CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

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AMYOTROPHIC LATERAL SCLEROSIS RESEARCH PROGRAM

VISION

Improve treatments and find cures for people with ALS

MISSION

Fund impactful research to develop ALS treatments

PROGRAM GOALS GUIDING THE ALSRP

- Preclinical treatment discovery research
- Preclinical treatment validation
- Better define ALS subtypes, therapeutic responses and prognosis
- Early-phase clinical trials to de-risk interventions and improve clinical care

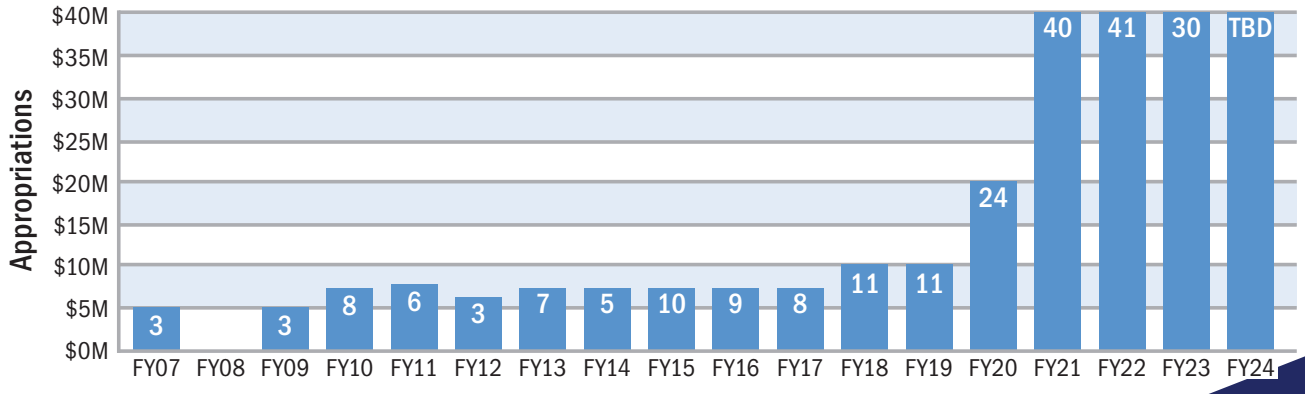
PROGRAM HISTORY

In FY07, Congress appropriated ALS-specific research funding, and the DOD redirected a $5M appropriation from Army Research, Development, Test, and Evaluation funding to initiate the ALSRP as a broadly competed, peer-reviewed research program managed by the CDMRP. Recommendations from stakeholders resulted in a focus on leveraging new ALSRP funds with other mechanisms of federal and non-federal funding to promote development of ALS therapeutics. The benefits of the research from this program extend to Warfighters and their Family members, as well as retirees and other beneficiaries of the Military Health System. Since the initial appropriation in 2007, the goal of the ALSRP has been to expedite the pathway from bench science to clinical trials for new therapeutic approaches and to fund scientifically meritorious research in accordance with directives received from Congress.

PROGRAM RELEVANCE TO MILITARY HEALTH

After identifying that ALS was occurring in Gulf War Veterans at an unexpected rate, the VA established a registry to identify cases of ALS in military Veterans and requested that the National Academies conduct an independent assessment of the relationship between military Service and the development of ALS. **The results noted that Veterans from all eras, not just the Gulf War, had an increased incidence of ALS.** In 2008, the VA established a presumption of Service connection, and in 2010 the Centers for Disease Control and Prevention, CDC, launched the National ALS Registry. Two subsequent reports on data findings from the National ALS Registry reaffirmed that military Service is a risk factor; however, the etiology of ALS and its linkage to military Service remains largely unknown.

ALSRP CONGRESSIONAL APPROPRIATION (FY07-FY24*) with number of awards made



*FY08–no appropriation

02/2024

PROGRAM PORTFOLIO:

The ALSRP funds a therapeutic pipeline, from early ideas to pilot clinical trials, focusing on mechanism-specific biomarkers to guide treatment selection and efficacy.

Early Ideas and Therapeutic Development

- **SRT-055:** The ALSRP is funding investigations of a potent and selective inhibitor of a cell death regulator, ASK1, called SRT-055. The investigator anticipates that SRT-055 will revert hyperexcitability and prevent cell death in ALS patient-derived motor neurons and improve survival time in animal models of ALS.
- **RASRx1902:** The ALSRP is funding investigations into the biomarker development for the evaluation of mas agonist RASRx1902 in ALS. The investigator has secured follow-on funding and is moving forward with submission of an Investigational New Drug, IND, application.

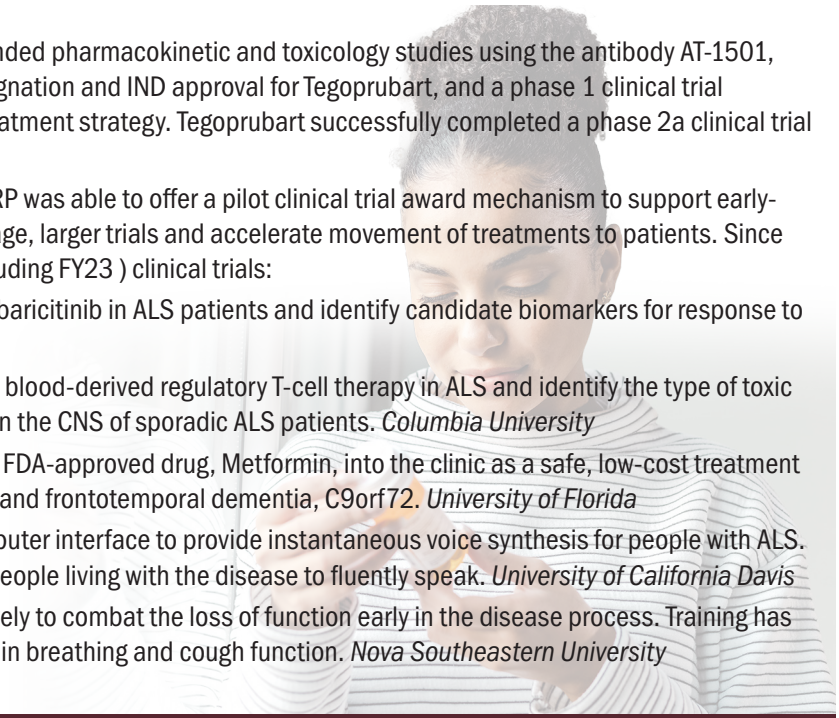
Clinical Trials

ALSRP support in early stages of therapeutic development of several targets has led to clinical trials, including:

- **Prosetin:** The ALSRP funded both early idea investigations and later pharmacology, safety and efficacy profiles of prosetin, the potent kinase inhibitor that the team found to be efficacious across multiple models of ALS. This motor neuron-protective agent is now moving through clinical trials as a potential therapeutic for ALS (NCT05279755).
- **Pimozide:** The ALSRP funded large-scale screens of thousands of FDA-approved drugs to identify pimozide. This is now in a national clinical trial in Canada (funded by ALS Canada and Brain Canada, NCT03272503).
- **Human Neural Progenitor Cells Secreting Glial Cell-Derived Neurotrophic Factor:** The ALSRP funded preclinical studies that contributed to a California Institute of Regenerative Medicine grant moving this approach into clinical trials in patients (NCT02943850).
- **Tegoprubart (Formerly AT-1501):** The ALSRP funded pharmacokinetic and toxicology studies using the antibody AT-1501, Tegoprubart. The FDA granted Orphan Drug Designation and IND approval for Tegoprubart, and a phase 1 clinical trial determined Tegoprubart to be safe as an ALS treatment strategy. Tegoprubart successfully completed a phase 2a clinical trial in May 2022 (NCT04322149).

With the increased appropriation in FY21, the ALSRP was able to offer a pilot clinical trial award mechanism to support early-phase clinical trials to de-risk and improve later stage, larger trials and accelerate movement of treatments to patients. Since then, the ALSRP has funded six (total number, including FY23) clinical trials:

- **Baricitnib:** Will assess safety and tolerability of baricitinib in ALS patients and identify candidate biomarkers for response to baricitinib. *Massachusetts General Hospital*
- **REGALS:** Will test the safety and efficacy of cord blood-derived regulatory T-cell therapy in ALS and identify the type of toxic immune cells circulating in the blood and found in the CNS of sporadic ALS patients. *Columbia University*
- **Metformin:** Aim to rapidly move a well-tolerated FDA-approved drug, Metformin, into the clinic as a safe, low-cost treatment for the most common genetic cause of both ALS and frontotemporal dementia, C9orf72. *University of Florida*
- **Brain Computer Interface:** Testing a brain-computer interface to provide instantaneous voice synthesis for people with ALS. Team will develop a neuroprosthetic device for people living with the disease to fluently speak. *University of California Davis*
- **Respiratory Training:** Aims to intervene proactively to combat the loss of function early in the disease process. Training has the potential to improve the trajectory of decline in breathing and cough function. *Nova Southeastern University*



Clinical Outcomes and Biomarkers

- **Rasch-Built Outcome Measures to Improve Clinical Trials:** Building and refining an ALS outcome measure toolbox containing a widely accessible patient-reported questionnaire to assess overall disability and a novel objective exam-based scale to assess overall motor strength using Rasch methodology. *Emory University*

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