The Congressionally Directed Medical Research Programs

Amyotrophic Lateral Sclerosis Research Program

Presented by

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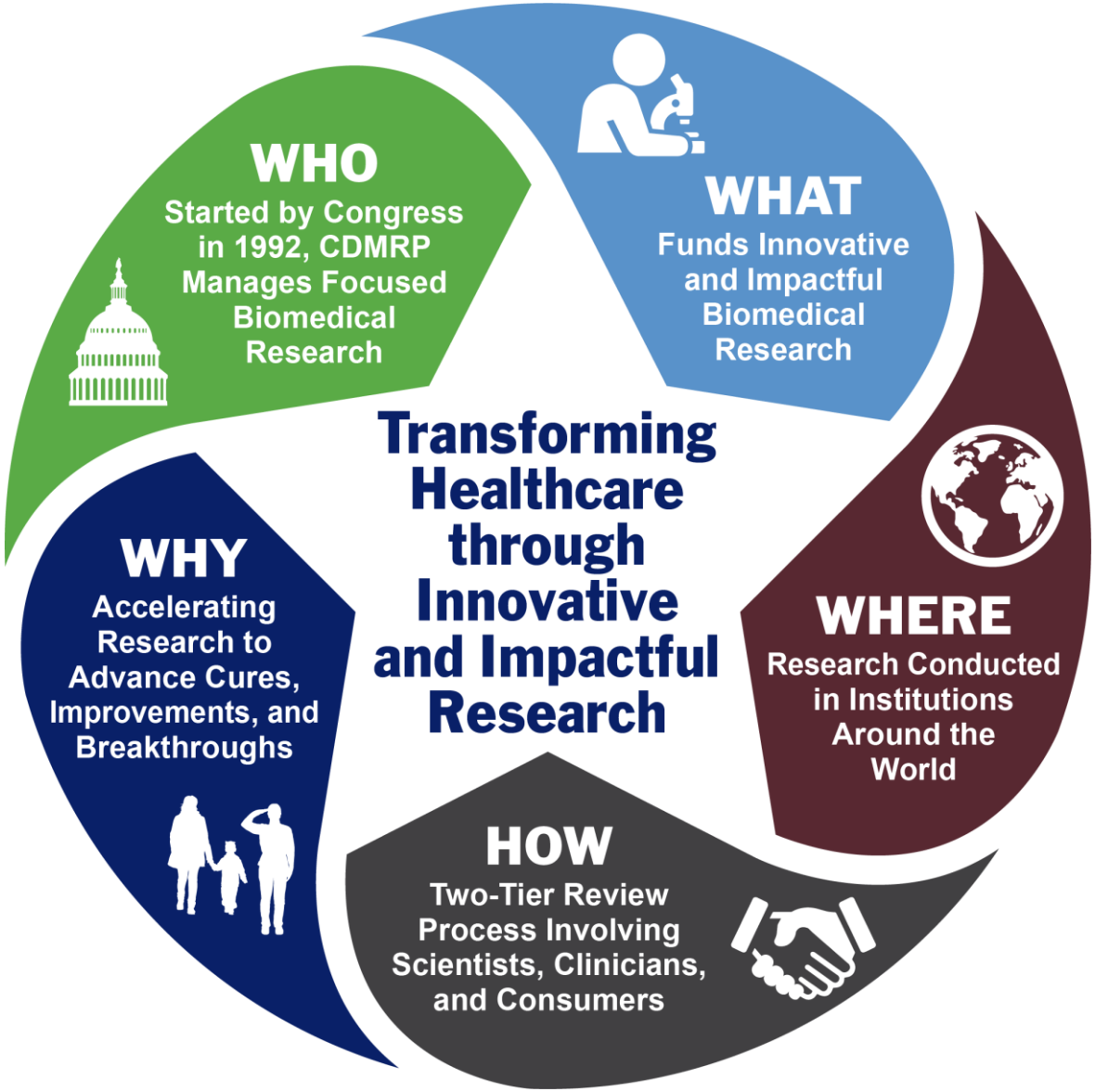
*Transforming Healthcare through Innovative and **Impactful** Research*

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

About CDMRP



Consumers are the “True North” and foundation of the CDMRP

Mission

Responsibly manage collaborative research that discovers, develops, and delivers health care solutions for Service Members, Veterans and the American public

https://cdmrp.health.mil

About ALSRP

Vision: *Improve treatments and find cures for people with ALS*

Mission: *Fund impactful research to develop ALS treatments*

Total Congressional Appropriation (through FY23): **$229.4M**

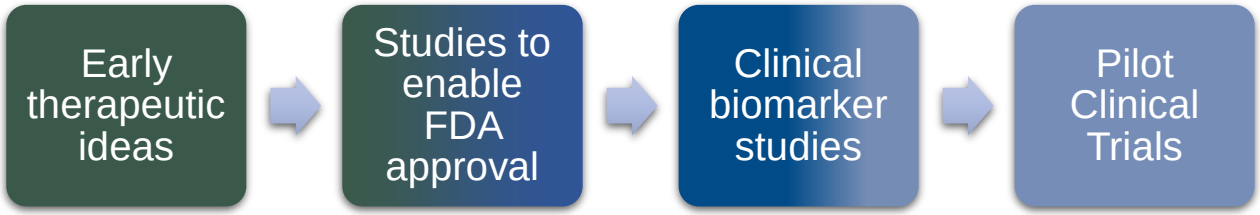
Objective: Collect, manage, and analyze data about persons with ALS

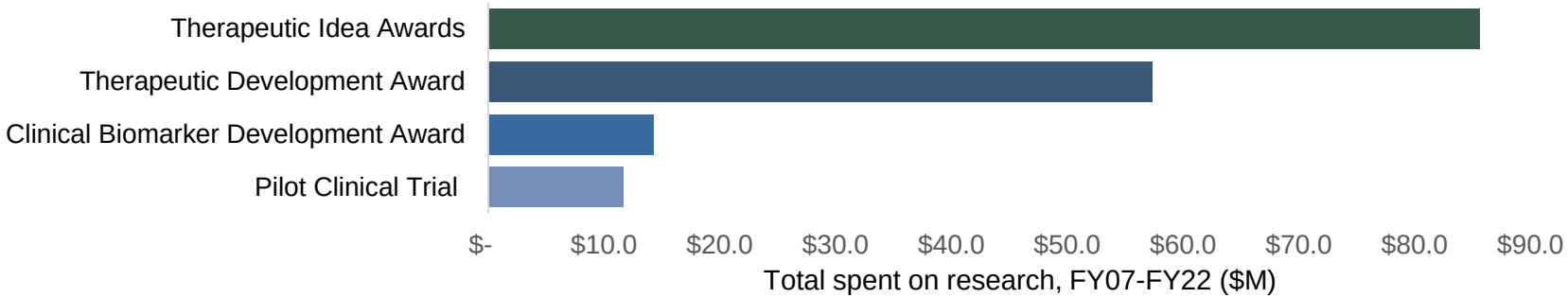
Objective: Seek fundamental knowledge about the brain and nervous system and use that knowledge to reduce the burden of neurological disease for all people

DOD ALSRP
Objective: Promote responsible translational science; expedite the pathway from bench science to clinical trials; de-risk and improve the impact of later stage trials.

Objective: Advance treatments to patients through clinical trials and precision medicine

Largest dedicated funder of early-stage innovative ALS therapeutic development





ALSRP Portfolio Highlights

Prosetin

Columbia University/Project ALS

2015 - initial development of a small molecule kinase inhibitor to prevent ER stress-mediated motor neuron death; preclinical assessments also funded by Project ALS
2020 - IND-enabling studies and manufacturing scale-up
2022 – First patient receives PRO-101 during a Phase 1 clinical study of prosetin (WITH a specific biomarker in hand)

- **8 Investigation New Drug (IND)** designations for ALSRP-funded therapeutics
- **Nerve-on-a-Chip®** system could revolutionize ALS therapeutic development.
- Pilot clinical trial: “Safety Assessment and Biomarker Identification for **Metformin** to inform future trials”
- Pilot clinical trial: “A **Brain-Computer Interface** for Voice Synthesis in People with ALS”






Therapeutic Development Challenges and Opportunities

Therapeutic Development

Therapeutic Specificity – Understanding efficacy by ALS subtype to better inform responsiveness to treatment.

Biomarkers - Therapeutic development should include the analysis of biosamples to improve time to diagnosis, better define subtypes, determine optimal treatments.

Data generation and sharing – Centralized data sharing to ensure both positive and negative outcomes are widely shared.

Clinical Trial Design

Alternative, non-pharmacological options – Experimental drug treatments based on symptom onset are inaccessible to many given the time it takes to obtain a diagnosis. Research is needed on alternate options that provide positive impact to patients' lives.

Patient and Community Collaboration in Clinical Trial design– Involving individuals living with ALS who collaborate and contribute equitably to the study, to ensure facilitation of accessible, efficient, and humane clinical trials.

Biomarker-Driven Trials – Clinical trial outcomes should be tied to quantifiable biomarkers that inform treatment response, to de-risk, improve, and accelerate later-stage, larger clinical trials.

Questions?
For more information, please visit:
cdmrp.health.mil

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More Information:

https://cdmrp.health.mil/alsrp

News & Project Highlights

News & Highlights

- Department of Defense Amyotrophic Lateral Sclerosis Research Program Anticipated Funding Opportunities for Fiscal Year 2021 (FY21)
- FY20 ALSRP Recommended for Funding List
- New study shows common diabetes drug improves symptoms in genetic form of ALS in mice (external link)
- Novel ALS therapeutic intervention shows promise in preclinical trials
- ALSRP Program Summary Sheet
- Research Resources
- More…

Contact us

Feedback

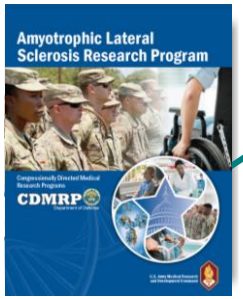
Click here to provide feedback/comments to the ALSRP

Amyotrophic Lateral Sclerosis

***Vision** - Improve treatment and find a cure for ALS*

Amyotrophic Lateral Sclerosis (ALS), also known as "Lou Gehrig's disease," is a degenerative neurological disorder without a cure. For reasons that are not well understood, the nerve cells in the brain and spinal cord that control voluntary muscle movement gradually deteriorate. ALS can be difficult to diagnose because the initial symptoms are both subtle and vague and can be attributed to a number of other conditions. Average life expectancy after diagnosis ranges between 3 to 5 years from the onset of symptoms. It is estimated that 5-10% of all ALS cases are inherited (familial disease) while the remaining 90-95% are sporadic, with unknown etiology and risk factors. There is currently no known cure or therapy to effectively halt the progression of 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.

The ALSRP is guided by a vision to improve treatment and find a cure for ALS. Through its award mechanisms and funding recommendations, the ALSRP specifically supports innovative and impactful research targeting development of new therapeutics for ALS.



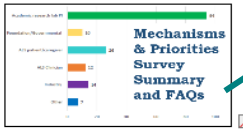
» Click on Image to View Program Booklet

Program Book

Strategic Plan

» Click on Image to View Strategic Plan

Survey Response and FAQs



ALSRP Supported Initiatives

- Research Resources

Awards FY07 – FY22

Congressional Appropriations | Funding Summary | Programmatic Panels | Peer Review Participants

Two-Tier Review Participants

ALS Resources Initiative

Research Resources

A list of resources made broadly available to the ALS Research Community.

- Animal Models
- **Biorepositories**
  - Biofluids and Cell Lines
  - Postmortem Tissues
- ALS Data Sets and Data Analysis/Visualization Platforms
- Antibodies and Other Reagents

Amyotrophic Lateral Sclerosis Research Program

Impactful Research to Develop ALS Treatments

CDMRP
Congressionally Directed Medical Research Programs

Congressional Appropriations

FY07, FY09-FY23: $229.4M total

Vision: Improve treatments and find cures for people with ALS

Congressional Intent: To leverage program funds with other mechanisms of support to promote development of ALS therapeutics.

With a growing portfolio of preclinical therapeutic candidates supported by biomarkers and IND-enabling studies, the program is uniquely positioned to expand support into early-phase clinical trials.

Scope of the Problem

30,000 people in the U.S. **live with ALS**

Average life expectancy is **2-5 years** from diagnosis

ALS is ***always*** **fatal**

No known therapies to effectively stop, significantly slow, or reverse progression

Relevance to the Military

Service Members are more likely than civilians to develop ALS

- Scientific evidence demonstrates that those who serve in the military—regardless of branch, location, or peace time or time of war—are at a greater risk of dying from ALS than if they had never served
- Reasons for increased risk have been linked to chemical exposure, traumatic injury, viral infection, and intense physical activity; however, no definitive link has been established

1 in 6 people living with ALS are **Veterans**

4,540 Veterans received care for ALS in 2020*

~1,055 Veterans with new onset ALS each year

The Department of Veterans Affairs implemented regulations to establish a "Presumption of Service Connection" for ALS

*Veterans Health Administration data

ALS Research Pipeline

DISEASE MODELING/IDENTIFICATION OF TARGETS | **THERAPEUTIC TESTING AND VALIDATION** | **CLINICAL TRANSLATION**

Epidemiology → Biology → Scientific Model Systems → Target *Discovery* → Target *Validation* → Clinical Development → Clinical Trials → Standard of Care, Control, Survivorship

CDC
Objective: Estimate cases, understand who, examine connections, improve care

NIH
Objective: Seek fundamental knowledge about the brain and nervous system and use that knowledge to reduce the burden of neurological disease

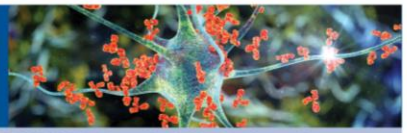
DOD ALSRP
Objective: Expedite the pathway from bench science to clinical trials for new therapeutic approaches aimed at controlling or curing ALS

Industry
Objective: Advance treatments to patients through clinical trials, precision medicine, and assistive technology

ALSRP Research Breakthroughs — Making a Difference

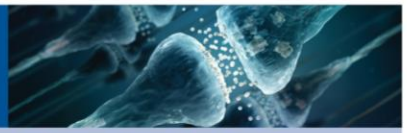
Treatment Approaches Now in Clinical Trials

Antibody Therapy AT-1501



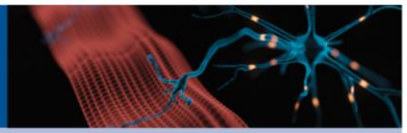
Humanized anti-CD40LG IgG antibody blocks damaging inflammation in motor neurons

GDNF-Expressing Neural Progenitor Cells



Transplanted cells secrete growth factor GDNF, which protects and stimulates neurons

Neuroleptic Pimozide



FDA-approved drug for narcolepsy that strengthens electrical connections between nerves and muscles to slow ALS progression

Treatment Approaches That Have Transitioned to Industry

- **Combination Therapy:** Increased penetration/ bioavailability of FDA-approved Riluzole in combination with the membrane pump inhibitor Elacridar
- **Copper Carrier:** Delivery of copper to damaged cells in the CNS using the copper carrier CuATSM

- **microRNAs:** Genetic manipulation of microRNA Mir-155 to reduce inflammation
- **Screening Platforms:** Motor neuron analysis software that leads to the identification of novel therapeutic targets
- **Inhibitor Proteins:** Small molecule inhibitor Apilimod to eliminate toxic protein aggregates that cause neurodegeneration

- **Iron Regulation:** Infusion of apo-h-ferritin to remove iron and extend life span
- **Drug Repurposing:** Use of Duchenne Muscular Dystrophy drug RASRx1902 to decrease neurological deficits and neuronal death

"I was a Prowler Pilot. I trained in Pensacola and then Meridian. And then up to Whidbey Island. After that I did some anti-terror operations in East Africa and then administrative work when I got sick. I had no genetic disposition, no family history of ALS. The ALSRP is a very promising program because it is focused on therapeutic ideas for the aggressive development of a treatment. I was blown away by the scientists working on this; they're trying to get us where we need to go. The ALSRP has really given me a lot of hope because I've learned that we know a lot more about what's going on than we did even last year. Every year I go, I'm amazed at how much the body of knowledge has grown. It's exponential, so we're going to get there. I guarantee it."

Matt Bellina, ALS Therapy Development Institute