Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Amyotrophic Lateral Sclerosis Research Program

Therapeutic Development Award

Funding Opportunity Number: W81XWH-09-ALSRP-TDA

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Objectives

The Amyotrophic Lateral Sclerosis Research Program (ALSRP) was established in fiscal year 2007 (FY07) with a $5 million (M) appropriation to fund peer-reviewed research for effective treatments and a cure for this disease. The program was not funded in FY08 but returned in FY09 with another $5M appropriation.

B. Award Description

As the vision of the FY09 ALSRP is to improve treatments for ALS, the Therapeutic Development Award is being offered to support preclinical development of therapeutics for amyotrophic lateral sclerosis (ALS). Investigators are encouraged to undertake preclinical studies of novel and existing agents. The Therapeutic Development Award is restricted to research in 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 therapeutics for ALS. Studies focused on basic science research that will not directly inform therapeutic development do not meet the intent of the award mechanism. Additionally, ***clinical trials will not be allowed***.

Therapeutic Development Award proposals are limited to the areas of programmatic interest listed below. Proposals must focus on one or more of these areas to be considered for funding. Proposals that do not focus on at least one of the following areas will be administratively withdrawn.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 identify lead agents for ALS treatment and be an asset for the ALS research community;
- Validation or refinement of preclinical model systems to assess potential therapeutics may serve as an adjunct objective for studies proposed under this award mechanism, as they may also provide an improved tool for the ALS research community;
- Development of pharmacologic agents through the Adsorption, Distribution, Metabolism, Excretion and Toxicity (ADMET) phase;
- Design and implement production of therapeutics and/or delivery systems using current Good Manufacturing Practices (cGMP) for use in advanced preclinical and future clinical trials;
- Development of pharmacologic agents to the Investigational New Drug (IND) stage in order to initiate Phase 1 clinical trials ***after*** the award's completion.

Proposals must include ***preliminary data*** relevant to the phase(s) of the preclinical development process covered by the proposed research. The proposal should include a clear statistical plan of analysis, if appropriate.

The preclinical drug development process may require resources beyond those available at a single institution. 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 or study rather than an additive set of subprojects (i.e., the combined efforts of the collaboration must provide greater benefit than the sum of individual research initiatives). ***If a collaboration is proposed, letters confirming/supporting the collaboration are required***. If the collaboration is multi-institutional, participating institutions will ensure the success of the collaboration by resolving potential intellectual and material property issues and by removing institutional 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. Also, due to the nature of the work involved in the development process, biotechnology or pharmaceutical companies are welcome to apply. Whether a biotechnology or pharmaceutical company applies for this mechanism as an individual submitter or as part of a collaboration, the company is expected to leverage its own resources to complement the funding provided for the study by this award.

It is the responsibility of the Principal Investigator (PI) to clearly and explicitly articulate what impact the project may have on therapeutic development for ALS.

Use of human subjects and human biological substances: Because these awards are designed for preliminary 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]). ***Studies that do not qualify for exempt status during review at any level 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. Additional information regarding exempt status may be found on the US Army Medical Research and Materiel Command (USAMRMC) Human Research Protection Office website (https://mrmc.amedd.army.mil/rodorphrpo.asp) and the Application Instructions and General Information, Appendix 6, for this award mechanism.

C. Eligibility

Independent investigators at all academic levels (or equivalent) are eligible to submit proposals. Refer to the Application Instructions and General Information, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **3** years.
- The maximum allowable funding for the entire period of performance is **$1,500,000** in direct costs.
- The applicant may request the entire maximum direct cost amount for a project that may be less than the maximum 3-year period of performance. More cost-effective studies that do not request the full available funding amount are encouraged.

- Regardless of the period of performance proposed, the applicant may not exceed the maximum direct cost. In addition to the direct costs, indirect costs may be proposed in accordance with your institution's negotiated rate agreement.

Within the guidelines provided in the Application Instructions and General Information, funds can cover:

- Salary
- Research supplies
- Equipment
- Clinical costs (Clinical trials are not allowed)
- Travel between collaborating institutions
- Travel to scientific/technical meetings
- Travel to one CDMRP-hosted meeting between investigators

The Office of the Congressionally Directed Medical Research Programs (CDMRP) expects to allot all of the $5M FY09 ALSRP appropriation to fund two or three TDA applications, depending on the quality and number of proposals received as well as the individual proposed budgets. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent on the availability of federal funds for this program.

E. Award Administration

Refer to the Application Instructions and General Information, Appendix 5, for general award administration information.

II. TIMELINE FOR SUBMISSION AND REVIEW

Proposal submission is a two-step process consisting of (1) pre-application submission and (2) proposal submission. ***Pre-application submission is a required first step***.

- **Pre-Application Submission Deadline: July 15, 2009, 5:00 p.m. Eastern Time**
- **Invitation to Submit Proposal: August 28, 2009**
- **Proposal Submission Deadline: October 15, 2009, 11:59 p.m. Eastern Time**
- **Peer Review: December 2009**
- **Programmatic Review: February 2010**

Awards will be made approximately 4 to 6 months after receiving a funding notification letter, but no later than September 30, 2010.

III. SUBMISSION PROCESS STEP

Proposal submission is a two-step process consisting of (1) a pre-application submission through the CDMRP eReceipt system (https://cdmrp.org/) and (2) an application submission through Grants.gov (http://www.grants.gov/).

PIs and organizations identified in the application submitted through Grants.gov should be the same as those identified in the pre-application. If there is a change in PI or organization after submission of the pre-application, the PI must contact the eReceipt help desk at ***help@cdmrp.org*** or 301-682-5507.

The Government reserves the right to reject duplicative applications submitted to different award mechanisms within the same program or to other CDMRP programs.

A. Step 1 – Pre-Application Components and Submission

Pre-application submission is the required first step. The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the CDMRP eReceipt system by ***5:00 p.m. Eastern time on the deadline date***. Refer to the Application Instructions and General Information for detailed information.

- Proposal Information
- Proposal Contacts
- Collaborators and Conflicts of Interest (COI)
- **Preproposal Narrative**: The Preproposal Narrative has a ***three-page limit*** inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the preproposal. The preproposal narrative should address the following:
    - **Research Idea:** State the ideas and reasoning on which the proposed work is based.
    - **Research Strategy:** Concisely state the project's objectives and specific aims.
    - **Impact:** State how the proposed work will directly inform therapeutic development for ALS.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application are:

- **References:** One-page limit.
- **Biographical Sketches:** Include biographical sketches for the PI and other key collaborators.

Pre-Application Screening: Pre-applications will be screened by the ALSRP Integration Panel (IP), composed of scientists, clinicians, and consumer advocates. The pre-application screening criteria are as follows:

- **Research Idea:** How the described research focuses specifically on treatments for ALS. How the rationale will support preclinical development of therapeutics for ALS.
- **Research Strategy:** How the specific aims support the research idea.
- **Impact:** How the study addresses an important problem related to ALS. If successful, how the study will lead to improved treatments for ALS.

B. Step 2 – Application Components and Submission

Application submissions will not be accepted unless the PI has been invited. Do not submit an application unless a letter of invitation has been received. Applications must be submitted electronically by the Authorized Organizational Representative (AOR) through Grants.gov (***www.grants.gov***).

Each application submission must include the completed application package of forms and attachments identified in www.grants.gov for the US Army Medical Research Acquisition Activity (USAMRAA) Program Announcement/Funding Opportunity. In addition to the specific instructions below, please refer to the Application Instructions and General Information for detailed requirements of each component.

The package includes:

1. **SF-424 (R&R) Application for Federal Assistance Form**

2. **Attachments Form**

   - **Attachment 1: Project Narrative (20-page limit)**

     Describe the proposed project in detail using the outline below. The project narrative must include preliminary data that is relevant to ALS and the proposed project.

     - **Background:** Present the ideas and reasoning behind the proposed work. Cite relevant literature. Describe previous experience most pertinent to this project.
     - **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
     - **Specific Aims:** Concisely explain the project's specific aims to be funded by this application. If the proposed work is part of a larger study, present only tasks that the Department of Defense award would fund.
     - **Research Strategy:** Describe the study design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. If human subjects or human biological samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples. Describe the statistical plan, if appropriate for the research proposed. ***This award may not be used to conduct clinical trials.***

- **Attachment 2: Supporting Documentation**
  - References Cited
  - Acronyms and Symbol Definitions
  - Facilities & Other Resources
  - Letters of Institutional Support (two-page limit per letter)

    If the PI is a practicing clinician, the institution must clearly demonstrate a commitment to the clinician's research, by indicating that an appropriate amount of the investigator's time will be devoted to the proposed research.
  - Description of Existing Equipment (no page limit)
  - Publications and/or Patent Abstracts (five document limit)
  - Intellectual and Material Property Plan (if applicable)
  - Letters of Collaboration (if applicable, two-page limit per letter)
- **Attachment 3: Technical Abstract (one-page limit)**
- **Attachment 4: Public Abstract (one-page limit)**
- **Attachment 5: Statement of Work (SOW, three-page limit)**
- **Attachment 6: Detailed Budget and Justification**
- **Attachment 7: Impact Statement (one-page limit)**

  Explain how the expected results of the study will make an original and important contribution to the goal of advancing ALS treatments and its impact on patient care. Describe the potential clinical applications, benefits, and risks.
- **Attachment 8: Claim of Exemption Form (if applicable)**
- **Attachment 9: Federal Agency Financial Plan (if applicable)**
- **Attachments 10-15: Subaward Detailed Budget and Justification (if applicable)**

3. Research & Related Senior/Key Person Profile (Expanded Form)

- PI Biographical Sketch (four-page limit)
- PI Current/Pending Support
- Key Personnel Biographical Sketches (four-page limit each)
- Key Personnel Current/Pending Support

4. Research & Related Project/Performance Site Location(s) Form

IV. INFORMATION FOR APPLICATION REVIEW

A. Proposal Review and Selection Overview

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review of proposals against established criteria for determining scientific merit. The second tier is a programmatic review that compares submissions to each other and recommends proposals for funding based on scientific merit, overall goals of the program, and the specific intent of the award mechanism. Additional information about the two-tier review process used by the CDMRP may be found at http://cdmrp.army.mil/fundingprocess

The peer review and programmatic review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each tier of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Institutional personnel and PIs are prohibited from contacting persons involved in the application 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 institution's application. Violations by panelists or PIs that compromise the confidentiality of the peer review and programmatic review processes may also result in suspension or debarment of their employing institutions from Federal awards. Furthermore, it is a crime for Federal officials to disclose confidential information of one party to another third party (Title 18 United States Code 1905).

The Government reserves the right to review all applications based on one or more of the required attachments or supporting documentation (e.g., Impact Statement).

B. Review Criteria

1. Peer Review: All proposals will be evaluated according to the following criteria. Research Strategy and Translational Potential are of equal importance.

- **Research Strategy (preliminary data are required)**
  - How 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 hypothesis or objectives, aims, experimental design, methods, and analyses are developed (if the proposal is hypothesis-driven). Alternatively, whether the study has clearly identified endpoints (if the proposal is productdriven).
  - How well the applicant acknowledges potential problems and addresses alternative approaches.
  - (As appropriate) How the outlined chemical synthetic pathways for modification of lead compounds or the formulation of potential delivery

systems are based in rational design.

- **Translational Potential**
  - How the project addresses one or more of the programmatic interests stated in the program announcement.
  - How the study will make an impact on the development of therapeutics for ALS.
  - For projects involving hypothesis-driven research, the potential impact on the concepts or methods that drive the development of therapeutics for ALS.
  - For projects involving product-driven research, the potential impact on patient lives.

The following criteria will not be scored but may impact the overall evaluation of the application and are listed in order of decreasing importance.

- **Personnel**
  - How the research team's background and expertise are appropriate to develop the proposed product or, for hypothesis-driven proposals, to conduct the proposed research.
  - Appropriateness of the levels of effort for 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.
- **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 institutional support.
  - If multi-institutional, 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 the award mechanism.
- **Application Presentation**
  - How the writing and components of the application influenced the review.

2. Programmatic Review: The following criteria are used by programmatic reviewers to make funding recommendations that maintain the program's broad portfolio:

- Ratings and evaluations of the peer reviewers,
- Program portfolio balance,
- Programmatic relevance,
- Relative impact, and
- Adherence to the intent of the award mechanism.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by Integration Panel (IP) members and recommended for funding to the Commanding General, US Army Medical Research and Materiel Command. The highest scoring applications from the first tier of review are not automatically recommended for funding. All applications are carefully considered to ensure that the funds available are allocated to those proposals that best fulfill the goals, objectives, and areas of encouragement of the program.

V. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eReceipt 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.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

The following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).

B. Modifications

- Pages exceeding the specified limits will be removed for all documents other than the Preproposal Narrative or Project Narrative.
- Documents not requested will be removed.

- ***NEW for FY09:*** Following the application deadline, the applicant may be contacted by email from CDMRP with a request to provide certain missing supporting documents (excluding those listed directly above in Section A, Rejection). The missing documents must be provided by 5:00 p.m. Eastern time on the second full business day following the date the email was sent. Otherwise, the application will be peer reviewed without the missing documents.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- FY09 IP member(s) is found to be involved in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY09 IP members may be found at ***http://cdmrp.army.mil/alsrp/panel09***
- Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs.
- The application does not conform to this funding opportunity description to an extent that precludes appropriate scientific peer and programmatic review.
- Direct costs as shown on the detailed budget form exceed the maximum allowed by the award mechanism.
- Inclusion of URLs, with the exception of links to published references.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be requested to provide the findings of the investigation to the USAMRAA Contracting/Grants Officer for a determination of the final disposition of the application.

VI. CONTACT INFORMATION

A. Program Announcement/Funding Opportunity, application format, or required documentation: To view all funding opportunities offered by the CDMRP, perform a Grants.gov basic search using the CFDA Number 12.420. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079
Fax: 301-619-7792
Email: ***cdmrp.pa@amedd.army.mil***

B. eReceipt system: Questions related to pre-application components through the CDMRP eReceipt system should be directed to the eReceipt help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time.

Phone: 301-682-5507
Website: ***https://cdmrp.org***
Email: ***help@cdmrp.org***

C. Grants.gov contacts: Questions related to application submission through the Grants.gov (http://www.grants.gov/) portal should be directed to the Grants.gov help desk, which is available Monday through Friday, 7:00 a.m. to 9:00 p.m. Eastern time. Deadlines for application submission are 11:59 p.m. Eastern time on the deadline date. Please note that the CDMRP help desk is unable to answer questions about Grants.gov submissions.

Phone: 800-518-4726
Email: ***support@grants.gov***

Grants.gov will notify PIs of changes made to this Program Announcement/Funding Opportunity and/or application package ONLY if the PI subscribes to the mailing list by clicking on the "send me change notification emails" link on the Opportunity Synopsis page for this announcement. If the PI does not subscribe and the application package is updated or changed, the original version of the application package may not be accepted.