicate whether the proposed research involves a change that increases the risks associated with using the product.
    - State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).
- If the product is not currently regulatory agency-approved, -licensed, or -cleared, state the planned indication/use.
    - Indicate whether the product would be classified as a drug, device, biologic, or combination product.
    - Indicate whether the FDA has confirmed the proposed classification.
    - Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.
- ***If an FDA IND or IDE is required, the application must be submitted to the FDA prior to the FY24 ALSRP Pilot Clinical Trial Award application submission deadline. Similarly, if regulatory approval is required from an international regulatory agency, it must be submitted prior to submitting the ALSRP PCTA application.*** The data presented here should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical trial.
    - Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s).

- Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold).
    - ❖ If the IND or IDE application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold.
    - ❖ If an active IND or IDE for the investigational product is in effect, but an amendment is needed to include the proposed trial, describe the type and nature of the amendment(s) and the timeline for submission. Indicate whether the amendment increases the risk of the intervention.
    - ❖ If available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed.
- Provide a summary of any previous meetings with the FDA on development of this product. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.

– If the clinical trial will be conducted at international sites, provide equivalent information and supporting documentation relevant to the product indication/label and regulatory approval and/or filings in the host country(ies).

– Describe the overall regulatory strategy and product development plan that will support the planned product indication/label. Include a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of regulatory agency meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.

○ **Attachment 9: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as "Personnel.pdf".** The Study Personnel and Organization attachment should include the components listed below.

– **Organizational Chart:** Provide an organizational chart that identifies key members of the study team and provides an outline of the governing structure for multi-institutional studies.

- Identify collaborating organizations, centers, and/or departments and name each person's position on the project.
- Include any separate laboratory or testing centers. Identify the data and clinical coordinating center(s) and note any involvement from Contract Research Organizations, as appropriate.

- Identify and provide justification for the inclusion of international sites, as appropriate.
- If applicable, identify the Regulatory Agency sponsor and any external consultants or other experts who will assist with Regulatory Agency sponsor applications. While there is no specified format for this information, a table(s) or diagram is recommended.
- Note: This item may be made available for programmatic review.

– **Study Personnel Description:** Briefly describe the composition of the study team, including roles of the individuals listed in the organizational chart on the project.

- Study coordinator(s) should be included.
- Describe how the levels of effort for each individual are appropriate to successfully support the proposed research.
- Describe relevant background and qualifications that demonstrate appropriate expertise to accomplish the proposed work, including previous interactions with the relevant Regulatory Agency, if applicable.

– **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial involves more than one institution, clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions.

- Provide a regulatory submission plan for the master protocol and master consent form by the lead institution.
- If the research involves more than one institution, a single IRB is required for all institutions located in the United States.
- If applicable, describe how communication and data transfer between/among the collaborating institutions will occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.

○ **Attachment 10: Community Collaboration Plan (no page limit). Required, upload as "Community.pdf".** Refer to Section II.B for more details regarding the Community collaboration requirement. This attachment must be written in a manner that will be ***readily understood by readers without a background in science or medicine at or around the eighth-grade level.***

– **Community Collaboration Statement:** Describe the collaborative research approach that will be used (e.g., Lived experience consultant, partnership with community-based organization, Community advisory board, co-researcher model). Detail when and how the approach will be used within the research project, how input

will be meaningfully incorporated into the research design, execution, and dissemination, and explain how this best serves the ALS community.

- Include the names of at least one community partner (person with ALS, a family member and/or caregiver, representative of a community-based organization) who will provide advice and consultation throughout the planning and implementation of the research project.

- Describe any training, co-learning, or capacity-building activities that will be provided to both scientific researchers and Community members on collaborative research approaches, decision-making, and equitable participation.

– **Letters of Community Collaboration (two-page limit per letter):** Provide a letter signed by each Community partner confirming their role and commitment to participate on the research team. The letter should include a mention of why the qualifications and background of the individual will benefit the proposed research project. If a community-based organization will be engaged, the letter of commitment should be signed by BOTH the organization point of contact participating and the organization's leadership endorsing the collaboration.

○ **Attachment 11: Clinical Impact Statement (two-page limit): Upload as "Impact.pdf".** Attachment must be written in a manner that will be ***readily understood by readers without a background in science or medicine at or around the eighth-grade level.***.

– Describe how the intervention itself offers significant potential impact for individuals affected by ALS, to include subpopulations. Projects may have outcomes that focus on specific subpopulations of ALS patients or potentially even individual patients. Potential impact is not whether a therapy is ready at the conclusion of the trial, but rather if the outcomes will improve and accelerate future larger trials.

– Biomarker-Driven Interventions Focus Area (if applicable): Describe how the outcomes of the proposed project will de-risk and improve the design of anticipated later phase trials of the biomarker-driven intervention under investigation or will optimize components of established ALS clinical care.

– Clinical Care Focus Area (if applicable): Clearly demonstrate how this trial will provide near-term impact on patient care. Describe how the intervention represents an improvement over currently available interventions and/or standards of care.

○ **Attachment 12: Transition Plan (three-page limit): Upload as "Transition.pdf".** All applicants should contemplate and provide a plan outlining a practical trajectory to full clinical implementation for the research they are proposing, and how this will ultimately translate to benefits for the intended recipients. Applicants should identify what are **the next immediate logical steps following the period of performance** and consider how those steps would be successfully achieved.

- Describe the **immediate next logical step** to progress the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Include:
    - The schedule needed, with defined milestones, for that next step. If this step is immediately executable for clinical use, describe what is needed next to implement. If another clinical study is required, describe why this additional study is needed and whether that will bring the outcomes to stage ready to execute and implement.
    - Describe the scientific, technical, and/or regulatory requirements needed to advance the intervention. Include steps necessary for regulatory approval, as applicable.
    - Describe collaborations and other resources that will be used to help progress the trial to the next stage of development or clinical implementation (e.g., clinical partners, commercial partners, manufacturing partners, clinical practice guideline development/execution committees, training providers/resources, funding considerations). Include considerations of intellectual property, ownership rights, licensing, and commercialization plans, as applicable here. Applicants are encouraged to work with their Technology Transfer Office (or equivalent).
- **Describe how feedback from the ALS community will be integrated** into the progression of this research and continued development of the intervention. Outline the plan for disseminating the knowledge to the research, lived experience, clinical, and care communities.

- **Attachment 13: Biomarker Statement (no page limit), required for projects under the Biomarker-Driven Intervention Focus Area only: Upload as "Biomarker.pdf".** Applicants must clearly describe a biomarker-driven approach and its potential to de-risk and improve the design of anticipated later-stage trials. Preliminary biomarker characterization must consider qualification criteria described in relevant ALS biomarker literature. See Section II.B, Award Information, for more information on relevant ALS biomarker literature. Provide the following information:
    - **Biomarker(s) Description:**
        - Describe the biomarker(s) and the basis for potential utility. Biomarkers may reference levels of analytes in fluids or samples, radiologically measured parameters, event time frames, or any other objectively measured values used to reach a single interpretation.
        - Specify the aspect of the biomarker that is measured and the form in which it is used for biological interpretation.
    - **Purpose in ALS Drug Development:**

- Describe how the proposed biomarker(s) will de-risk subsequent development efforts by demonstrating target engagement, pharmacodynamics, or refinement of patient selection.

- Describe the extent to which the biomarker results will be used to steer the development process.

- Describe how the biomarker characterization considers qualification criteria described in relevant ALS biomarker literature. ***The inclusion of a decision-tree diagram that explicitly illustrates the application of the biomarker(s) and includes the actions that would be taken based on the biomarker results is recommended.***

- Describe the extent to which implementation of the biomarker in clinical settings is feasible, including how easily and reliably the biomarker may be employed in future clinical trials of the proposed therapeutic. ***Include a description of regulatory considerations for use in ALS clinical trials or clinical practice.***

- **Attachment 14: Representations *(Extramural Submissions Only)*: Upload as "RequiredReps.pdf".** All extramural applicants must complete and submit the Required Representations template available on eBRAP (https://ebrap.org/eBRAP/public/Program.htm). For more information, see the General Application Instructions, Appendix 8, Section B, Representations.

- **Attachment 15: Suggested Intragovernmental/Intramural Budget Form *(if applicable)*: Upload as "IGBudget.pdf".** If an intramural DOD organization will be a collaborator in performance of the project, complete a separate budget using the "Suggested Intragovernmental/Intramural Budget Form", available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). The budget should cover the entire period of performance for each intramural DOD site and include a budget justification as instructed. The ***total*** costs per year for each subaward (direct and indirect costs) should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section V.A.(e), for additional information and considerations.

(c) Research & Related Personal Data: For extramural submissions, refer to the General Application Instructions, Section IV.B.(c), and for intramural submissions, refer to the General Application Instructions, Section V.A.(c), for detailed instructions.

(d) Research & Related Senior/Key Person Profile (Expanded): For extramural submissions, refer to the General Application Instructions, Section IV.B.(d), and for intramural submissions, refer to the General Application Instructions, Section V.A.(d), for detailed instructions.

- **PI Biographical Sketch (five-page limit):** Upload as "Biosketch_LastName.pdf".

- **PI Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".

- **Key Personnel Biographical Sketches (five-page limit each):** Upload as "Biosketch_LastName.pdf".

- **Key Personnel Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".

(e) Research & Related Budget: For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), for detailed instructions.

- **Budget Justification (no page limit):** For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Section L, for instructions. For intramural submissions, refer to General Application Instructions, Section V.A.(e), Budget Justification Instructions.

(f) Project/Performance Site Location(s) Form: For extramural submissions, refer to the General Application Instructions, Section IV.B.(f), and for intramural submissions, refer to the General Application Instructions, Section V.A.(f), for detailed instructions.

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(g), for detailed instructions.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form and upload through Grants.gov.

- **Intramural DOD Subaward:** Complete a separate "Suggested Intragovernmental/Intramural Budget Form" for each intramural DOD subaward and upload as a single document titled **IGBudget.pdf** to Grants.gov as Attachment 15.

II.D.2.c. Applicant Verification of Full Application Submission in eBRAP

Independent of submission type, once the full application is submitted it is transmitted to and processed in eBRAP. At this stage, the PI and organizational representatives will receive an email from eBRAP instructing them to log into eBRAP to review, modify, and verify the full application submission. Verification is strongly recommended but not required. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in the "Full Application Files" tab in eBRAP. However, eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the program announcement. ***The Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline. If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the full application submission deadline.*** Other application components, including subaward budget(s) and subaward budget justification(s), may be changed until the end of the

application verification period. The full application cannot be modified once the application verification period ends.

II.D.3. Unique Entity Identifier (UEI) and System for Award Management (SAM)

The applicant organization must be registered as an entity in SAM (https://www.sam.gov/content/home) and receive confirmation of an "Active" status before submitting an application through Grants.gov. Organizations must include the UEI generated by SAM in applications to this funding opportunity.

II.D.4. Submission Dates and Times

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Failure to meet either of these deadlines will result in submission rejection.

All submission dates and times are indicated in Section I, Overview of the Funding Opportunity.

II.D.5. Funding Restrictions

The maximum period of performance is **4** years.

The application's direct costs budgeted for the entire period of performance should not exceed **$2M**. If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

All direct and indirect costs of any subaward or contract must be included in the direct costs of the primary award.

The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **4** years.

For this award mechanism, direct costs may be requested for (not all-inclusive):

- Travel in support of multidisciplinary collaborations.
- Travel costs for one investigator to travel to one scientific/technical meeting per year. The intent of travel costs to scientific/technical meetings is to present project information or disseminate project results from the FY24 ALSRP Pilot Clinical Trial Award.

Must not be requested for:

- Preclinical research costs
- Costs for travel to scientific/technical meeting(s) beyond the limits stated above.

II.D.6. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

To determine technical merit, all applications will be individually evaluated according to the following **scored criteria**, which are of equal importance:

- **Clinical Impact in the Intended Population**
    - How well the intervention provides significant potential impact for individuals living with ALS.
    - To what extent the sample population represents the targeted patient population that might benefit from the proposed intervention, to include specific subpopulations of ALS patients or potentially even individual patients.
    - *Biomarker Driven Intervention Focus Area only*: Whether the outcomes of the proposed project will de-risk and improve the design of anticipated later phase trials of the biomarker-driven intervention under investigation or will optimize components of established ALS clinical care.
    - *Clinical Care Focus Area only*: To what extent the trial provides near-term impact on patient care. Whether the intervention represents an improvement over currently available interventions and/or standards of care.
- **Rationale for the Intervention**
    - How well the scientific rationale for the proposed clinical trial is supported by the preliminary data; critical review and analysis of the literature; relevant ongoing, planned, or complete clinical trials; and/or laboratory/preclinical evidence.
    - To what degree the application includes preclinical and/or clinical evidence to support the safety and stability (as appropriate) of the intervention.
    - How the intervention compares with currently available interventions, interventions currently in clinical trial, and/or standards of care.

- **Clinical Trial Design**
    - How well the study questions, hypotheses and/or objective(s), experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective and purpose.
    - How well the inclusion/exclusion criteria and group assignment process meet the needs of the proposed clinical trial.
    - Whether there is adequate evidence of support, indicating availability of the intervention from its source (if applicable), for the duration of the proposed clinical trial.
    - Recruitment, Accrual, and Feasibility:
        - How well the application addresses the availability of patients for the clinical trial and the prospect of their participation.
        - The degree to which the recruitment, informed consent, screening, and retention processes for study participants will meet the needs of the proposed clinical trial.
        - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate mitigation plans to resolve them.
        - To what extent the proposed clinical trial might affect the daily lives of the individuals participating in the study.
        - Whether the distribution of the proposed enrollment on the basis of sex/gender, race, and/or ethnicity is appropriate for the proposed research.
- **Data Management and Statistical Plan**
    - To what degree the methods used for data collection, including confidentiality, are suitable for the planned study.
    - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
    - Whether subpopulations are sufficiently powered for comparative analysis with the base population from which they are derived to produce meaningful outcomes.
    - Whether analysis of group differences on the basis of sex/gender, race, and/or ethnicity are considered and are appropriate for the proposed research.
- **Biomarker Plan** ***(not applicable for applications under the Clinical Care Focus Area)***
    - How well a biomarker-driven approach and its potential to improve the design of anticipated later-stage trials is described.

- Whether biomarker(s) and data analysis are relevant to a specific therapeutic/class of therapeutics or to a specific type of ALS (such as a particular genetic mutation) and demonstrate potential to improve patient selection, efficiency, and interpretation.

- How well the preliminary biomarker characterization includes qualification criteria described in relevant ALS biomarker literature.

- The extent to which implementation of the proposed biomarker in clinical settings is feasible.

- **Regulatory Strategy and Transition Plan**

  - How the regulatory strategy and development plan to support the product indication or product label change, if applicable, are appropriate and well-described.

  - Whether the application includes documentation that the study is exempt from FDA or other international agency regulation, or that the IND or IDE application (and/or international equivalent) has been submitted to the FDA and/or relevant international regulatory agency, as appropriate.

  - How well the documentation provided supports the feasibility of acquiring an active IND or IDE (and/or international equivalent) covering the proposed trial, if applicable.

  - For investigator-sponsored regulatory exemptions (e.g., IND, IDE, or other international equivalent), whether there is evidence of appropriate institutional support.

  - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.

  - Whether the identified immediate next logical step of development and/or commercialization is realistic.

  - Whether the schedule and milestones for bringing the intervention to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into clinical practice, and/or approval by the FDA) are achievable.

  - How well the application identifies collaborations and resources needed to realize the immediate next step for the intervention, including intellectual property ownership/access rights, industry and clinical partners.

  - To what extent feedback from the ALS community is integrated into the translation of the intervention to the next stage of development and commercialization, and planned dissemination to the community is described.

- **Ethical Considerations**

  - Whether the population selected to participate in the trial stands to benefit from the knowledge gained.

- Whether the level of risk to study participants is sufficiently minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
- To what degree privacy and confidentiality issues are appropriately considered.
- To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
- Whether an independent clinical trial monitor (or clinical research associate) with expertise consistent with the nature of the potential risk(s) is identified.

- **Personnel and Communication**
  - Whether the composition, background, expertise, and levels of effort of the study team is appropriate to accomplish the proposed trial.
  - How well the input of the community partner (e.g., person with ALS, family member and/or caregiver, representative of a community-based organization) is meaningfully integrated and incorporated into the needs assessment, planning, design, execution, analysis, and/or dissemination of the research.
  - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures, site coordination) meet the needs of the proposed clinical trial.

In addition, the following **unscored criteria** will also contribute to the overall evaluation of the application:

- **Data and Resources Sharing Plan**
  - How well a plan for data sharing, as it pertains to biosample/data collection and analyses that would be of broad interest to ALS therapy development, is described.
  - Whether existing, publicly available, curated ALS repositories/data platforms or other resources with relevant repository parameters and mechanisms for broad access to data and samples are considered.
  - Whether the plan describes organizational and technical capabilities sufficient to share project data in a timely manner.

- **Environment**
  - Whether the scientific environment, clinical setting, institutional commitment, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).

- **Budget**
    - Whether the **direct** costs exceed the allowable direct costs as published in the program announcement.
    - Whether the budget is appropriate for the proposed research.
- **Application Presentation**
    - To what extent the writing, clarity, and presentation of the application components influence the review.

II.E.1.b. Programmatic Review

To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following criteria are used by programmatic reviewers:

- Ratings and evaluations of the peer reviewers
- Relevance to the priorities of the Defense Health Program and FY24 ALSRP, as evidenced by the following:
    - Adherence to the intent of the award mechanism
    - Relative clinical impact
    - Programmatic relevance to ALSRP
    - Program portfolio composition

II.E.2. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding General, USAMRDC. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in Section II.E.1.b, Programmatic Review.*** Additional information about the two-tier process used by the CDMRP can be found at https://cdmrp.health.mil/about/2tierRevProcess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement declaring that application and evaluation information will not be disclosed outside the review panel. Violations of confidentiality can result in the dissolution of a panel(s) and other corrective actions. In

addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review and approval process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review and approval process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to a third party is a crime in accordance with 18 USC 1905.

II.E.3. Integrity and Performance Information

Prior to making an assistance agreement award where the federal share is expected to exceed the simplified acquisition threshold, as defined in 2 CFR 200.1, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in SAM.

An applicant organization may review SAM and submit comments on any information currently available about the organization that a federal awarding agency previously entered. The federal awarding agency will consider any comments by the applicant, in addition to other information in the designated integrity and performance system, in making a judgment about the applicant's integrity, business ethics, and record of performance under federal awards when determining a recipient's qualification prior to award, according to the qualification standards of the Department of Defense Grant and Agreement Regulations (DoDGARs), Section 22.415.

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Each applicant organization and PI will receive email notification when the funding recommendations are posted to eBRAP. At this time, each PI will receive a peer review summary statement on the strengths and weaknesses of the application and an information paper describing the funding recommendation and review process for the ALSRP award mechanisms. The information papers and a list of organizations and PIs recommended for funding are also posted on the program's page within the CDMRP website.

If an application is recommended for funding, after the email notification is posted to eBRAP, a government representative will contact the person authorized to negotiate on behalf of the recipient organization.

Only an appointed USAMRAA Grants Officer may obligate the government to the expenditure of funds to an extramural organization. No commitment on the part of the government should be inferred from discussions with any other individual. ***The award document signed by the Grants Officer is the official authorizing document (i.e., assistance agreement).***

Intra-DOD obligations of funding will be made according to the terms of a negotiated Inter-Agency Agreement and managed by a CDMRP Science Officer.

Funding obligated to ***intragovernmental and intramural DOD organizations*** will be sent through the Military Interdepartmental Purchase Request (MIPR), Funding Authorization Document (FAD), or Direct Charge Work Breakdown Structure processes. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intragovernmental and intramural DOD investigators and collaborators must coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

An organization may, at its own risk and without the government's prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new award. For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Pre-Award Costs section, and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), Pre-Award Costs section, for additional information about pre-award costs.

If there are technical reporting requirement delinquencies for any existing CDMRP awards at the applicant organization, no new awards will be issued to the applicant organization until all delinquent reports have been submitted.

II.F.2. PI Changes and Award Transfers

The organizational transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

Unless otherwise restricted, changes in PI will be allowed at the discretion of the Grants Officer, provided the intent of the award mechanism is met.

An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

Refer to the General Application Instructions, Appendix 7, Section F, for general information on organization or PI changes.

II.F.3. Administrative and National Policy Requirements

Applicable requirements in the DoDGARs found in 32 CFR, Chapter I, Subchapter C, and 2 CFR, Chapter XI, apply to grants and cooperative agreements resulting from this program announcement.

Refer to the General Application Instructions, Appendix 7, for general information regarding administrative requirements.

Refer to the General Application Instructions, Appendix 8, for general information regarding national policy requirements.

Refer to full text of the latest DoD R&D General Terms and Conditions and the USAMRAA General Research Terms and Conditions: Addendum to the DoD R&D General Terms and Conditions for further information.

Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to register the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 6, Section F, for further details.

Applications recommended for funding that involve animals, human data, human specimens, human subjects, or human cadavers must be reviewed for compliance with federal and DOD animal and/or human subjects protection requirements and approved by the USAMRDC Office of Human and Animal Research Oversight (OHARO), prior to implementation. This administrative review requirement is in addition to the local Institutional Animal Care and Use Committee (IACUC), IRB, or Ethics Committee (EC) review. Refer to the General Application Instructions, Appendix 6, for additional information.

II.F.4. Reporting

Quarterly and Annual Technical Reports, as well as a final technical report, will be required. Technical reports must be prepared in accordance with the Research Performance Progress Report (RPPR).

The Award Terms and Conditions will specify whether additional and/or more frequent reporting is required.

The Award Terms and Conditions will specify if additional and/or more frequent reporting is required.

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the final progress report. Use the one-page template "Award Expiration Transition Plan," available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) under the "Progress Report Formats" section. The Award Expiration Transition Plan must outline whether and how the research supported by this award will progress and must include source(s) of funding, either known or pending.

PHS Inclusion Enrollment Reporting Requirement: Enrollment reporting on the basis of sex/gender, race, and ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP.

Enrollment reporting on the basis of sex/gender, race, and ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP.

Awards resulting from this program announcement may entail additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have federal contract, grant, and cooperative agreement awards with a cumulative total value greater than $10M are required to provide information to SAM about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a federal award. These recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 8, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

Questions regarding program announcement content or submission requirements as well as technical assistance related to pre-application or intramural application submission

Phone: 301-682-5507

Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

Questions regarding Grants.gov registration and Workspace

Phone: 800-518-4726; International 1-606-545-5035

Email: support@grants.gov

II.H. Other Information

II.H.1. Program Announcement and General Application Instructions Versions

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 901Ta. The program announcement numeric version code will match the General Application Instructions version code 901.

II.H.2. Administrative Actions

After receipt of full applications, the following administrative actions may occur.

II.H.2.a. Rejection

The following will result in administrative rejection of the full application:

- Pre-application was not submitted.

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Intervention (Attachment 5) is missing.
- Human Subject Recruitment and Safety Procedures (Attachment 6) is missing.
- Data Management and Sharing (Attachment 7) is missing.
- Regulatory Strategy (Attachment 8) is missing.

II.H.2.b. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.

II.H.2.c. Withdrawal

The following may result in administrative withdrawal of the full application:

- An FY24 ALSRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation, including letters of support/recommendation. ***A list of the FY24 ALSRP Programmatic Panel members can be found at https://cdmrp.health.mil/alsrp/panels/panels24***.
- The application fails to conform to this program announcement description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Applications that include names of personnel from either of the CDMRP peer or programmatic review companies. For FY24, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.health.mil/about/2tierRevProcess).
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP.

- Applications submitted by a federal government organization (including an intramural DOD organization) may be withdrawn if (a) the organization cannot accept and execute the entirety of the requested budget in current fiscal year (FY24) funds and/or (b) the federal government organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to collaborators.
- Application includes research data that are classified and/or proposes research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The PI does not meet the eligibility criteria.
- A community partner (e.g., person with ALS, family member and/or caregiver, representative of a community-based organization) is not included on the research team as required by this program announcement.
- An IND or IDE application (and/or international equivalent) has not been submitted prior to the application submission deadline for an FDA-regulated (and/or relevant international regulatory agency) study.
- The proposed project includes preclinical research.
- For the Biomarker-Driven Focus Area, if the Biomarker Statement (Attachment 13) is missing.

II.H.2.d. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

II.H.2.e. Other Funding Opportunities

The ALSRP is committed to leveraging efforts with other funding organizations to accelerate progress in ALS research. At the time of funding notifications, the ALSRP may inform highly rated, unfunded applicants about opportunities to provide their ALSRP applications and peer review summary statements to non-governmental funders, who will determine the specific criteria for funding consideration.

II.H.3. Full Application Submission Checklist

Full Application Components	Uploaded
SF424 Research & Related Application for Federal Assistance *(Extramural submissions only)*	☐
Summary (Tab 1) and Application Contacts (Tab 2) *(Intramural submissions only)*	☐
Attachments	
Project Narrative – Attachment 1, upload as "ProjectNarrative.pdf"	☐
Supporting Documentation – Attachment 2, upload as "Support.pdf"	☐
Technical Abstract and Lay Abstract – Attachment 3, upload as "TechAbs.pdf"	☐
Statement of Work – Attachment 4, upload as "SOW.pdf"	☐
Intervention – Attachment 5, upload as "Intervention.pdf"	☐
Human Subject Recruitment and Safety Procedures: Upload as Attachment 6 with file name "HumSubProc.pdf"	☐
Data Management: Upload as Attachment 7 with file name "Data_Manage.pdf"	☐
Regulatory Strategy: Upload as Attachment 8 with the file name "Regulatory.pdf"	☐
Study Personnel and Organization: Upload as Attachment 9 with file name "Personnel.pdf"	☐
Community Collaboration Plan: Upload as Attachment 10 with file name "Community.pdf" if applicable	☐
Clinical Impact Statement: Upload as Attachment 11 with file name "Impact.pdf"	☐
Transition Plan: Upload as Attachment 12 with file name "Transition.pdf"	☐
Biomarker Statement: Upload as Attachment 13 with file name "Biomarker.pdf" if applicable	☐
Representations *(Extramural submissions only)* – Attachment 14, upload as "RequiredReps.pdf"	☐
Suggested Intragovernmental/Intramural Budget Form (*if applicable)* – Attachment 15, upload as "IGBudget.pdf"	☐
Research & Related Personal Data	☐
Research & Related Senior/Key Person Profile (Expanded)	☐
Attach PI Biographical Sketch (Biosketch_LastName.pdf)	☐
Attach PI Previous/Current/Pending Support (Support_LastName.pdf)	☐
Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person	☐
Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person	☐

Research & Related Budget *(Extramural submissions only)* Include budget justification	☐
Budget *(Intramural submissions only)* Include budget justification	☐
Project/Performance Site Location(s) Form	☐
Research & Related Subaward Budget Attachment(s) Form *(if applicable)*	☐
Additional Application Components	☐
Confidential Letters of Recommendation	☐

APPENDIX 1: ACRONYM LIST

ALS	Amyotrophic Lateral Sclerosis
ALSRP	Amyotrophic Lateral Sclerosis Research Program
BEST	Biomarkers, EndpointS, and Other Tools
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
eBRAP	Electronic Biomedical Research Application Portal
ET	Eastern Time
FAD	Funding Authorization Document
FDA	Food and Drug Administration
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
IND	Investigational New Drug
IPR	In-Progress Review
IRB	Institutional Review Board
LAR	Legally Authorized Representative
LOI	Letter of Intent
M	Million
MB	Megabytes
MIPR	Military Interdepartmental Purchase Request
NIH	National Institutes of Health
NINDS	National Institute of Neurological Disorders and Stroke
PCTA	Pilot Clinical Trial Award
PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
SAM	System for Award Management
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
UEI	Unique Entity Identifier

URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code
VA	U.S. Department of Veterans Affairs