Program Announcement for the Department of Defense
Defense Health Program

Amyotrophic Lateral Sclerosis Research Program Therapeutic Development Award

Funding Opportunity Number: HT942525ALSRPTDA

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) Therapeutic Development Award (TDA) supports research ranging from preclinical validation of therapeutic leads through Food and Drug Administration (FDA) Investigational New Drug (IND)-enabling studies. The proposed studies are expected to be empirical in nature and product driven. Applicants with limited Amyotrophic Lateral Sclerosis (ALS) experience are strongly encouraged to include collaborators with substantial experience in the relevant ALS model systems, endpoints, and pathophysiology.

Applications supported by this award must begin with lead compounds in hand and must already demonstrate proof-of-concept efficacy data in at least one appropriate preclinical model system of ALS, including whole animal and cellular model systems.

Distinctive Features: ***Mechanism-specific, predictive/cohort-selective, target engagement, and pharmacodynamic biomarker development, in parallel to the main therapeutic effort, is a critical component of the FY25 ALSRP Therapeutic Development Award***. If appropriate 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 apparent in the application. Development of biomarkers for the purposes of diagnosis, prognosis, or measurement of general disease progression without consideration of the therapeutic development process will not be supported.

Therapeutic candidates which have already been granted an IND are not appropriate for this mechanism.

Funding Details: The Congressionally Directed Medical Research Programs (CDMRP) expects to allot approximately $9.8 million (M) to fund approximately four Therapeutic Development Award applications with direct cost caps of $1.5M. 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: Initial

Funding Opportunity Number: HT942525ALSRPTDA

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 Therapeutic Development Award

The FY25 ALSRP Therapeutic Development Award supports research ranging from preclinical validation of therapeutic leads through FDA IND-enabling studies. The proposed studies are expected to be empirical in nature and product driven. Applicants with limited ALS experience are strongly encouraged to include collaborators with substantial experience in the relevant ALS model systems, endpoints, and pathophysiology. Candidate therapeutics that already have been granted an IND are not appropriate for the TDA

Applications supported by this award must begin with lead compounds in hand and must already demonstrate proof-of-concept efficacy data in at least one appropriate preclinical model system of ALS, including whole animal and cellular model systems.

Examples of activities that will be supported by this award include.

- Lead optimization including confirmation of candidate therapeutics obtained from screening or by other means, including optimization of potency and pharmacological properties and testing of derivatives and sister compounds.
- Validation of preliminary efficacy findings, building on initial discoveries from pilot studies (e.g., ALSRP Therapeutic Idea Awards) through expansion on assessed ALS model systems, extended dose-response characterization, or extended timepoints to more robustly establish therapeutic potential.
- IND-enabling studies to include: compound characterization; absorption, distribution, metabolism, and excretion studies; studies on formulation and stability leading to Good Manufacturing Practice production methods; dose/response and toxicology studies in relevant model systems.
- Confirmation of candidate therapeutics obtained from screening or by other means, including optimization of potency and pharmacological properties and testing of derivatives and sister compounds.
- Applications supported by this award must begin with lead compounds in hand and must include preliminary data relevant to the phase of development, such as:
    - Proof of identity and purity.
    - Selectivity for the intended target over closely related targets.
    - Availability of primary and secondary in vitro bioactivity assays for optimization or structure–activity relationship studies.
    - Availability of clear efficacy data in at least one appropriate preclinical ALS model, with adequate power and methods.

3.1.1. Key Elements for the TDA

Mechanism-specific, predictive/cohort-selective, target engagement, and pharmacodynamic biomarker development, in parallel to the main therapeutic effort, is a critical component of the FY25 ALSRP Therapeutic Development Award (TDA). If appropriate 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 apparent in the application. Development of biomarkers for the purposes of diagnosis, prognosis, or measurement of general disease progression without consideration of the therapeutic development process will not be supported. Applicants seeking support for biomarker development independent of therapeutic development are encouraged to apply for the FY25 ALSRP Clinical Outcomes and Biomarkers Award (Funding Opportunity Number HT942525ALSRPCOBA).

For further information on biomarker Context of Use in ALS clinical trials, it is recommended that applicants consult the following resources:

- FDA/National Institutes of Health Biomarkers, EndpointS, and Other Tools (BEST) Resource (https://www.ncbi.nlm.nih.gov/books/NBK338448/)
- FDA Guidance Document – "Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment Guidance for Industry." September 2019. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/amyotrophic-lateral-sclerosis-developing-drugs-treatment-guidance-industry
- Verber, N.S., S.R. Shepheard, M. Sassani, et al. 2019. Biomarkers in Motor Neuron Disease: A State of the Art Review. *Frontiers in Neurology* 10:291. https://www.frontiersin.org/articles/10.3389/fneur.2019.00291/full
- van den Berg, L.H., E. Sorenson, G. Gronseth, et al. 2019. Revised Airlie House Consensus Guidelines for Design and Implementation of ALS Clinical Trials. *Neurology* 92(14):e1610-e1623. https://n.neurology.org/content/92/14/e1610
- Benatar, M., K. Boylan K, A. Jeromin, et al. 2016. ALS Biomarkers for Therapy Development: State of the Field and Future Directions. *Muscle Nerve* 53(2):169-182. https://doi.org/10.1002/mus.24979

For further information on new drug applications, biologics license applications, or applications for supplemental indications on the evidence to be provided to demonstrate effectiveness, it is recommended that applicants consult the following resources:

- FDA Guidance Document – "Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products." December 2019. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/demonstrating-substantial-evidence-effectiveness-human-drug-and-biological-products

For biomarker development efforts proposing the use large data sets for training predictive models, a discussion of mechanisms for addressing rigor in model design, training, and assessment should be provided. Depending upon the context, this might include: algorithmic designs to avoid overfitting, saliency analysis, feature attribution, node ablation, or other alternate strategies.

3.1.2. Other Important Considerations for the TDA

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.

Clinical trials are not allowed under this award mechanism. However, validation of treatment approaches in appropriately powered and controlled studies using biological correlates of disease activity and progression in preexisting, de-identified human specimens from well-characterized patient cohorts is permitted and is encouraged. Examples of acceptable sources for preexisting biosamples or datasets include controlled clinical trials, observational studies, publicly available biorepositories, and registries. A list of suitable resources can be found on the ALSRP web page. Other resources may be used, provided they have an adequate description of repository parameters and mechanisms for broad access. Active-duty military and/or Veteran patient populations or resources should be considered.

All clinical specimens must exist at the time of application submission; collection of new specimens will not be supported.

A clinical trial is defined in the Code of Federal Regulations, Title 45, Part 46.102 (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.

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 direct costs budgeted for the entire period of performance should not exceed **$1.5M**. 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 TDA.

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 for Candidate Therapeutic:** Concisely state the project's objectives to support development of a candidate therapeutic. Describe the lead compound(s) already in hand and include preliminary data relevant to the phase of development, including relevant physical, chemical, and/or biological properties and efficacy in at least one relevant ALS model with adequate power and methods.
  - **Clinical Impact:** State explicitly how the proposed work will have significant clinical impact on the target population, including specific ALS subtypes. Outline, in general terms, steps to transition the study outcomes to therapeutic application.
  - **Research Strategy (including a biomarker-driven approach):** Describe the project's specific aims supporting development of a candidate therapeutic. **Mechanism-specific** predictive/cohort-selective, target engagement, and pharmacodynamic biomarker development, in parallel to the main therapeutic effort, is a critical component of the research strategy. If mechanism-specific biomarkers are already available or currently in development, how the existing biomarkers will improve trial study design, patient selection, and efficiency or interpretation of the proposed ALS therapeutic approach must be described. **The existence or inclusion of mechanism-specific biomarker development in the Research Strategy is a requirement for all Therapeutic Development Award applications**, including research strategies focused on translational efficacy or on Chemistry, Manufacturing, and Controls processes.

- **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 (12-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.

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

  - **Rationale for Candidate Therapeutic:** Provide background information supporting validation and further development of a proposed lead compound(s) and its putative mechanism of action as a viable therapeutic approach. Explain how the proposed study is empirical in nature and product driven.
    - Provide the chemical (or biological) identities of the lead molecules(s) or limited group of specific lead compounds.

- Provide proof of identity and purity of the lead(s) (for small molecules, typically >95% by nuclear magnetic resonance, liquid chromatography–mass spectrometry [LC-MS], melting point, etc., with no single impurity >0.5%. For biologics, often by high-performance liquid chromatography, LC-MS, immunochemistry, nucleotide or amino acid sequence analysis, etc.). Describe other physical, chemical, and/or biological properties of the lead(s) as appropriate.
- Provide clear efficacy data in at least one relevant preclinical ALS model, with adequate power and methods.

– **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.

– **Research Strategy and Specific Aims:** Concisely explain the project's specific aims to be funded by this award. Provide a well-developed, well-integrated research plan that explains how the research plan will meet the research goals and milestones. Describe the study design, methods, models, and analyses (including appropriate controls) in sufficient detail for assessment of feasibility. Explain how the study design and methods support rational design, translatability, and promise of the approach. Describe how each study is designed to achieve reproducible and rigorous results, including controls.

- Describe how the existing or proposed biomarker(s) will demonstrate target engagement, help refine individual patient or patient subgroup selection, and clarify the biological impact of a potential therapeutic. Describe how qualification criteria described in relevant ALS biomarker literature is being addressed. ***Additional details of the biomarker effort(s) should be provided in Attachment 6, Biomarker Statement.***
- For efficacy studies involving preclinical ALS models, describe the rationale for the choice of model(s), and the dose(s) of the drug.
- Describe the chemical synthetic pathways associated with proposed lead compound(s) and the feasibility of modification and/or formulation of potential delivery systems.
- Provide data to support use of primary and secondary in vitro bioactivity studies for optimization or structure–activity relationships.
- Provide data to support target selectivity, engagement, and desirable activity at the intended target.
- Describe the statistical plan, including power analysis, for the research proposed.
- Address potential pitfalls and problem areas and present alternative methods and approaches.

– **Clinical Impact:** State explicitly how the proposed work will have significant clinical impact including the target population. Outline, in general terms, steps to transition the study outcomes to therapeutic application. ***Additional details describing impact should be provided in Attachment 7, Impact Statement.***

– **Transition Readiness:** Explain how the proposed approach will prepare the candidate therapeutic for the transition to clinical studies. Outline the steps required to achieve regulatory submissions (e.g., IND). ***Additional details describing a transition plan should be provided in Attachment 8, Transition Plan.***

- **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. 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.
  - **Sex as a Biological Variable Strategy (two-page limit *is recommended*)**: 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. If needed, provide a strong rationale for proposing a single-sex study, based on justification from scientific literature, preliminary data, or other relevant considerations. Refer to the CDMRP Directive on Sex as a Biological Variable in Research for additional information.
  - **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.

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

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

  - **Background:** Present the scientific rationale behind the proposed research project.
  - **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.
  - **Product:** Describe the therapeutic product to be developed and the validated biomarker(s) or biomarker development/characterization proposed.
  - **Impact:** Summarize briefly how the proposed project will impact ALS therapeutic development and the ALS community.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf".** The lay abstract is used by all reviewers and addresses issues of particular interest to the affected community. ***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. ***Do not duplicate the technical abstract.***

  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.

  - Summarize the objectives and rationale for the proposed research.
  - What population will the research help, and how will it help them?
  - What are the likely contributions of the proposed research project to advancing research, patient care, and/or quality of life?
  - What type of ALS patients will it help, how will it help them, and when will this likely happen?

- **Attachment 5: Statement of Work (three-page limit): Upload as "SOW.pdf".** Refer to eBRAP for the "Suggested SOW Format".

  For the Therapeutic Development Award, refer to the "Example: Assembling a Generic Statement of Work", for guidance on preparing the SOW.

- **Attachment 6: Biomarker Statement (no page limit): Required for all applications. 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 TDA, for more information on relevant ALS biomarker literature.

  Provide the following information:

  - **Biomarker(s) Description:** Describe the biomarker(s) and the theoretical or empirical basis for its potential utility. Biomarkers may reference levels of analytes in fluids or samples, radiologically measured parameters, 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 biomarkers will demonstrate target engagement, help refine individual patient or patient subgroup selection, and/or clarify biological impact of a potential therapeutic. Describe the extent to which the biomarker results will be used to steer the development process. Describe how the preliminary biomarker characterization addresses qualification criteria described in relevant ALS biomarker literature. ***The inclusion of a decision-tree diagram that explicitly illustrates the application of the biomarkers and includes the actions that would be taken based on the biomarker results is recommended.*** Describe how easily and reliably the biomarkers may be implemented in eventual clinical trials of the proposed novel therapeutic. **Include a description of regulatory considerations for use in future ALS clinical trials.**

- **Attachment 7: Impact Statement (one-page limit): Upload as "Impact.pdf".** Describe how the proposed work will impact development of therapeutics for ALS. Articulate a pathway to making a clinical impact for individuals with, or at risk for, ALS. **This should be written in a manner readily understand by readers without background in science or medicine, at or around the eighth-grade level.** Specifically highlight how the research will achieve the following by the end of the performance of period:

  - Advance the development of a groundbreaking ALS therapeutic.
  - Further validation biomarkers in a parallel with the main therapeutic effort for use in eventual clinical trials.
  - Prime the therapeutic and/or biomarkers for rapid clinical impact in the intended patient populations (including subpopulations).
  - Lead to meaningful improvements in patient care.
  - If applicable, describe how the anticipated outcomes of the proposed study will make an impact in understanding health differences between sexes.

- 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.

- **Attachment 8: Transition Plan (three-page limit): Upload as "Transition.pdf".** Describe/discuss the methods and strategies proposed to move the product to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Outline the regulatory strategy. The post-award transition plan should include the components listed below.
  - The development and/or commercialization strategy.
  - The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication. Describe in detail the FDA regulatory strategy, to include considerations for compliance with Good Manufacturing Practice, Good Laboratory Practice, and Good Clinical Practice guidelines, if appropriate.
  - Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., partners, internal/external funding opportunities to be applied for).
  - For knowledge products, a description of collaborations and other resources that will be used to provide continuity of development including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. A "knowledge product" is a non-materiel product that addresses an identified need, topic area, or capability gap, is based on current evidence and research, aims to transition into medical practice, training, tools, or to support materiel solutions (systems to develop, acquire, provide, and sustain medical solutions and capabilities), and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.
  - A schedule and milestones for transitioning the technology or knowledge product to the next level of development (next-phase clinical trials, transition to industry, delivery to the military or civilian market, incorporation into clinical practice, or approval by the FDA). Include identification of the FDA regulatory strategy (if appropriate).
  - A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 9: Animal Research Plan (three-page limit), if applicable: Upload as "AnimalPlan.pdf".** When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be submitted to the Institutional Animal Care and Use Committee (IACUC) as the Animal Research Plan. The Animal Research Plan should address the following points for each proposed animal study:
  - Describe consideration of the guidelines for working with ALS animal models.
  - Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) were chosen to address the scientific objectives and, where appropriate, the study's relevance to human biology.
  - For efficacy studies, provide the rationale for the dose and route of administration for the drug(s).

- Summarize the procedures to be conducted. Describe how the study will be controlled.
- Describe the randomization and blinding procedures for the study, and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.
- Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.
- Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, statistical methods for data analysis, and identification of the primary endpoint(s).
- Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with the FDA, if applicable.

○ **Attachment 10: 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 11: 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 information.

- **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 HT942525ALSRPTDA from Grants.gov or eBRAP, depending on which submission portal will be used.

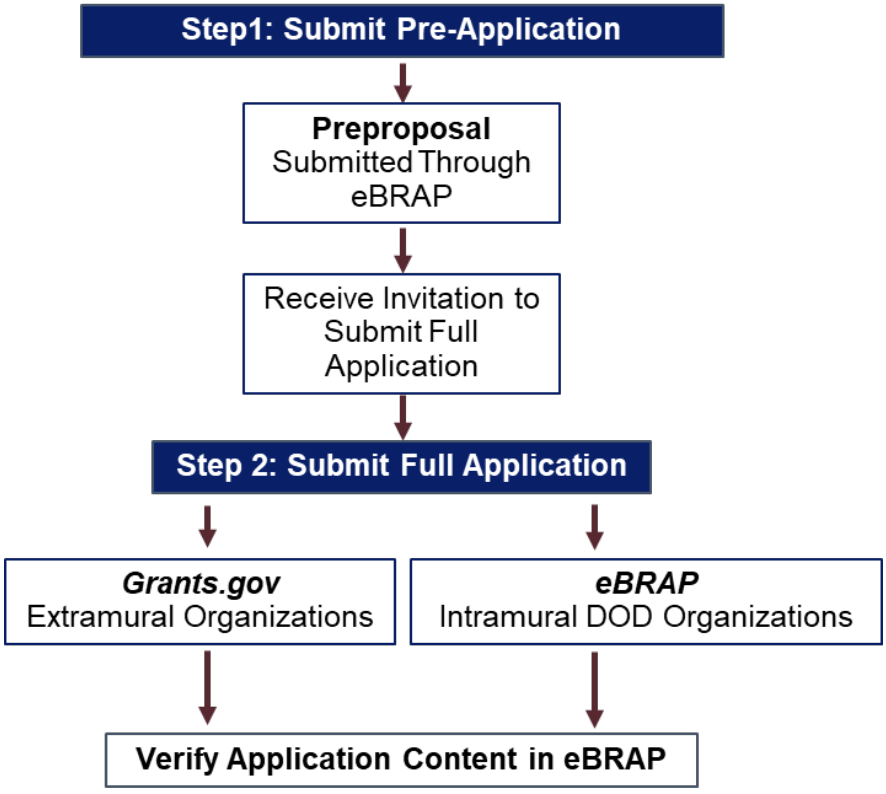
5.2. Unique Entity Identifier and System for Award Management

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.

Refer to the General Application Instructions, Section III.A, 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; the transmission to eBRAP may take up to 48 hours. 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 for Candidate Therapeutic:** How well the project's objectives support the development of a candidate therapeutic. The extent to which the preliminary data support the proposed phase of development, including clear efficacy in at least one appropriate ALS model, with adequate power and methods, and relevant physical, chemical, and/or biological properties. Candidate therapeutics that already have been granted an IND are not appropriate for the TDA
- **Clinical Impact:** How the proposed work will have significant clinical impact on the target population, including specific ALS subtypes. How well the steps to transition the study outcomes to therapeutic application are outlined.
- **Research Strategy (including a biomarker-driven approach):** How well the project's specific aims and feasibility support the development of a candidate therapeutic. Whether appropriate mechanism-specific biomarkers exist or plans for their development are included in the study design and how the biomarker will indicate target engagement,

pharmacodynamics, and/or predict whether a specific therapeutic will be effective in an individual patient or patient subgroup.

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***:***

- **Rationale for Candidate Therapeutic**
  - How strongly the project background supports the applicant's reasoning that the proposed therapeutic approach is feasible for validation and further development and the extent to which the study is product driven.
  - Whether further preclinical development of an identified bioactive compound or group of lead compounds is supported by clear efficacy in at least one ALS-relevant model system, with adequate power and methods.
  - How well the project's objectives support the development of a candidate therapeutic. Candidate therapeutics that already have been granted an IND are not appropriate for the TDA.
  - Whether the lead compounds(s) is already in hand.
- **Research Strategy and Feasibility**
  - How well the experimental design, methods, and analyses, including statistical analyses, support the study outcomes.
  - To what extent the theoretical arguments and/or empirical data support use of the proposed biomarkers for target engagement, biological effect, and/or to predict whether the therapeutic will be effective in individual patients or patient subgroups.
  - How well the preliminary biomarker characterization addresses qualification criteria described in relevant ALS biomarker literature. How well regulatory considerations for use in future ALS clinical trials are described.
  - How well the applicant identifies potential pitfalls and problem areas and addresses alternative methods and approaches.
  - 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.

For manufacturing/chemistry manufacturing and controls/IND-enabling studies:

- How appropriate and well-developed the primary and secondary in vitro bioactivity assays are for optimization or structure–activity relationship studies.
- How appropriate and well-developed the described target engagement and selectivity assays are for measurement of desirable activity at the intended target, for assessing artifacts, and for assessing the potential for undesirable activities at related but unintended targets.
- How feasible modifications and/or formulations of potential delivery systems are for the outlined chemical synthetic pathways associated with the lead compound(s).

For studies involving animal research:

- How well the animal species, strain, and model(s) being used can address the scientific objectives.
- For efficacy studies, whether the drug dose(s) and route(s) of administration are justified.
- How well each animal study considers the guidelines for working with ALS animal models and how well it is designed to achieve the objectives, including the relevance of endpoints/outcome measures to be used.
- The extent to which each study is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.

- **Transition Readiness**
  - If applicable, whether data will be appropriately reported and documented to support a regulatory filing with the FDA.
  - Whether the schedule and milestones for bringing the product to the next level of development (next-phase clinical trials, transition to industry, delivery to the military or civilian market, incorporation into clinical practice, or approval by the FDA) are achievable.
  - Whether the funding strategy described to bring the product to the next level of development (e.g., specific potential industry partners, specific funding opportunities to be applied for) is reasonable and realistic.
  - How the regulatory strategy and the development plan to support the planned product label, if applicable, are appropriate and well-described.
  - Whether the risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
  - How well the application identifies intellectual property ownership, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this program announcement.
  - The extent to which the use of the proposed biomarkers(s) will enhance future clinical trials, and the feasibility of their implementation in clinical settings.
- **Clinical Impact**
  - To what extent does the proposed research advance the development of a novel ALS therapeutic.
  - To what extent the research further validates biomarkers in parallel with the main therapeutic effort for use in eventual clinical trials.
  - To what extent the therapeutic and/or biomarkers will be ready for clinical implementation in the intended patient populations (including subpopulations/subtype of ALS) at the conclusion of the proposed project.
  - If applicable, to what extent the anticipated outcomes of the proposed study will make an impact in understanding health differences between sexes.

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**:

- **Personnel**
  - How appropriate the expertise and levels of effort are for successful conduct of the proposed work.
  - How appropriate the research team members' backgrounds and expertise are for development of the proposed product and conduct of the proposed research.
- **Budget**
  - Whether the budget is appropriate for the proposed research.
- **Environment**
  - To what extent the scientific environment and level of institutional support is appropriate for the proposed research project.
  - How well the research requirements are supported by the availability of and accessibility to facilities and resources.
  - To what extent the quality and level of institutional support are appropriate for the proposed research project.
- **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.
  - Program portfolio composition.
  - Relative impact, including transition potential, and/or military benefit

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. Feedback (e.g., a critique of the pre-application's strengths and weaknesses) is **not** 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 OUSD R&E 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 1.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.

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 IACUC, Institutional Review Board, or Ethics Committee review. Refer to the General Application Instructions, Appendix 6, for additional information.

8.2. Reporting

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

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 five-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

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_01b. 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.

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.
- 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 clinical trial is proposed.
- The invited application proposes a different research project than that described in the pre-application.

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"	☐
Technical Abstract – Attachment 3, upload as "TechAbs.pdf"	☐
Lay Abstract – Attachment 4, upload as "LayAbs.pdf"	☐
Statement of Work – Attachment 5, upload as "SOW.pdf"	☐
Biomarker Statement – Attachment 6, upload as "Biomarker.pdf"	☐
Impact Statement – Attachment 7, upload as "Impact.pdf"	☐
Transition Plan – Attachment 8, upload as "Transition.pdf"	☐
Animal Research Plan – Attachment 9, upload as "AnimalPlan.pdf"	☐
Representations ***(Grants.gov submissions only)*** **– Attachment 10, upload as "RequiredReps.pdf"**	☐
Suggested Intragovernmental/Intramural Budget Form ***(if applicable)*** **– Attachment 11, 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
BEST	Biomarkers, EndpointS, and Other Tools
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
eBRAP	Electronic Biomedical Research Application Portal
ET	Eastern Time
FAD	Funding Authorization Document
FY	Fiscal Year
IACUC	Institutional Animal Care and Use Committee
IND	Investigational New Drug
LC-MS	Liquid Chromatography–Mass Spectrometry
M	Million
MIPR	Military Interdepartmental Purchase Request
OUSD R&E	Office of the Under Secretary of Defense for Research and Engineering
PDF	Portable Document Format
PI	Principal Investigator
SAM	System for Award Management
SciENcv	Science Experts Network Curriculum Vitae
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
TDA	Therapeutic Development Award
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