Thank you for joining the weekly webinar!

We are admitting audience members from the waiting room.

Please allow a few moments for the webinar to begin.

HEALEY ALS Platform Trial

Monthly EAP Update – November 9, 2023

Massachusetts General Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL

Healey & AMG Center

Sean M. Healey & AMG Center for ALS
at Massachusetts General Hospital

TACKLE ALS "DON'T BE SORRY LETS BEAT THIS"

ALS ASSOCIATION

MDA Muscular Dystrophy Association

SALSA For a Cure

alsFINDINGaCURE

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

IAM ALS

TAMBOURINE

NCRI NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BARROW Neurological Institute

ALS ONE

RUN2REVIVE MIND · BODY · POTENTIAL

Berry Consultants Statistical Innovation

1850 MELIORA

ucb

biohaven pharmaceuticals

CLene NANOMEDICINE

prilenia

THE ARTHUR M. BLANK FAMILY FOUNDATION

BASEBALL WINTER MEETINGS SAN DIEGO 2019

SEELOS THERAPEUTICS

Calico

DENALI THERAPEUTICS

AMG The AMG Foundation

Multi-PIs – Healey Center for ALS at MGH

- Suma Babu, MBBS, MPH
  - Assistant Professor of Neurology, Harvard Medical School
- James Berry, MD, MPH
  - Winthrop Family Scholar in ALS Sciences
  - Averill Healey Endowed Chair in ALS
  - Director, MGH Neurological Clinical Research Institute (NCRI)
- Sabrina Paganoni, MD, PhD
  - Co-Director, MGH Neurological Clinical Research Institute (NCRI)

MASSACHUSETTS GENERAL HOSPITAL
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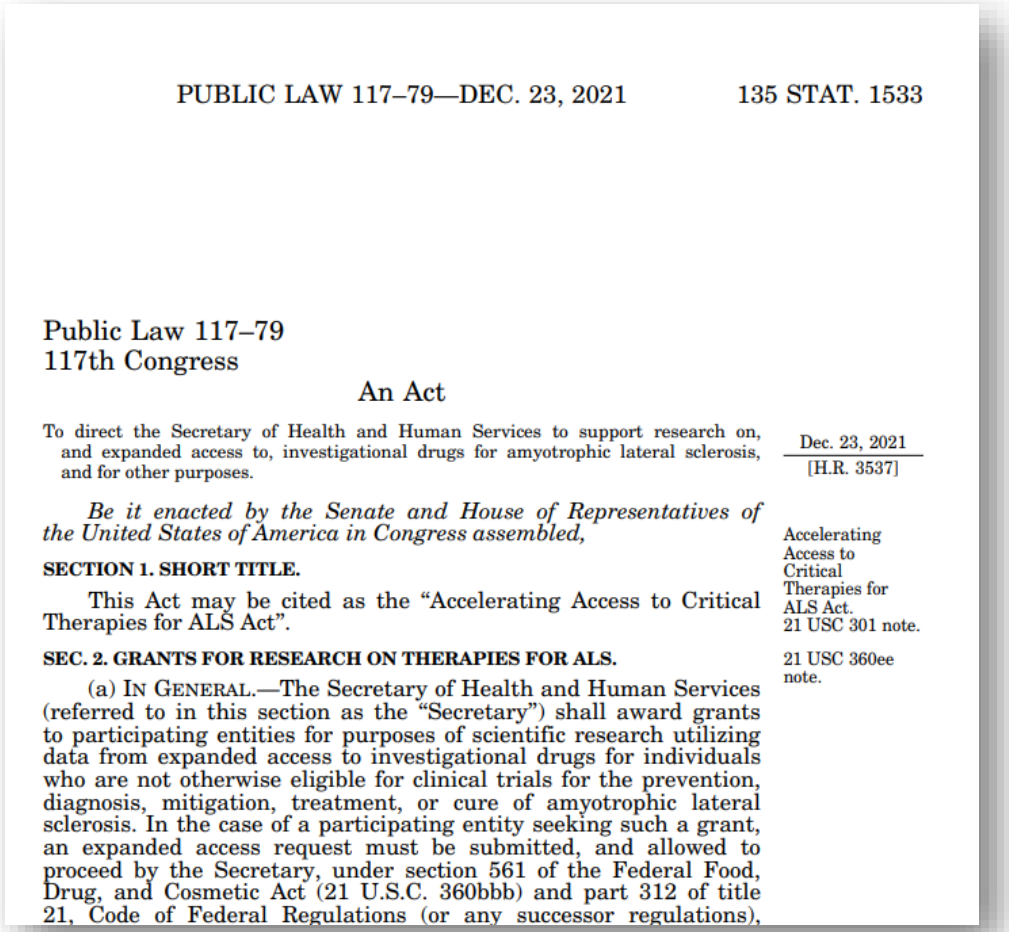
ACT for ALS- A new opportunity to expand access and collect real world data in parallel to clinical trials via EAP

- Signed into law on Dec 23, 2021
- Grants for Research on Therapies via Intermediate-Size EAPs for ALS
- NIH U01 grant mechanism



PUBLIC LAW 117–79—DEC. 23, 2021 135 STAT. 1533

Public Law 117–79
117th Congress

An Act

To direct the Secretary of Health and Human Services to support research on, and expanded access to, investigational drugs for amyotrophic lateral sclerosis, and for other purposes.

Dec. 23, 2021
[H.R. 3537]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

Accelerating Access to Critical Therapies for ALS Act.
21 USC 301 note.

This Act may be cited as the "Accelerating Access to Critical Therapies for ALS Act".

SEC. 2. GRANTS FOR RESEARCH ON THERAPIES FOR ALS.

21 USC 360ee note.

(a) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section as the "Secretary") shall award grants to participating entities for purposes of scientific research utilizing data from expanded access to investigational drugs for individuals who are not otherwise eligible for clinical trials for the prevention, diagnosis, mitigation, treatment, or cure of amyotrophic lateral sclerosis. In the case of a participating entity seeking such a grant, an expanded access request must be submitted, and allowed to proceed by the Secretary, under section 561 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb) and part 312 of title 21, Code of Federal Regulations (or any successor regulations),

Expanded Access Protocol (EAP): What is it & for who is it?

- “a pathway for patients with a serious and life-threatening disease to access an investigational product (IP) treatment outside of clinical trials when there are no comparable or satisfactory therapies available.”

- For patients who do not qualify to participate in a clinical trial. The criteria for participation in an EAP are generally broad and inclusive

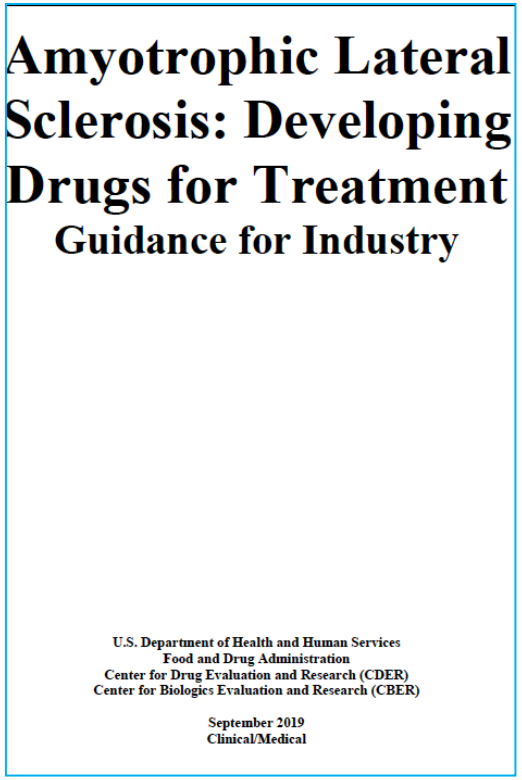
FDA encourages EAPs while developing drugs for ALS

➢ Long term safety data:

"*During development, sponsors should collect safety data, including data from open-label studies or expanded access programs, from patients across the spectrum of disease stages and severities, and whenever possible, data from patients who may not have been included in effectiveness studies but in whom, based on other data, the use of the drug following approval is likely.* " [Page 4]

➢ Generalizability of safety and efficacy data:

"*There is a need to understand the safety and effectiveness of investigational drugs for ALS across disease stages….. An acceptable approach could include enrollment of a broad population with the conduct of the primary analysis in a study subset defined based on clinical characteristics and/or biomarkers, and analyses of the broader population being secondary and supportive* " [Page 3]


Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

September 2019
Clinical/Medical

Trehalose EAP

More info: clinicaltrials.gov NCT05597436

National Institute of Neurological Disorders and Stroke

Healey & AMG Center
Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital

Massachusetts General Hospital
Neurological Clinical Research Institute

Study Design

- Planned enrollment: 70 pALS at up to 25 sites
- Weekly IV infusions of trehalose, 90.5 mg/mL, at a dose of 0.75 g/kg
- Infusions may take place at the study center or at home

Cohort 1 (Trehalose Naïve)

- Patients who do not qualify for any reasonably accessible ongoing clinical trial.

Cohort 2 (RGE Rollover)

- Patients who have completed Regimen E of the HEALEY ALS Platform Trial and are not eligible for enrollment in another treatment regimen of the platform study.

Site Startup Overview

Startup
Q4 2022 > Q1 2023

Enrollment
Q1 2023 > Q1 2024

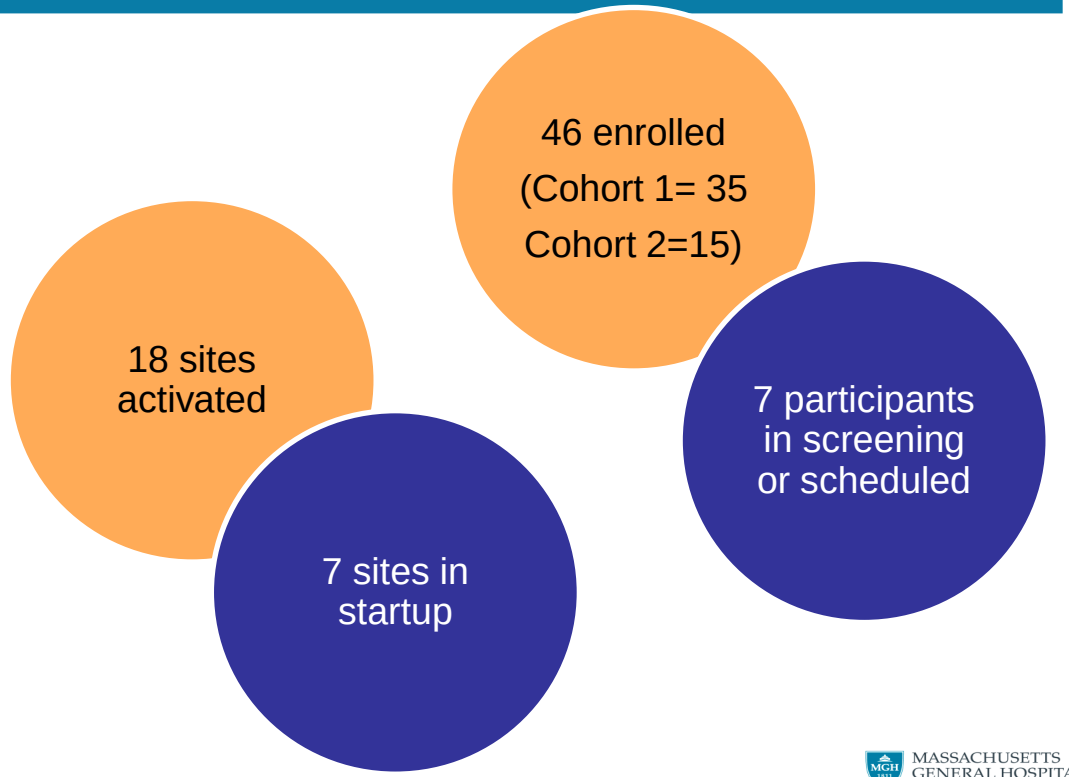
Treatment Follow-up
Q1 2023 > Q3 2024

Closeout and Reporting
Q4 2024 > Q1 2025

Study Startup | *Site activation and enrollment*

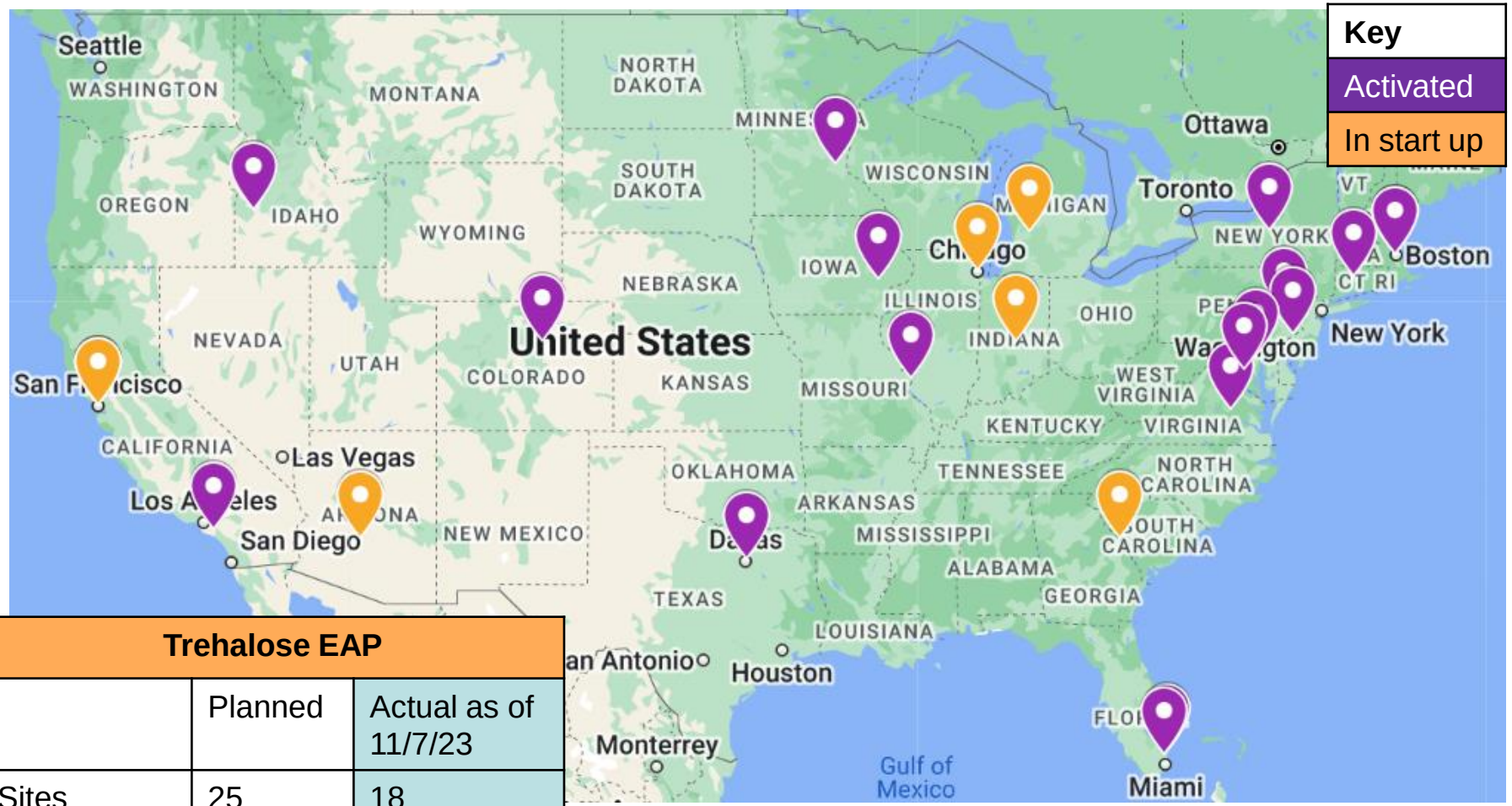
Key elements for site activation:

- Clinical Site Agreement (CSA)
- sIRB approval
- Regulatory Document Collection
- Local Requirements (IRB, infusion center, pharmacy, etc.)



Data cut 11/7/23

Study Sites & Enrollment updates: ~70% enrolled in 7 months since site activation!



Trehalose EAP		
	Planned	Actual as of 11/7/23
Sites	25	18 *Nearing activation: 3*
Participants	70	46 *In screening/ scheduled: 7*

- ✓ Massachusetts General Hospital
- ✓ Texas Neurology
- ✓ Saint Alphonsus
- ✓ Holy Cross Hospital
- ✓ Virginia Commonwealth
- ✓ Nova Southeastern University
- ✓ University of Iowa
- ✓ Washington University School of Medicine
- ✓ University of Colorado, Anschutz
- ✓ Hospital for Special Care
- ✓ George Washington University, MFA
- ✓ SUNY Upstate Medical University
- ✓ University of California, Irvine
- ✓ University of Minnesota
- ✓ University of Maryland School of Medicine Baltimore
- ✓ Thomas Jefferson University
- ✓ Beth Israel Deaconess Medical Center
- ✓ Lehigh Valley Health Network

Two additional NIH funded EAPs to be enrollment ready by Spring 2024

Home - Neurology - ALS - News

PRESS RELEASE · OCT | 5 | 2023

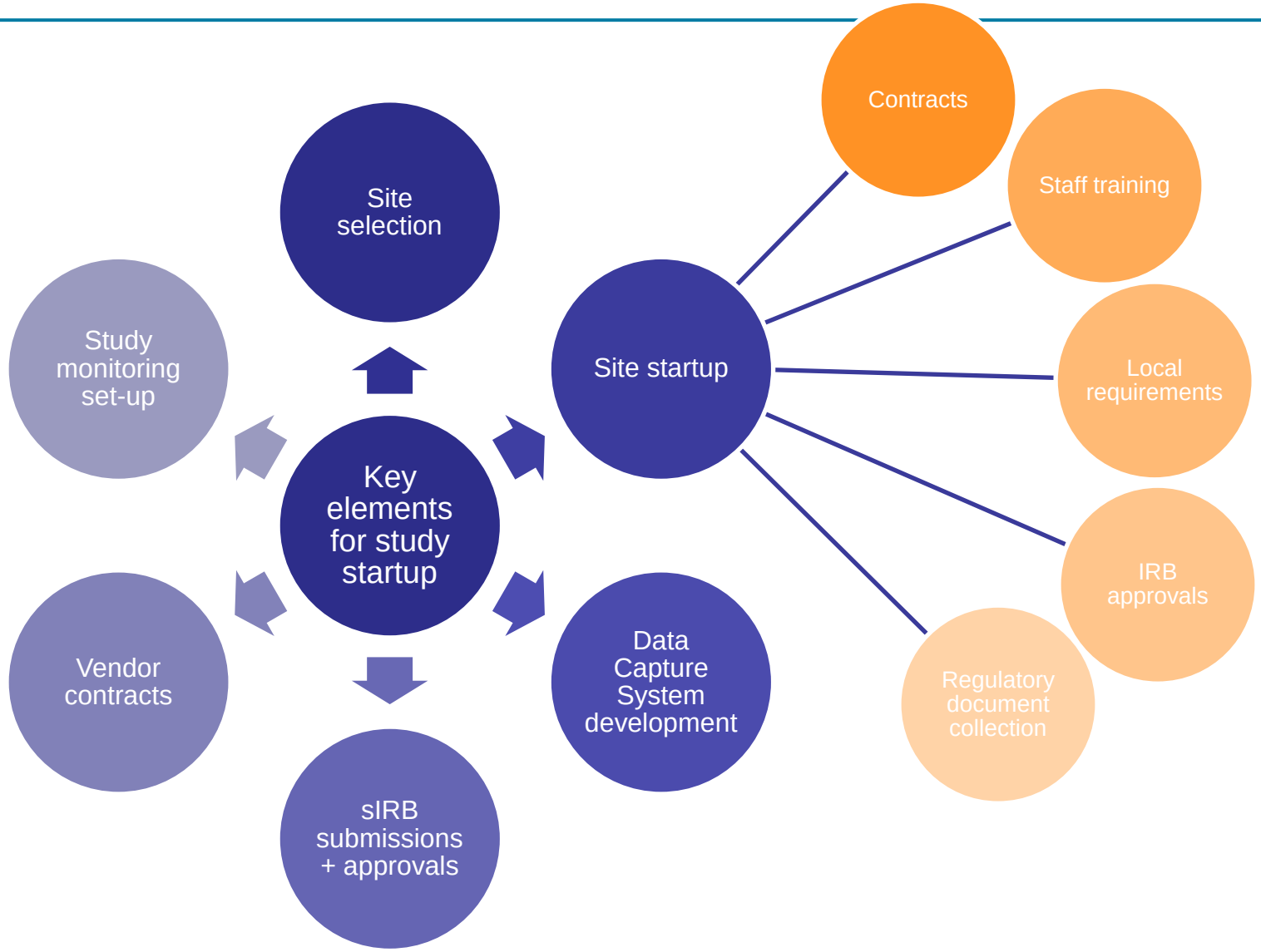
Sean M. Healey & AMG Center for ALS awarded NIH U01 Grant to support Expanded Access to Pridopidine in Collaboration with Prilenia Therapeutics

Home - Neurology - ALS - News

PRESS RELEASE · OCT | 5 | 2023

Sean M. Healey & AMG Center for ALS awarded NIH U01 Grant to support Rapa Therapeutics' Expanded Access Protocol of Epigenetically Reprogrammed RAPA-501

We are currently in the startup phase for these two 2 new EAPs



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Pridopidine EAP2

More info: clinicaltrials.gov NCT06069934

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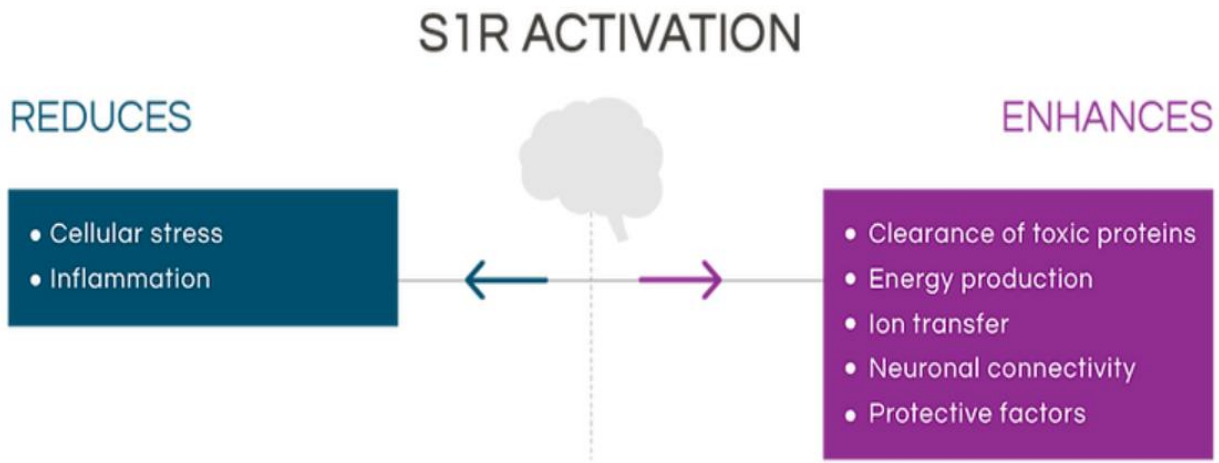
Pridopidine EAP

- 45 sites
- Target enrollment: 200 ALS individuals who:
  - do not qualify for clinical trials at the enrolling site and
  - have established care at a specialized ALS center
- Same dose as platform trial: 45 mg twice daily Oral

Pridopidine is a Sigma-1 receptor (S1R) agonist

prilenia.com/about-pridopidine



- Prior clinical data from Healey ALS Platform Trial:
  - demonstrates a favorable safety and tolerability profile
  - did not meet primary and secondary endpoints in the Platform Trial, but showed benefit in slowing bulbar and speech decline

RAPA-501 EAP

More info will be available on clinicaltrials.gov soon

National Institute of Neurological Disorders and Stroke

Healey & AMG Center
Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital

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Rapa-501 EAP

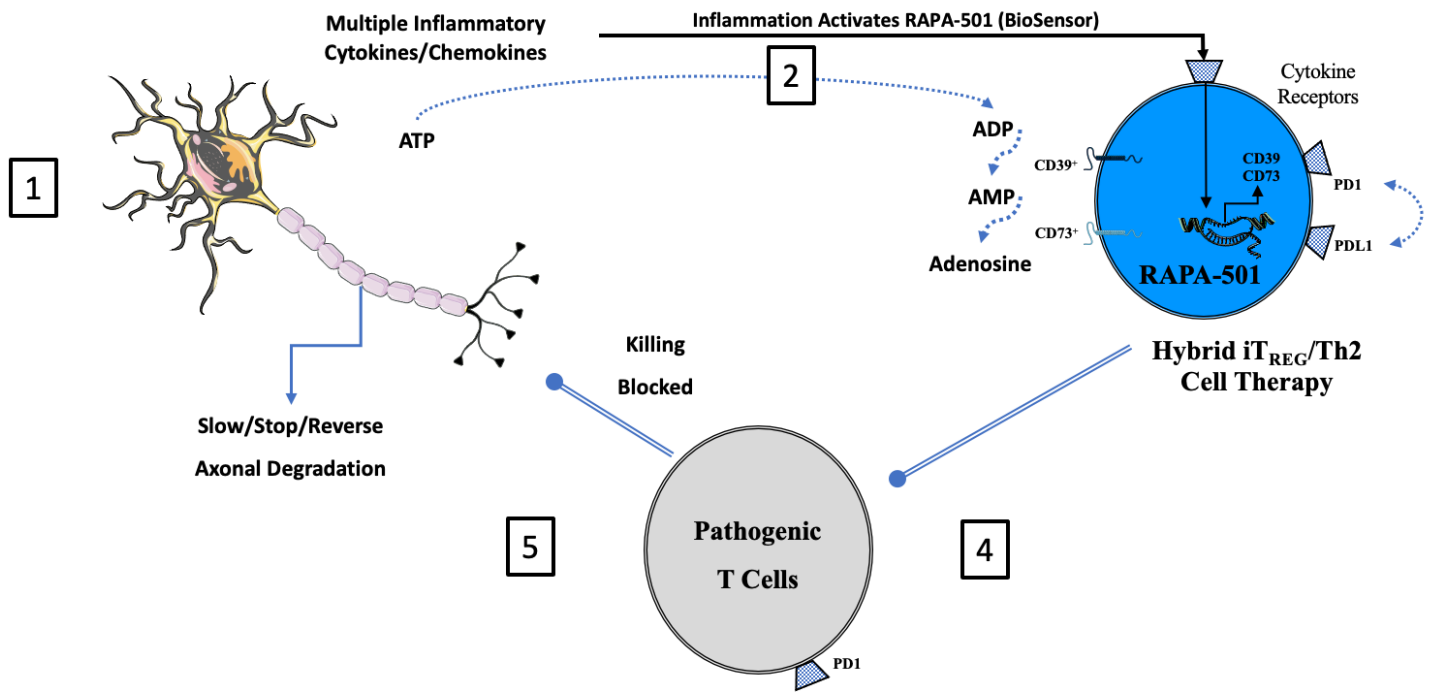
- Up to 10 sites

- Target enrollment: 40 ALS individuals who
  - do not qualify for clinical trials at the enrolling site
  - have established care at a specialized ALS center and
  - have a vital capacity ≤ 50% predicted

- Treatment with RAPA-501 infusions

RAPA-501 Mechanism of Action

Induced (i)T_{REG} Cell With Hybrid Th2 Anti-Inflammatory Function



- In ALS pathogenic T cells facilitate axonal degradation and injury.
- Activated RAPA-501 can inhibit pathogenic Th1 cells, which will reduce T cell killing of motor neurons to slow ALS pathogenesis.

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For the most up to date information on EAPs, visit the Sean M. Healey & AMG Center for ALS website:

Additional information on EAPs:

- FDA
  - fda.gov/news-events/expanded-access/expanded-access-information-patients
- Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS)
  - neals.org/als-trials/expanded-access