Program Announcement for the Department of Defense
Defense Health Program

Amyotrophic Lateral Sclerosis Research Program Pilot Clinical Trial Award

Funding Opportunity Number: HT942525ALSRPPCTA

Pre-Application Due: June 6, 2025

Application Due: August 27, 2025

This program announcement must be read in conjunction with the General Application Instructions, version CD25_01.

Content

Before You Begin

- **Active SAM.gov, eBRAP.org, and Grants.gov registrations are required for application submission.** User registration for each of these websites can take several weeks or longer. Each applicant must ensure their registrations are active and up to date prior to application preparation.
- **Read the funding opportunity announcement in the order it is written before beginning to prepare application materials**. It is the responsibility of the applicant to determine whether the proposed research meets the intent of the funding opportunity and that all parties meet eligibility requirements.

Who to Contact for Support

eBRAP Help Desk

301-682-5507
help@eBRAP.org

Questions regarding funding opportunity submission requirements, as well as technical assistance related to pre-application or intramural application submission.

Grants.gov Contact Center

800-518-4726
International: 1-606-545-5035
support@grants.gov

Questions regarding Grants.gov registration and Workspace.

This document uses internal links; you can go back to where you were by pressing Alt + left arrow key (Windows) or command + left arrow key (Macintosh) on your keyboard.

1. Basic Information About the Funding Opportunity

Summary: The fiscal year 2025 (FY25) Amyotrophic Lateral Sclerosis Research Program (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 Amyotrophic Lateral Sclerosis (ALS). Projects may range from phase 1 to small-scale phase 2 trials.

Applications must address one of the following focus areas:

> **Biomarker-Driven Interventions:** Disease-modifying interventions, with mechanism-specific biomarkers to predict which clinical trial participants are likely to respond, demonstrate target engagement, and effects on the intended biological pathway.
>
> **Clinical Care:** Improving aspects of clinical care and symptom management for ALS.

Distinctive Features: Funding from this award mechanism must support a clinical trial.

Projects proposing a therapeutic intervention (drug, biologic, and/or device) must incorporate biomarkers specific to the intervention into the trial design.

All applications are required to incorporate a Community Collaboration Plan, as described in Attachment 8 to optimize research impact.

The clinical trial should begin no later than 12 months after the award date or 18 months for FDA-regulated studies.

Funding Details: The Congressionally Directed Medical Research Programs (CDMRP) expects to allot approximately $5.6 million (M) to fund approximately two Pilot Clinical Trial Award applications with total cost caps of $2.8M. The maximum period of performance is three years. It is anticipated that awards made from this FY25 funding opportunity will be funded with FY25 funds, which will expire for use on September 30, 2031. Awards supported with FY25 funds will be made no later than September 30, 2026.

Submission and Review Dates and Times

- **Pre-Application (Preproposal) Submission Deadline:** 5:00 p.m. Eastern Time (ET), June 6, 2025

  Invitation to Submit an Application: July 10, 2025
- **Application Submission Deadline:** 11:59 p.m. ET, August 27, 2025
- **End of Application Verification Period:** 5:00 p.m. ET, September 3, 2025
- **Peer Review:** October 2025
- **Programmatic Review:** December 2025

Announcement Type: Modified

Funding Opportunity Number: HT942525ALSRPPCTA

Assistance Listing Number: 12.420

2. Eligibility Information

2.1. Eligible Applicants

2.1.1. Organization

Extramural and intramural organizations are eligible to apply***, including foreign and domestic organizations, for-profit and non-profit organizations, and public or private 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.

2.1.2. Principal Investigator

Independent investigators at all career levels may be named by their organization as the Principal Investigator (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.

Individuals affiliated with an eligible organization are eligible to be named as PI regardless of ethnicity, nationality, or citizenship status.

2.2. Cost Sharing

Cost sharing is not an eligibility requirement.

2.3. Other

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

3. Program Description

The U.S. Army Medical Research Acquisition Activity (USAMRAA) is soliciting applications to this funding opportunity using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The CDMRP at the U.S. Army Medical Research and Development Command (USAMRDC) is the program office managing this FY25 funding opportunity as part of the ALSRP. 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 FY24 totaled $269.4M. The FY25 appropriation is $40M.

3.1. Intent of the Pilot Clinical Trial Award

The FY25 ALSRP Pilot Clinical Trial Award supports the rapid implementation of clinical trials with the potential to have a significant impact on the treatment or symptom management of ALS. Proposed projects may range from phase 1 to small-scale phase 2 trials.

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 Research Resource is available on the CDMRP website. PIs seeking funding for a preclinical research project should consider one of the other FY25 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 11, 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.

3.1.1. Focus Areas for the PCTA

To meet the intent of the funding opportunity, applications to the FY25 ALSRP Pilot Clinical Trial Award must address one of the following focus areas. Applicants will be required to select either the **Biomarker-Driven Interventions** or the **Clinical Care** focus area:

Biomarker-Driven Interventions: Disease-modifying interventions, with mechanism-specific predictive, and/or pharmacodynamic biomarkers. **Biomarker Driven Intervention Trials** 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 Care: Improving aspects of clinical care and symptom management for ALS. **Clinical Care Focus Area Trials** should aim to improve aspects of patient care and ALS symptom management.

3.1.2. Key Elements for the PCTA

- **Impact:**
  - Biomarker-Driven Interventions: Impact from these pilot clinical trials is not based on how soon the therapy may be to approval at the end of the proposed work, but rather if the outcomes will substantially de-risk and inform the design of anticipated later-phase trials of the intervention under investigation. The potential impact may include just specific subpopulations of ALS patients or potentially even individual patients.
  - Clinical Care: Trials designed to improve aspects of ALS clinical care and/or symptom management should have near-term impact on people living with ALS.
- **Employing Community Collaborations to Optimize Research Impact Is Required.** Research funded by the FY25 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 FY25 ALSRP Pilot Clinical Trial Award must incorporate a Community Collaboration to provide advice and consultation throughout the planning and implementation of the research project.

  The Community Collaboration participants should have meaningful and ongoing input on all aspects of the project, which can 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 of Community Collaborations include:

  - **Person(s) Living with ALS, Family Member(s), and/or Caregiver(s):** The research team includes persons with ALS, their family members, or caregivers (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 a partnership 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 living 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.

3.1.3. Other Important Considerations for the PCTA

The ALSRP aims to improve the health, care, and well-being of military Service Members, Veterans, their families, and the American public affected by ALS. Evidence from scientific

research suggests a mutually inclusive relationship between ALS and military service, with a higher rate of incidence in the Veteran population, without any known reason(s) for this incidence. Knowledge, information, products, or technologies gained from the proposed research should advance research that is of significance to Service Members, Veterans, and/or their Families.

A clinical trial is defined in the Code of Federal Regulations, 45 CFR 46.102 as a research study in which one or more human subjects 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. An ***intervention*** includes both physical procedures by which information or biospecimens are gathered and manipulations of the subject or the subject's environment that are performed for research purposes.

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

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.

- **Clinical Trial Start Date and Intervention Availability:** The proposed clinical trial should 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.

3.2. CDMRP-wide Encouragements

The following encouragements are broadly applicable across many CDMRP programs, including the ALSRP. Investigators are encouraged to consider addressing these areas in their applications if doing so is appropriate for their line of research and meets the intent of this funding opportunity.

Innovative research involving nuclear medicine and related techniques to support early diagnosis, more effective treatment, and improved health outcomes of Service Members and their Families is encouraged. Such research could improve diagnostic and targeted treatment capabilities through noninvasive techniques and may drive the development of precision imaging and advanced targeted therapies.

The CDMRP encourages research on health areas and conditions that affect women uniquely, disproportionately, or differently from men. Such research should relate anticipated project findings to improvements in women's health outcomes and/or advancing knowledge for women's health.

3.3. Funding Instrument

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

3.4. Funding Details

Period of Performance: The maximum period of performance is **three** years.

Cost Cap: The application's total costs budgeted for the entire period of performance should not exceed **$2.8M**. 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 **three** years.

The appropriateness of the budget for the proposed research will be assessed during peer review.

Direct Cost Restrictions: For this award mechanism, direct costs:

May be requested for (not all-inclusive):

- Travel in support of multi-institutional collaborations.
- Costs for one investigator to travel to one scientific/technical meeting per year. The intent of travel to scientific/technical meetings should be to present project information or disseminate project results from the ALSRP Pilot Clinical Trial Award.

- Research subject compensation and reimbursement for trial-related out-of-pocket costs (e.g., travel, lodging, parking, costs associated with caregiving, and resources/equipment to enable participation).

4. Application Contents and Format

4.1. Application Overview

Application submission is a two-step process requiring both a ***pre-application*** submitted via the Electronic Biomedical Research Application Portal (eBRAP) and a ***full application*** submitted through eBRAP or Grants.gov. Depending on the submission portal, certain aspects of the application will differ.

Intramural DOD organizations submitting a full application should follow instructions for submission through eBRAP.

Extramural organizations submitting a full application must follow instructions for submission through Grants.gov.

4.2. Step 1: Pre-Application Components

Pre-application submissions must include the following components.

Note: Upload documents as individual PDF files unless otherwise noted.

- **Preproposal Narrative (three-page limit):** The Preproposal Narrative page limit 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 that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

  The Preproposal Narrative should include the following:

  - **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 led to the development of the proposed clinical trial.
  - **Clinical Trial:** Describe the clinical intervention and phase of clinical trial proposed. Applications submitted under the Clinical Care Option must describe a clinical trial to improve aspects of clinical care and symptom management. All applicants must describe a plan for project readiness by the application deadline with respect to availability of and access to clinical reagents and experimental therapeutics that meet regulatory compliance guidelines, availability of and access to appropriate subject population(s), and submission of an Investigational New Drug (IND) or Investigational Device Exemption (IDE) application to the FDA, if applicable.
  - **Use of Biomarkers:** For investigation of novel therapeutic approaches, describe the use of predictive, and/or pharmacodynamic biomarkers to improve trial design, patient selection, efficiency, and interpretation. ***Not required for applications submitted to the Clinical Care Option.***
  - **Impact in the Intended Population:** Describe how the outcomes of the therapeutic approach will de-risk, improve, and accelerate the design of anticipated later phase trials of the intervention under investigation or will improve aspects of ALS clinical care and symptom management. Describe how the intervention itself offers significant potential impact for individuals affected by ALS. Projects may have outcomes that focus on specific subpopulations of ALS patients.

- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application ***must be uploaded as individual files*** and are limited to the following:
    - **References Cited (one-page limit):** List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, reference title, and reference source, including volume, chapter, page numbers, and publisher, as appropriate).
    - **List of Abbreviations, Acronyms, and Symbols:** Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
    - **Key Personnel Biographical Sketches: *All biographical sketches should be uploaded as a single combined file.*** Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

4.3. Step 2: Full Application Components

Applicants must receive an invitation to submit a full application. Uninvited full application submissions will be rejected.

Each application submission must include the completed full application package for this program announcement. See Appendix 1 for a checklist of the full application components.

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

IMPORTANT: When completing the SF424 R&R, enter the eBRAP log number assigned during pre-application submission into Block 4a – Federal Identifier.

(b) Attachments:

Each attachment of 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. It should be clear from this description that the proposed study meets the definition of a clinical trial.

  The Project Narrative should be structured in accordance with the outline below. If necessary, additional subheadings may be used.

  - **Background:** Describe in detail the scientific rationale for the study. Provide a review and analysis of the available literature and completed/ongoing studies relevant to the proposed clinical trial.
    - Describe the preliminary studies and/or preclinical data that support 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.

If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source(s) of prior funding. Identify the specific portions of the study that will be supported with funds from this award.

– **Intervention:** Identify the intervention to be tested. Include the following components, as applicable: intervention type (drug, device, behavioral, surgical, etc.), complete name and composition, source, general concept of design, administration route. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights, along with access to the intervention itself, for conduct of the clinical trial. As applicable, appropriate letters of commitment should be provided in Attachment 2: Supporting Documentation demonstrating the study team's access to the intervention(s) for the duration of the clinical trial. Describe how the intervention addresses current clinical needs and how it compares with currently available interventions and/or standards of care.

– **Objectives/Specific Aims/Hypotheses:** Describe the purpose of the proposed study with detailed objectives. State the hypothesis/research question to be tested in the proposed clinical trial and detail the specific aims that will address the hypothesis/research question. Indicate whether the research addresses health areas and conditions that affect women uniquely, disproportionately, or differently from men.

– **Study Design:** Describe the proposed clinical trial in sufficient detail to evaluate its appropriateness and feasibility, relating to both the scientific success of the study and setting reasonable expectations for what study participants will experience.

- Describe the type of study to be performed. Outline the proposed clinical trial methodology and study variables in sufficient detail to demonstrate a clear course of action and justification. Describe the interaction with the human subject, including the study intervention that they will experience, and include the dose and administration route. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the study participant will experience.
- Provide a schedule (e.g., flowchart or diagram) of study intervention(s), evaluation(s), and follow-up procedures, including, if applicable, the biospecimen that will be collected along with the collection schedule and amount. Describe measures to ensure consistency of dosing (e.g., active ingredients for nutritional supplements, rehabilitation interventions). Define each arm/study group of the proposed trial, if applicable, and describe how group assignment will occur. Include a description of controls, as appropriate. Specify the approximate number of study participants to be enrolled. Indicate whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.

- Define all endpoints/outcome measures relevant to the objective of the study, explain why they were chosen, and describe how, when, and where they will be measured. Include all evaluations that will be made for study purposes. If questionnaires or other research data collection instruments will be used, include a copy of them within Attachment 2: Supporting Documentation. Describe the reliability and validity of the selected endpoint/outcome measure and evaluation along with the applicable quality standards. Explain how the results of evaluations and/or data collection instruments will be used to meet the objectives of the study (or to monitor safety of human subjects).
- Briefly describe the study population and the inclusion and exclusion criteria that will be used to meet the needs of the proposed clinical trial. Additional details should be provided in Attachment 5: Study Population Recruitment and Safety Plan.

– **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.

– **Biomarker Plan (Required for Biomarker-Driven Interventions Focus Area Only):** Development of mechanism-specific (1) predictive/cohort-selective, (2) target engagement, and (3) pharmacodynamic biomarkers should be incorporated into the application. If mechanism-specific biomarkers are already available or currently in development, how the existing biomarkers will improve trial design, patient selection, and efficiency or interpretation of the proposed ALS therapeutic approach must be described. Preliminary biomarker characterization must address qualification criteria described in relevant ALS biomarker literature. *Briefly* describe how the proposed biomarker and data analysis is relevant to a specific therapeutic/class of therapeutics. Additional details of the biomarker effort should be provided in Attachment 11, Biomarker Statement.

– **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.

- Include a complete power analysis to demonstrate that the proposed clinical trial's anticipated sample size is appropriate to meet the objectives of the study. Describe all clinical and statistical justifications and assumptions that support the sample size calculations. Explain any anticipated subgroup analyses and demonstrate that such analyses will be appropriately powered.
- Describe the strategy for how sex will be considered as a biological variable. This strategy should include a brief discussion of what is currently known regarding sex differences in the applicable research area. Clearly articulate how sex as a biological variable will be factored into the data analysis plan and how data will be collected and disaggregated by sex. Refer to the CDMRP Directive on Sex as a Biological Variable in Research for additional information.

- **Pitfalls and Mitigation Strategy:** Describe potential challenges and discuss alternative methods/approaches that may be employed to overcome them.

- **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 Support (two-page limit per letter *is recommended*):** Provide individual letters signed by collaborating individuals and/or organizational officials demonstrating that the PI has the support and resources necessary for the proposed work for the duration of the proposed clinical trial. Letters from the PI's Department Chair, or appropriate organization official, should also confirm that the PI(s) meet eligibility criteria. If applicable, provide a letter of support, signed by the lowest-ranking person with approval authority, confirming participation of intramural DOD collaborator(s) and/or access to military populations, databases, or DOD resources. If applicable, provide a letter of support signed by the U.S. Department of Veterans Affairs (VA) Facility Director(s), or individual designated by the VA Facility Director(s), confirming access to VA patients, resources, and/or VA research space.
  - **Data and Research Resources Sharing Plan:** Describe the type of data or research resources (e.g., bio-specimen, analysis tool/software, training material) to be made publicly available as a result of the proposed work. Describe how data and resources generated during the period of performance will be shared with the research community and other affected communities, including clinical trial participants. Include the name of the repository(ies) where scientific data and resources arising from the proposed clinical trial 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. In cases where the study participant

could potentially derive medical or other benefit from the information, explain whether the results of screening and/or study participation will be shared with the participant or their primary care provider, including results from any screening or diagnostic tests performed as part of the study. Refer to CDMRP's Policy on Data & Resources Sharing for more information about CDMRP's expectations for making data and research resources publicly available.

- **Questionnaires and Other Research Data Collection Instruments, if applicable (no page limit):** Include a copy of the most recent version of questionnaires, data collection forms, rating scales, interview guides, or other instruments. This should include any drafts that are currently in use or underdevelopment. 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: Abstracts (two-page limit): Upload as "Abstracts.pdf".** The technical and lay abstracts are 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.
  - **Hypothesis/Objective(s):** State the hypothesis to be tested and/or 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 clinical trial will have a significant impact on the research field and/or treatment or management of ALS.

  Lay abstracts should address the points outlined below in a manner that will be readily understood by readers without a background in science or medicine. Avoid overuse of scientific jargon, acronyms, and abbreviations. ***Do not duplicate the technical abstract.***

  - Summarize the objectives and rationale for the proposed research.
  - 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 eBRAP for the "Suggested SOW Format".

  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.

- **Attachment 5: Study Population Recruitment and Safety Plan (no page limit): Upload as "StudyPopPlan.pdf".** Include the components listed below.

- **Enrollment Distribution:** Provide anticipated enrollment table(s) with the proposed enrollment distributed on the basis of sex race, and ethnicity using the Public Health Service (PHS) Inclusion Enrollment Report. The enrollment table(s) should be appropriate to the objectives of the study.
- **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. If limiting inclusion by age, race, ethnicity, or sex, provide strong rationale based on justification from scientific literature, preliminary data, or other relevant considerations. 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. Describe how the study population represents the population anticipated to benefit from the intervention.
- **Study Population Availability:** Demonstrate that the research team has access to the proposed study population at each site. Describe the approximate number, pertinent demographic information, and other relevant characteristics of the study population at each enrollment site. Indicate whether the actual size of available study population may be affected by ongoing clinical trials that compete for the same population. If the proposed research involves access to military and/or VA patient populations and/or DOD or VA resources or databases, describe the access at the time of submission and include a plan for maintaining access as needed throughout the proposed research. Also include a plan for obtaining any required data sharing, memorandum of understanding, or other agreements required to access and publish data. Refer to the General Application Instructions, Appendix 4, for additional considerations.
- **Recruitment and Retention Process:** Explain methods for identification of potential study participants (e.g., medical record review, obtaining sampling lists, health care 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. 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 human subjects enrolled in the study. If study participants will be compensated, include a detailed description of and justification for the compensation plan. Describe the methods that will be employed to retain participants within the study. Discuss past efforts in recruiting and retaining study participants 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. Estimate the potential for participant loss to follow-up and how such loss will be handled/mitigated. Indicate whether the study team has considered barriers to clinical trial participation and, if applicable, how the team aims to mitigate or overcome these barriers.
- **Women and Minorities Recruitment/Retention Strategy:** Describe the strategy for recruitment and retention specific to women and minorities in the clinical trial appropriate to the objectives of the study.
- **Informed Consent Process:** Specifically describe the plan for obtaining informed consent from study participants. Include information regarding the timing and location of the consent process. If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, describe the plan to obtain assent

(agreement) from those with capacity to provide it, or a justification for a waiver of assent. Appendix 6 of the General Application Instructions contains additional considerations unique to DOD sponsored research.

- **Risks/Benefits Assessment:**
  - **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention). 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 Regulatory Agency (if applicable) will be managed and conducted. Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. 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.
  - **Potential benefits:** Describe known and potential benefits of the study to the human subjects 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 human subjects are reasonable in relation to the anticipated benefits to the human subjects and others that may be expected to result.

- **Attachment 6: 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 prompts and provide supporting documentation as applicable.
  - State the product/intervention name.

  For products/interventions that do not require regulation by a Regulatory Agency:

  - Provide evidence that the clinical trial does not require regulation by a Regulatory Agency. Submissions providing "not applicable," "none," or similar responses do not satisfy this request. No further information for this attachment is required.

  For products that require regulation by a Regulatory Agency:

  - Describe the overall regulatory strategy and product development plan that will be performed during the project's period of performance to support the planned product indication/label. Include, as appropriate, a description of the regulatory application submission strategy.
    - State whether the product is FDA-approved, -licensed, or -cleared, and marketed in the United States. If the product is marketed in the United States, state the product label indication. State whether the proposed research involves a change to the approved label indication.
    - If the product is not currently FDA-approved, -licensed, or -cleared, state the planned indication/use and whether an IND or IDE application was submitted. ***If an IND or IDE is required, the application must be submitted to the FDA prior to the FY25 ALSRP Pilot Clinical Trial Award application submission deadline.*** The IND or IDE 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.

- Provide a summary of any meetings the research team had with regulatory agencies or consultants regarding the proposed research. Include key outcomes, action items, and recommendations. If available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed.
- 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).

- **Attachment 7: 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, including the location of the organization. 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.
  - **Study Personnel Description:** Describe the composition of the study team in enough detail to determine whether the team includes relevant subject matter expertise to accomplish the proposed work. Include the roles of individuals named in the organizational chart along with any external consultants or advisors who will provide critical guidance and input to the study team (e.g., statistician, regulatory expert, commercialization consultant, clinical ethicist, patient advocate). Study coordinator(s) should be included. Describe how the levels of effort for each individual are appropriate to successfully support the proposed clinical trial.
  - **Study Management Plan:** Describe the day-to-day management of the proposed clinical trial. 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. 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. Provide a plan for resolving intellectual and material property issues among participating organizations.
- **Attachment 8: Community Collaboration Plan (no page limit). Required, upload as "Community.pdf".** Refer to Section 3.2.2 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***.
  - **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). 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(s) with ALS, a family member(s) and/or caregiver(s), representative of a community-based organization or community advisory board) 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/advisory board 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 9: Impact Statement (two-page limit): Upload as "Impact.pdf".** The impact statement summarizes the potential short- and long-term impact of the proposed clinical trial. The statement should address the points outlined below written ***in a manner that will be readily understood by readers without a background in science or medicine***.

– Summarize the potential benefit(s) of the intervention and/or research outcome of the proposed clinical trial as it relates to the FY25 ALSRP focus area(s).

– 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.

– **Biomarker-Driven Interventions Focus Area:** 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. 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.

– **Clinical Care Focus Area:** Describe how the trial will improve aspects of patient care and ALS symptom management. Clinical Care Focus Area Trials should have near-term impact on people living with ALS. Describe how the intervention represents an improvement over currently available symptom management strategies and/or aspects of ALS multidisciplinary care.

– Detail the anticipated research outcome(s) that will be directly attributed to the results of the proposed clinical trial and describe the anticipated benefits of these outcomes for individuals and the research field. Describe any relevant controversies, treatment issues, or health disparities that will be addressed by the proposed clinical trial.

– Explain the long-range vision for how implementation/dissemination of the intervention and/or research outcome(s) will improve patient care and/or quality of

life for the target population. Describe how the intervention represents an improvement over currently available interventions and/or standards of care.

- If applicable, describe how the anticipated outcomes of the proposed study will make an impact in understanding health differences between sexes.
- If applicable, indicate to what extent the project findings are anticipated to lead to improvements in women's health outcomes and/or advancements in knowledge for women's health.
- If applicable, describe how knowledge, information, products, or technologies gained from the proposed research advance research that is of significance to Service Members, Veterans, and/or their Families.
- Describe any potential challenges that might limit the impact of the proposed clinical trial, including barriers to implementation or acceptance by users.

- **Attachment 10: Post-Award Transition Plan (three-page limit): Upload as "Transition.pdf".** Discuss the anticipated methods and strategies necessary to move the anticipated research outcome (e.g., intervention, product, methodology, finding) to the next phase of development (e.g., clinical trials, commercialization, and/or delivery to the civilian or military market), assuming a positive outcome from the proposed clinical trial. Investigators are encouraged to work with their organization's Technology Transfer Office (or equivalent) to develop the transition plan. Applicants are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development when preparing the transition plan. ***The post-award transition plan should:***
  - Name the project's anticipated research outcomes including knowledge products and/or clinical products for development. A "knowledge product" is a non-materiel product that aims to transition into medical practice, training, tools, or to support materiel solutions; and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.
  - Include a timeline with defined milestones describing the logical next steps to advance the research outcome to the next stage of clinical development/implementation/dissemination. Include steps regarding Regulatory Agency approval as appropriate.
  - Describe collaborations and other resources (e.g., clinical partners, commercial partners, manufacturing partners, clinical practice guideline development/execution committees, training providers/resources) that are in place or will be established to execute the steps described above. Include a discussion of the funding strategy necessary to transition the research outcome to the next level of investigation, development, and/or commercialization. This may include commercial sponsorship, venture capital, federal or non-federal funding opportunities, etc.
  - As appropriate, discuss ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award. Include a plan for resolving intellectual and material property issues among participating organizations. If the intellectual property rights are not owned by the applicant, PI, or a member of the study team, describe the planned next steps necessary to make the product available to the target population.
  - **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 11: Biomarker Statement (no page limit), required for projects under the Biomarker-Driven Intervention Focus Area only: Upload as "Biomarker.pdf". Development of mechanism-specific** (1) predictive/ cohort-selective, (2) target engagement, and (3) pharmacodynamic biomarkers should be incorporated into the application. If mechanism-specific biomarkers are already available or currently in development, how the existing biomarkers will improve trial design, patient selection, and efficiency or interpretation of the proposed ALS therapeutic approach must be described. Preliminary biomarker characterization must address qualification criteria described in relevant ALS biomarker literature. See Section 3.2.2 Key Elements for the PCTA, 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 mechanism-specific 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(s) 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 12: Representations *(Grants.gov submissions only)*: Upload as "RequiredReps.pdf".** All extramural applicants must complete and submit the "Required Representations" document that is available on eBRAP. For more information, see the General Application Instructions, Appendix 8, Section B, Representations.
- **Attachment 13: Suggested Intragovernmental/Intramural Budget Form *(if applicable)*: Upload as "IGBudget.pdf".** If an intramural DOD organization will be a collaborator in the performance of the project, complete a separate budget for that organization using the "Suggested Intragovernmental/Intramural Budget" form that is available for download on eBRAP. Refer to the General Application Instructions, Section V.B.(c), for instructions and considerations.

(c) Research & Related Personal Data: For detailed instructions for Grants.gov submissions, refer to the General Application Instructions, Section IV.C.(a); and for eBRAP submissions, refer to the General Application Instructions, Section V.B.(a).

(d) Research & Related Senior/Key Person Profile (Expanded): Complete a Profile for each person who will contribute in a substantive, meaningful way to the scientific development or execution of the proposed research project. A biographical sketch and full description of each PI and senior/key person's current/pending support information must be attached to the individual's profile in the Attach Biographical Sketch and Attach Current & Pending Support fields, respectively.

- **Biographical Sketch:** Upload as "Biosketch_LastName.pdf".

  The CDMRP staff and reviewers use biosketches to evaluate whether research teams are equipped with the expertise necessary to carry out the proposed research.

  Biosketches must conform to the federal-wide Biographical Sketch Common Form. To prepare their biosketch attachments, applicants may use the instructions provided in the General Application Instructions, Section IV.C.(b), for Grants.gov submissions; or General Application Instructions, Section V.B.(b), for eBRAP submissions; or may use a pdf form created in SciENcv for the National Institutes of Health (NIH) or the U.S. National Science Foundation (NSF).

- **Current/Pending Support:** Upload as "Support_LastName.pdf".

  Current and pending (other) support information are used to assess the capacity or any conflicts of commitment that may impact the ability of the individual to carry out the research effort as proposed. The information also helps to assess any potential scientific and budgetary overlap/duplication with the project being proposed.

  Current and pending support documentation must conform to the federal wide format. To prepare their Current and Pending Support form, applicants may use the instructions provided in the General Application Instructions, Section IV.C.(b), for Grants.gov submissions; or General Application Instructions, Section V.B.(b), for eBRAP submissions; or may use a pdf form created in SciENcv for NIH or NSF.

(e) Research & Related Budget: For detailed instructions for Grants.gov submissions, refer to the General Application Instructions, Section IV.C.(c); and for eBRAP submissions, refer to the General Application Instructions, Section V.B.(c).

- **Budget Justification (no page limit):** For instructions for Grants.gov submissions, refer to the General Application Instructions, Section IV.C.(c), Section L; for eBRAP submissions, refer to General Application Instructions, Section V.B.(c), Budget Justification Instructions.

(f) Project/Performance Site Location(s) Form: For detailed instructions for Grants.gov submissions, refer to the General Application Instructions, Section IV.C.(d); and for eBRAP submissions, refer to the General Application Instructions, Section V.B.(d).

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Grants.gov Submissions only)*: Refer to the General Application Instructions, Section IV.C.(e), for detailed instructions.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form and upload it through Grants.gov.
- **Intramural DOD Subaward:** Complete a separate "Suggested Intragovernmental/Intramural Budget Form" for each intramural DOD subaward.

Combine them into a single document, then upload the file to Grants.gov as an attachment named “IGBudget.pdf”.

4.4. Other Application Elements

- If recommended for funding, a data management plan compliant with Section 3.c, Enclosure 3, DoD Instructions 3200.12 will be requested.

- The government reserves the right to request a revised budget, budget justification and/or additional information for applications recommended for funding.

5. Submission Requirements

5.1. Location of Application Package

Download the application package components for HT942525ALSRPPCTA from Grants.gov or eBRAP, depending on which submission portal will be used.

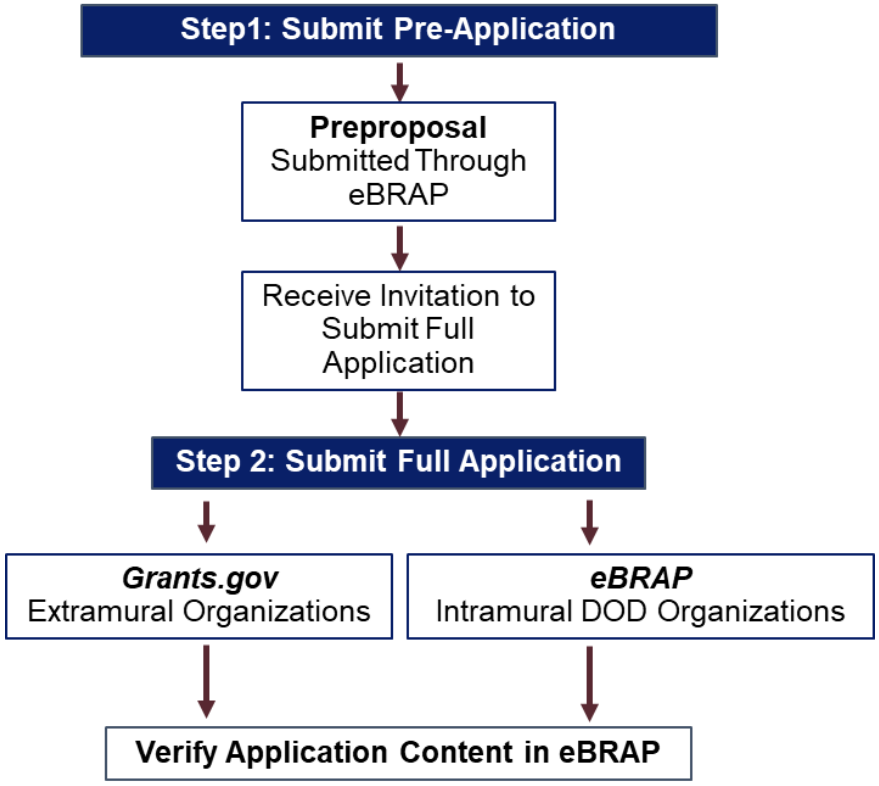
5.2. Unique Entity Identifier and System for Award Management

The applicant organization must be registered as an entity in the System for Award Management (SAM), SAM.gov, and receive confirmation of an "Active" status before submitting an application through Grants.gov. Organizations must include the unique entity identifier (UEI) generated by the SAM in applications to this funding opportunity and maintain an active registration in the SAM at all times during which it has an active Federal award or an application under consideration. More information regarding SAM registration can be found in the General Application Instructions, Section IV.A.

5.3. Submission Instructions

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

Application Submission Workflow



5.3.1. Pre-Application Submission

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.

When starting the pre-application, applicants will be asked to select a “Mechanism Option”. Be sure to select the correct option appropriate to your pre-application:

Application Includes:	Select Option:
Biomarker-Driven Interventions	PCTA-BDI
Clinical Care	PCTA-CC

Refer to the General Application Instructions, Section III.B, for considerations and detailed instructions regarding pre-application submission.

5.3.2. Full Application Submission

Grants.gov Submissions: Full applications from extramural organizations *must* be submitted through the Grants.gov Workspace. Refer to the General Application Instructions, Section IV, for considerations and detailed instructions regarding Grants.gov submissions.

eBRAP Submissions: Only intramural DOD organizations may submit full applications through eBRAP. Full applications from extramural organizations, including non-DOD federal organizations, received through eBRAP will be withdrawn. Refer to the General Application Instructions, Section V, for considerations and detailed instructions regarding eBRAP submissions.

5.3.3. Applicant Verification of Full Application Submission in eBRAP

Independent of submission portal, 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 the 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 through the appropriate portal 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.

5.4. Submission Dates and Times

The pre-application and full application submission process should be started early to avoid missing deadlines. Regardless of submission portal used, all pre- and full application components must be submitted by the deadlines stipulated in 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.***

All submission dates and times are indicated in Section 1, Basic Information above.

5.5. Intergovernmental Review

Not applicable for this funding opportunity.

6. Application Review Information

6.1. Application Compliance Review

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).

While it is allowable to propose similar research projects to different programs within CDMRP or to other organizations, duplication of funding or accepting funding from more than one source for the same research is prohibited. See the CDMRP's full position on research duplication.

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.

Members of the FY25 ALSRP Programmatic Panel should not be involved in any pre-application or full application including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation, including personal letters of support/recommendation for the research and/or PI. Programmatic panel members ***may*** provide letters to confirm PI eligibility and access to laboratory space, equipment, and other resources necessary for the project if that is part of their regular roles and responsibilities (e.g., as Department Chair). ***A list of the FY25 ALSRP Programmatic Panel members can be found on the CDMRP website.***

Additional restrictions and associated administrative responses are outlined in Section 9.2, Administrative Actions.

6.2. Review Criteria

6.2.1. Pre-Application Screening Criteria

To determine the technical merits of the pre-application and the relevance to the mission of the Defense Health Program and the ALSRP, pre-applications will be screened based on the following criteria:

- **Rationale:** Whether there is strong scientific rationale, preliminary studies and/or preclinical data to justify the proposed intervention.
- **Clinical Trial:** Whether the pre-application describes a feasible plan for clinical trial readiness by the application submission deadline.
- **Use of Biomarkers** (*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.
- **Impact in the Intended Population:** Whether the proposed project will improve aspects of ALS clinical care and symptom management or offers significant potential impact for individuals affected by ALS.

6.2.2. Peer Review Criteria

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.
  - *Clinical Care focus area only:* To what extent the trial provides near-term impact on the care of people living with ALS. Whether the intervention represents an improvement over currently available symptom management strategies and/or standards of care.
  - If applicable, to what extent the anticipated outcomes of the proposed study will make an impact in understanding health differences between sexes.
- **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 specific aims/hypotheses/research question, study design, experimental methods, data collection procedures, and evaluations are designed to address the clinical objective and purpose of the study.
  - 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.
  - Whether the strategy for considering sex as a biological variable is appropriate to the objectives of the study or whether the justification for a single sex study is sufficiently strong.
  - To what degree the planned route and schedule of study intervention(s), evaluations(s), and follow-up procedures is reasonable for study participants to experience.
  - How well potential challenges and alternative strategies are discussed.

- **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, race, and/or ethnicity is appropriate for the proposed research.
- **Statistical Plan and Data Analysis**
  - To what degree the statistical model and data analysis plan are suitable for the planned study objectives.
  - To what degree the sample size projections are adequate to ensure proper power for the study, and as applicable, any subgroup analysis.
- **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.
  - How well the preliminary biomarker characterization includes qualification criteria described in relevant ALS biomarker literature. How well the project's biomarker will indicate target engagement, pharmacodynamics, and/or predict whether a specific therapeutic will be effective.
  - The extent to which implementation of the proposed biomarker in clinical settings is feasible.
- **Regulatory Strategy and Transition Plan**
  - To what extent the regulatory strategy and product development plan are well described and appropriate to support the product indication or product label change, if applicable.
  - Whether the application includes documentation that the study is exempt from regulatory agency oversight, or that the IND or IDE application (and/or international equivalent) has been submitted to the 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.
  - To what degree the next logical steps to be taken upon successful completion of the proposed clinical trial are realistic and appropriate to bring the research outcome(s) to the next stage of clinical development/implementation/dissemination.
  - To what degree the collaborations and other resources (e.g., clinical partners, commercial partners, manufacturing partners, clinical practice guideline development/execution committees, training providers/resources) intended to help advance the research outcome(s) are established and/or achievable.

- To what degree ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award are considered and planned for.
- 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 the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
  - To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study.
  - If applicable, to what degree barriers to clinical trial participation have been considered and/or addressed.
- **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 Collaborator (e.g., person(s) with ALS, family member(s) and/or caregiver(s), 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, multi-institutional structure governing the research protocol(s)) are appropriate and meet the needs of the proposed clinical trial. In addition, the following criteria will also contribute to the overall evaluation of the application, but will not be individually scored and are therefore termed **unscored criteria**:

- **Data and Resources Sharing Plan**
  - As applicable, 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.
- **Environment**
  - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
  - Whether there is evidence for appropriate institutional commitment from each participating institution.

- **Budget**
  - 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.

6.2.3. 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 FY25 ALSRP, as evidenced by the following:
  - Adherence to the intent of the funding opportunity
  - Relative clinical impact
  - Programmatic relevance to ALSRP
  - Program portfolio composition

6.3. Application Review and Selection Process

6.3.1. Pre-Application

Following the pre-application screening, Initiating PIs will be notified as to whether they are invited to submit full applications. The estimated date when PIs can expect to receive notification of an invitation to submit a full application is indicated in Section 1, Basic Information about the Funding Opportunity. No feedback (e.g., a critique of the pre-application's strengths and weaknesses) is provided at this stage. Because the invitation to submit a full application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

6.3.2. Full Application

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 6.2.3, Programmatic Review.*** Additional information about the two-tier process used by the CDMRP can be found on the CDMRP website.

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.

6.4. Risk, 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.

In accordance with National Security Presidential Memorandum and all associated laws, all fundamental research funded by the DoD must be evaluated for affiliations with foreign entities. All applicant organizations must disclose foreign affiliations of all key personnel named on applications. Failure to disclose foreign affiliations of key personnel shall lead to withdrawal of recommendations to fund applications. Applicant organizations may be presented with an opportunity to mitigate identified risks, particularly those pertaining to influence from foreign entities specified in law. Implementation of mitigation discussions and utilization of the DOD Component Decision Matrix must decrease risk of foreign influence in accordance with the above-mentioned laws and guidance prior to award.

7. Federal Award Notices

For each full application received, the organizational representative(s) and PI will receive email notification when the funding recommendations are posted to eBRAP, typically within six weeks after programmatic review. 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 application receipt 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 additional information about pre-award costs for Grants.gov submissions, refer to the General Application Instructions, Section I.D, Pre-Award Costs section; and for eBRAP submissions, refer to the General Application Instructions, Section I.D, Pre-Award Costs section.

8. Post-Award Requirements

8.1. 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 Terms and Conditions and the USAMRAA Research Terms and Conditions: Addendum to the DoD R&D Terms and Conditions for further information.

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.

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. Additionally, the CDMRP requires all funded Applicable Clinical Trials to register on ClinicalTrials.gov. Additional data reporting requirements will also apply to Applicable Clinical Trials supported under this funding opportunity. 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, prior to implementation. This administrative review requirement is in addition to the local Institutional Animal Care and Use Committee, IRB, or Ethics Committee review. Refer to the General Application Instructions, Appendix 6, for additional information.

8.2. Reporting

Quarterly and annual technical progress reports as well as a final technical progress report will be required. Technical reports must be prepared in accordance with the Research Performance Progress Report.

Enrollment reporting on the basis of sex, race, and ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available in eBRAP.

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

Award Expiration Transition Plan: An Award Expiration Transition Plan, using the template available on eBRAP, must be submitted with the final progress report.

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).

8.3. Additional Requirements

The PI shall prepare for and participate in annual, virtual In-Progress Progress Reviews (IPR) during the project's term of award. The invitation and format for the IPR will be provided by the Grants Officer's Representative at least 30 days prior to the scheduled date. This will generally follow submission of the annual technical progress report, which will be distributed to the ALSRP Programmatic Panel prior to the IPR meeting.

Unless otherwise restricted, changes in the PI or organization will be allowed on a case-by-case basis, 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 H, for general information on organization or PI changes.

9. Other Information

9.1. 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 CD25_01Td. The program announcement numeric version code will match the General Application Instructions version code CD25_01.

9.2. Administrative Actions

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

9.2.1. Rejection

The following will result in administrative rejection of the pre-application:

- Preproposal Narrative is missing.

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

- Project Narrative is missing.
- Budget is missing.
- Submission of an application for which a letter of invitation was not issued.
- Study Population Recruitment and Safety Plan (Attachment 5) is missing.
- Regulatory Strategy (Attachment 6) is missing.

9.2.2. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents.
- Documents not requested will be removed.

9.2.3. Withdrawal

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

- A member of the FY25 ALSRP Programmatic Panel is named as being involved in the development or execution of the research proposed or is found to have assisted in the pre-application or application processes.
- Applications that include names of personnel from either of the CDMRP peer or programmatic review companies for which conflicts cannot be adequately mitigated. For FY25, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website.
- 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) if: (a) the organization cannot accept and execute the entirety of the requested budget in FY25 funds; and/or (b) the federal government organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to collaborators.
- 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.
- Application includes research data that are classified and/or proposes research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns.
- The invited application proposes a different research project than that described in the pre-application.
- 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.
- The proposed research is not a clinical trial.
- For the Biomarker-Driven Focus Area, if the Biomarker Statement (Attachment 11) is missing.

9.2.4. 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.

9.3. 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 will 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.

Appendix 1. Full Application Submission Checklist

Full Application Components	Uploaded
SF424 Research & Related Application for Federal Assistance ***(Grants.gov submissions only)***	☐
Summary (Tab 1) and Application Contacts (Tab 2) ***(eBRAP submissions only)***	☐
Attachments	
Project Narrative – Attachment 1, upload as "ProjectNarrative.pdf"	☐
Supporting Documentation – Attachment 2, upload as "Support.pdf"	☐
Abstracts – Attachment 3, upload as "Abstracts.pdf"	☐
Statement of Work – Attachment 4, upload as "SOW.pdf"	☐
Study Population Recruitment and Safety Plan – Attachment 5, upload as "StudyPopPlan.pdf"	☐
Regulatory Strategy – Attachment 6, upload as "Regulatory.pdf"	☐
Study Personnel and Organization – Attachment 7, upload as "Personnel.pdf"	☐
Community Collaboration Plan – Attachment 8, upload as "Community.pdf"	☐
Impact Statement – Attachment 9, upload as "Impact.pdf"	☐
Post-Award Transition Plan – Attachment 10, upload as "Transition.pdf"	☐
Biomarker Statement – (*if applicable*) Attachment 11, upload as "Biomarker.pdf".	☐
Representations *(Grants.gov submissions only)* – Attachment 12, upload as "RequiredReps.pdf"	☐
Suggested Intragovernmental/Intramural Budget Form *(if applicable)* – Attachment 13, upload as "IGBudget.pdf"	☐
Research & Related Personal Data	☐
Research & Related Senior/Key Person Profile (Expanded)	☐
Attach Biographical Sketch for PI and Senior/Key Persons (Biosketch_LastName.pdf)	☐
Attach Current and pending (other) support for PI and Senior/Key Persons (Support_LastName.pdf)	☐
Budget **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 2. Acronym List

ALSRP	Amyotrophic Lateral Sclerosis Research Program
BDI	Biomarker-Driven Interventions
CC	Clinical Care
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
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
IDE	Investigational Device Exemption
IND	Investigational New Drug
IPR	In-Progress Progress Reviews
IRB	Institutional Review Board
M	Million
MIPR	Military Interdepartmental Purchase Request
NIH	National Institutes of Health
OUSD R&E	Office of the Under Secretary of Defense for Research and Engineering
PCTA	Pilot Clinical Trial Award
PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
SAM	System for Award Management
SciENcv	Science Experts Network Curriculum Vitae
SOW	Statement of Work
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