Program Announcement

for the

Defense Health Program

Defense Medical Research and Development Program

Department of Defense

Congressionally Directed Medical Research Programs

Amyotrophic Lateral Sclerosis Research Program

Therapeutic Development Award

Funding Opportunity Number: W81XWH-14-ALSRP-TDA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), May 13, 2014
- **Invitation to Submit an Application:** June 2014
- **Application Submission Deadline:** 11:59 p.m. ET, August 20, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, August 25, 2014
- **Peer Review:** October 2014
- **Programmatic Review:** December 2014

Change for Fiscal Year 2014: *The CDMRP eReceipt System has been replaced with the Electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.*

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

TABLE OF CONTENTS

I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2014 (FY14) Amyotrophic Lateral Sclerosis Research Program (ALSRP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The ALSRP was initiated in 2007 aimed at the preclinical assessment of therapeutics for amyotrophic lateral sclerosis (ALS). Appropriations for the ALSRP from FY07 through FY13 totaled $39.4 million (M). The FY14 appropriation is $7.5M.

The goal of the ALSRP is to contribute to a cure for ALS by funding innovative preclinical research to develop new treatments for ALS.

B. Award Information

The ALSRP Therapeutic Development Award mechanism was first offered in FY07. Since then, 153 Therapeutic Development Award applications have been received, and 14 have been recommended for funding.

The Therapeutic Development Award supports the preclinical assessment of therapeutics for ALS. The proposed studies are expected to be empirical in nature and product-driven but may have a hypothesis-driven approach, provided the focus is on therapeutics. It is anticipated that the agents and/or data generated from these awards will lead to the advancement of new therapies for ALS.

The Therapeutic Development Award mechanism is designed to support **preclinical** testing and development of therapeutics for ALS. Applications must include **preliminary data** relevant to the phase(s) of the preclinical development process covered by the proposed research. The application should include a clear statistical plan of analysis, if appropriate. Applicants must clearly and explicitly articulate what impact the project may have on therapeutic development for ALS. **Clinical trials will not be supported with this Program Announcement/Funding Opportunity.**

Therapeutic Development Award applications are limited to the areas of programmatic interest listed below. Applications must focus on one or more of these areas to be considered for funding. Applications that do not focus on at least one of the following areas will be administratively withdrawn.

- Development and/or validation of high-throughput screens to define targets with therapeutic potential or to identify lead agent candidates for ALS treatment and be an asset for the ALS research community;
- Development, modification, and/or validation of preclinical model systems in order to assess lead compounds and potential therapeutics by pharmacological and/or pharmacokinetic testing. Such models would also serve as improved tools for the ALS research community;

- Development and optimization of pharmacologic agents through Adsorption, Distribution, Metabolism, Excretion (ADME) studies, and toxicology testing, including Investigational New Drug (IND)-enabling pharmacology/toxicology testing;
- Formulation and stability studies, design and implementation of full-scale, pilot current Good Manufacturing Practice (cGMP) production of therapeutics and/or delivery systems for use in advanced preclinical and initial clinical trials;
- Development of pharmacologic agents up to IND submission to initiate Phase I clinical trials after the award's completion.

In contrast, investigators interested in more basic research focused on ALS therapeutics should consider the FY14 ALSRP Therapeutic Idea Award, which does not require preliminary data (***http://cdmrp.army.mil/funding/alsrp***).

If a therapeutic agent(s) or model(s) that is the subject of a Therapeutic Development Award application was initially developed under an ALSRP Therapeutic Idea Award (TIA), the applicant should describe the role of the TIA in that development.

The preclinical drug development process may require resources beyond those available at a single organization. Therefore, ***Therapeutic Development Awards are open to investigators participating in collaborations focused on identifying and/or testing lead agents for the treatment of ALS***. Collaborations should be dedicated to a single, preclinical development project rather than an additive set of subprojects. If a collaboration is proposed, letters confirming/supporting the collaboration are required. If the collaboration is multiorganizational, participating organizations should ensure the success of the collaboration by resolving potential intellectual and material property issues and by removing organizational barriers that might interfere with achieving high levels of cooperation. A proposed means to resolve these issues must be delineated in an Intellectual and Material Property Plan to be included with the application. Due to the nature of the work involved in the development process, biotechnology and pharmaceutical companies are invited to apply. Whether a biotechnology or pharmaceutical company applies for this mechanism as an individual applicant or as part of a collaboration, the company is expected to leverage its own resources to complement the funding provided by this award.

Use of human subjects and human anatomical substances: Because these awards are designed for preclinical studies, projects involving human subjects or specimens will not be supported unless they are exempt under Title 32, Code of Federal Regulations, Part 219, Section 101(b) (32 CFR 219.101[b]). ***Applications for studies involving human subjects or human anatomical substances that do not qualify for exempt status will be administratively withdrawn and will not be funded.*** For studies using only commercially available or de-identified specimens, a Claim of Exemption Form will be requested if the application is recommended for funding. Additional information regarding exempt status may be found on the U.S. Army Medical Research and Materiel Command (USAMRMC) Human Research Protection Office website (https://mrmc.amedd.army.mil/rodorphrpo.asp) and the Human Subject Resource Document at https://ebrap.org/eBRAP/public/Program Clinical trials are not permitted under this Program Announcement/Funding Opportunity.

New for FY14

All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The standards are described in Landis, S. C., et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nature* 2012, 490: 187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards are written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies. Projects that include research on animal models are required to submit Attachment 8, Animal Research Plan, as part of the application package to describe how these standards will be addressed. Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at http://www.nc3rs.org.uk/page.asp?id=1357.

The types of awards made under this Program Announcement/Funding Opportunity will be assistance agreements. Reference the General Application Instructions, Appendix 4, for additional information regarding award types.

The Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section L.

C. Eligibility Information

- Independent investigators at all academic levels (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **3** years.
- The maximum allowable direct costs for the entire period of performance are **$1,500,000** plus indirect costs.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total 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 **3** years.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

For this award mechanism, direct costs:

Must be requested for:

- Travel costs for the PI to disseminate project results at one DoD military research-related meeting to be determined by the CDMRP during the award performance period. Cost associated with travel to this meeting should be included in year 2 of the budget. These costs are independent of travel costs between collaborating organizations.

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment (Note: Cost sharing is encouraged for large equipment purchases)
- Consultation with scientific and/or technical experts (e.g., statisticians, editors)
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings in addition to the required meeting described above

The CDMRP expects to allot approximately $4.8M of the $7.5M FY14 appropriation to fund approximately 2 Therapeutic Development Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

New for FY14: ***The CDMRP has replaced its eReceipt System with eBRAP.*** Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at *https://ebrap.org/eBRAP/public/UserGuide.pdf)*. Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. ***Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*** If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov, provided there is no cause for administrative rejection of the application (see Section IV.A., Rejection).

Submission of applications that are essentially identical or 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.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-14-ALSRP-TDA.

B. Pre-Application Submission and Content Form

All pre-application components must be submitted by the PI through eBRAP (https://eBRAP.org/). Because the invitation to submit an 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.

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**

  It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  FY14 ALSRP Integration Panel (IP) members should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

- **Required Files – Tab 4**

  Notes: Upload document(s) as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

  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, etc.) 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:

  - **Research Strategy and Objectives:** State the rationale on which the proposed work is based. Concisely state the project's objectives, specific aims, and how it addresses an area of programmatic interest. Describe the outcome(s) of the proposed project.
  - **Impact:** Describe how the project will make an important contribution to ALS therapeutic development. Describe in general terms how the outcomes of the project, if successful, will be translated to the clinic and made available to ALS patients.
  - **Personnel:** Briefly state the qualifications of the PI, collaborators (if applicable) and key personnel to perform the described research project.

  Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application ***must be uploaded as individual documents*** and are limited to:

  - 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, title of reference, source of reference, 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 (four-page limit per individual).

- **Submit Pre-Application – Tab 5**

  This tab must be completed for the pre-application to be accepted and processed.

Pre-Application Screening

- **Pre-Application Screening Criteria**

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

  - **Research Strategy and Objectives:** How the scientific rationale supports the project objectives and feasibility. How well the pre-application defines a product that will support development of new ALS therapeutics and whether it addresses an area of programmatic interest.
  - **Impact:** How the project will make an important contribution to ALS research and/or therapeutic development. Whether general steps for clinical translation of the projected outcomes of the project were adequately described.
  - **Personnel:** How the qualifications of the PI and key personnel are appropriate to perform the proposed research project.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weakness) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Forms

Applications will not be accepted unless the PI has received notification of invitation.

Each application submission must include the completed application package of forms and attachments provided in Grants.gov for this Program Announcement/Funding Opportunity. The application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

New for FY14: Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification. The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a "Changed/Corrected Application" with the Previous Grants.gov Tracking ID ***prior to the***

application submission deadline (which occurs earlier than the end of the application verification period).

Grants.gov application package components: For the Therapeutic Development Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

   - **Attachment 1: Project Narrative (20-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, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and will result in administrative withdrawal of the application.

     Describe the proposed project in detail using the outline below. The project narrative must include preliminary data relevant to the phase(s) of the preclinical development process addressed by the proposed research.

     - **Background:** Present the ideas and reasoning behind the proposed work. Cite relevant literature. Describe previous experience most pertinent to this project.
     - **Objectives and Specific Aims:** Concisely explain the project's objectives and specific aims and their rationale. Show how the specific aims will support the proposed outcome(s) of the study/project. If the research is hypothesis-driven, state the hypothesis(es) to be tested.
     - **Research Strategy:** Describe the study design, methods, and analyses, including statistical analyses, where applicable, in sufficient detail for assessment of the application. Address planned statistical analyses for animal studies in Attachment 8, Animal Research Plan. Address potential problem areas and present alternative methods and approaches.

       As appropriate, address the following:

       - The suitability of the screening assays and preclinical models to be developed, modified, and/or validated for identification and/or assessment of therapeutic agents;
       - How well the applicant clearly demonstrates the intent to use the proposed tools or models for preclinical therapeutic testing or development, not for basic research;
       - How well the outlined chemical synthetic pathways for modification of lead compounds or the formulation of potential delivery systems are feasible and based in rational design.

- **Collaborations:** If a collaborative project is proposed, describe the expected working relationship between collaborators and how the expertise and resources of each collaborator will be brought to bear on the proposed project.

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested may result in the removal of those items or administrative withdrawal of the application.***
  - References Cited: List the references cited (including URLs if available) in the project narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
  - 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 or not 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 Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.
  - Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project.
  - Letters of Collaboration (if applicable): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
  - Intellectual Property
    - Background and Proprietary Information (if applicable): All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. Provide a list of all background intellectual property to be used in the project. Identify any proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.

- Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

  - Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section L for more information about the CDMRP 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. Of particular importance, programmatic reviewers typically do not have access to the full application and therefore rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

  Use the outline below:

  - Background: Present the ideas and reasoning behind the proposed work.
  - Objective/Hypothesis: State the objectives/hypothesis(es) to be tested. Provide evidence or rationale that supports the objectives/hypothesis(es).
  - Product: Describe the product or resource to be developed.
  - Specific Aims: State the specific aims of the study.
  - Study Design: Briefly describe the study design including appropriate controls.
  - Impact: Summarize briefly how the proposed project will impact the development of therapeutics for ALS.

- **Attachment 4: Lay Abstract (one-page limit):** Upload as "LayAbs.pdf."

  Do not duplicate the technical abstract. The lay abstract is used by all reviewers. Describe the scientific objective and rationale for the proposed project in a manner that will be readily understood by readers without scientific or medical backgrounds.

  Describe the ultimate applicability of the research.

  - What type of ALS patients will it help and how will it help them?
  - What are the potential clinical applications, benefits, and risks?
  - What is the projected time it may take to achieve a patient-related outcome?
  - What are the likely contributions of this study in advancing the development of therapeutics for ALS?

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Program Announcement and Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Therapeutic Development Award mechanism, use the SOW format example titled "SOW for Advanced Tech Development Research." The SOW must be in PDF format prior to attaching.

- **Attachment 6: Impact Statement (one-page limit):** Upload as "Impact.pdf." Explain how the expected results of the study will make an important contribution to ALS therapeutic development. For projects involving product-driven research, describe the potential impact of the product on patients' lives. For projects involving hypothesis-driven research, describe the potential impact of the concepts or methods to drive therapeutic development.
- **Attachment 7: Transition Plan (one-page limit):** Upload as "Transition.pdf." Describe potential methods and strategies to move the product to the next phase of development/clinical trials after successful completion of the award. The transition plan should include the following components:
    - Outline a funding strategy that could be used to bring the therapy to the next phase of development/clinical trials.
    - Describe collaborations and other resources that could be used to provide continuity of development.
    - Provide a brief schedule and milestones for bringing the therapy to the next phase of development/clinical trials.
- **Attachment 8: Animal Research Plan (five-page limit):** 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:
    - Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.
    - 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).

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information. ***Note: Some of the items in this attachment may be made available for programmatic review.***

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. ***The Project Narrative and Budget cannot be changed after the application***

submission deadline. Any other application component cannot be changed after the end of the application verification period.

E. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in application rejection.

F. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, U.S. Army Medical Research and Materiel Command (USAMRMC), based on (a) technical merit and (b) the relevance to the mission of the DHP and ALSRP and to the specific intent of the award mechanism. The highestscoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a non-disclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

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

   - **Research Strategy (preliminary data are required)**
     - How well the scientific rationale supports the feasibility and development of the proposed product as demonstrated by a critical review and analysis of the literature, preliminary data, and logical reasoning;
     - How well the hypotheses or objectives and aims are developed;
     - How well the experimental design, methods, and analyses support the study outcomes;
     - Whether the study is product-driven, whether the study has clearly identified endpoints, how appropriate are the selected endpoints for the proposed research;
     - How well the applicant identifies potential problems and addresses alternative approaches;

     For studies involving animal research:

     - How well the animal study (or studies) is designed to achieve the objectives, including the relevance of model and endpoints/outcome measures to be used.
     - How well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.

     And, as appropriate:

     - The suitability of the screening assays and preclinical models to be developed, modified, and/or validated for identification and/or assessment of therapeutic agents;
     - How well the applicant clearly demonstrates the intent to use the proposed tools or models for preclinical therapeutic testing or development, not for basic research;
     - How well the outlined chemical synthetic pathways for modification of lead compounds or the formulation of potential delivery systems are feasible and based in rational design.
   - **Impact and Translational Potential**
     - How the study will make an impact on the development of therapeutics for ALS;
     - For projects involving product-driven research, the potential impact on patients' lives, and the quality and feasibility of the Transition Plan;
     - For projects involving hypothesis-driven research, the potential impact of the concepts or methods to drive therapeutic development.

- **Adherence to the Award Intent**
    - How well the project addresses one or more of the areas of programmatic interests stated in the Program Announcement/Funding Opportunity.
- **Personnel**
    - How the research team's background and expertise are appropriate to develop the proposed product or, for hypothesis-driven projects, to conduct the proposed research;
    - How the levels of effort are appropriate for the successful development of the proposed product;
    - If multiple investigators are participating in the project, whether the letters of collaboration adequately describe all aspects of the collaborative effort.

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

- **Environment**
    - The appropriateness of the scientific environment for the proposed research;
    - How the research requirements are supported adequately by the availability of and accessibility to facilities and resources (including collaborative arrangements);
    - The quality and extent of organizational support, including the ability to support the therapy for the next level of clinical trials/development;
    - If multi-organizational, the quality and completeness of the Intellectual and Material Property Plan.
- **Budget**
    - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
    - To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations, the following equally considered criteria are used by programmatic reviewers:

    a. **Ratings and evaluations of the peer reviewers**

    b. **Relevance to the mission of the DHP and FY14 ALSRP, as evidenced by the following:**
        - Program portfolio composition
        - Adherence to the intent of the award mechanism
        - Programmatic relevance and relative impact

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

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

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and Project Narrative.
- Documents not requested will be removed.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These

modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- A FY14 ALSRP Integration Panel (IP) member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. A list of the FY14 ALSRP IP members can be found at http://cdmrp.army.mil/alsrp/panels/panels14.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The PI does not meet the eligibility criteria.
- The application is or includes a clinical trial or expedited clinical research.
- The application does not address any of the topic areas of programmatic interest described under Section I.B., Award Information.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution 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.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 5 for general information regarding national policy requirements.

D. Reporting

Refer to the General Application Instructions, Appendix 4, Section J, for general information on reporting requirements.

E. Award Transfers

Changes in PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

Refer to the General Application Instructions, Appendix 4, Section M, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the application package. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Impact/Transition Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	Innovation Statement: Upload as Attachment 7 with file name "Innovation.pdf."	
	Animal Research Plan: Upload as Attachment 8 with file name "AnimalPlan.pdf."	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
	Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.	