

HEALEY ALS Platform Trial

Weekly Q&A – Oct 27, 2022



Healey Center

Sean M. Healey & AMG Center
for ALS at Mass General



The AMG Foundation

The **1ST** Ever
ALS PLATFORM TRIAL

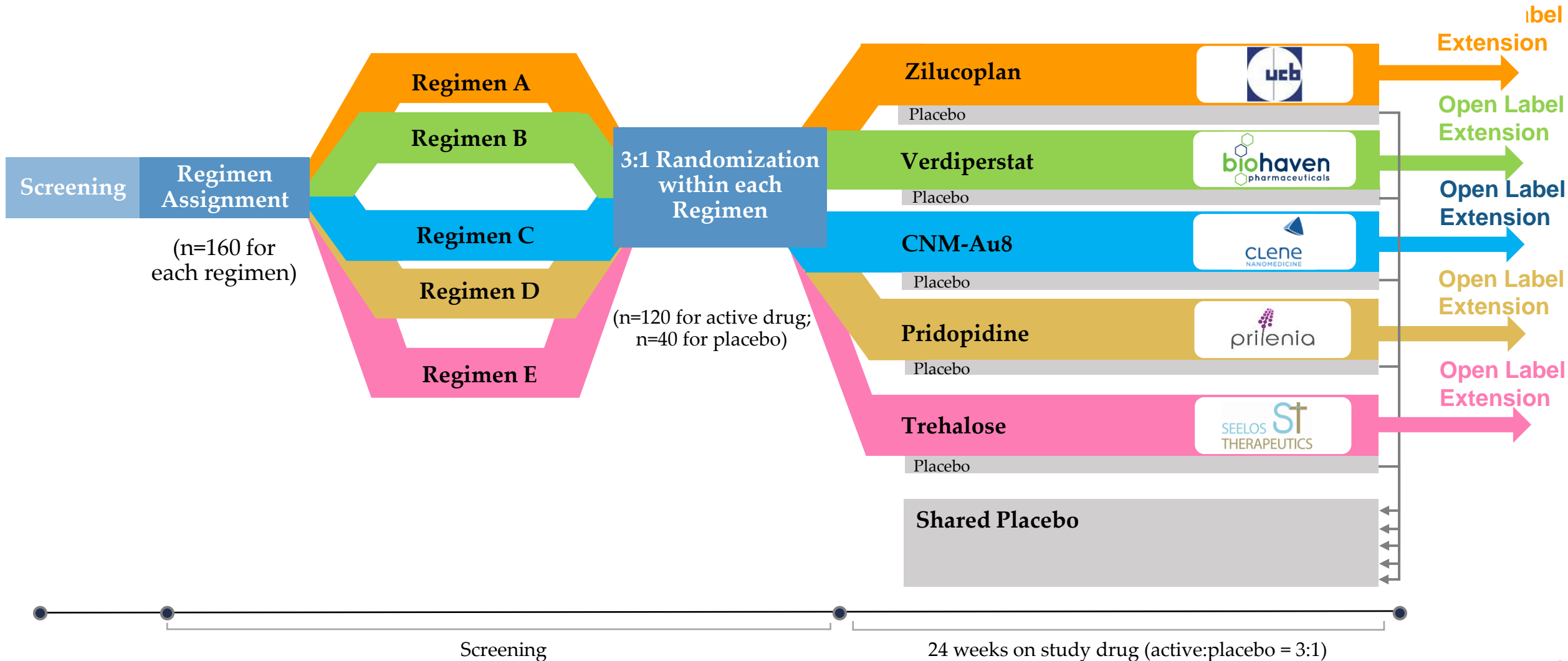
Video Link:



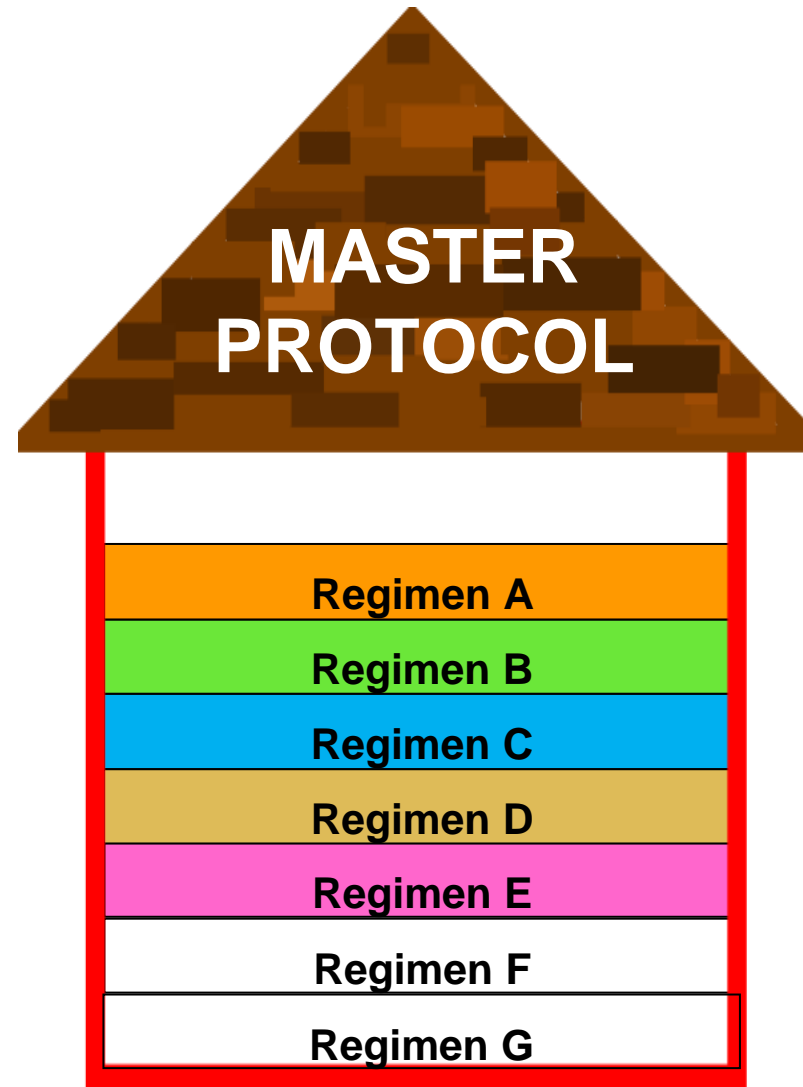
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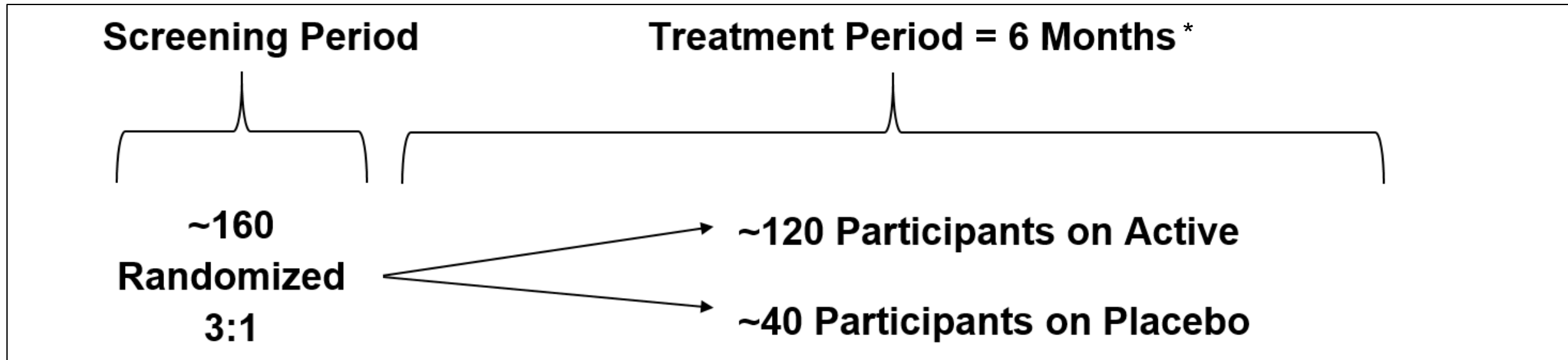
The goal of the HEALEY ALS Platform Trial is to screen drugs rapidly and efficiently, get solid answers, and determine next steps



The Platform Trial is Governed by a Master Protocol, a Common Protocol for Multiple Regimens



Common Protocol – Schema for Each Regimen



* Randomized Placebo-Controlled Treatment Period followed by Open Label Extension

Common Protocol – Endpoints

Primary Endpoint

- Change in disease severity through 24 weeks
- ALS Functional Rating Scale-Revised (ALSFRS-R) + Mortality
- Potential to provide confirmatory evidence with overall type I error of 5%

Secondary Endpoints

1. Change in respiratory function - slow vital capacity (SVC)
2. Change in muscle strength - hand held dynamometry (HHD)
3. Survival

Safety Endpoints

Biomarkers and Exploratory Endpoints (DNA, NfL, Speech app, Home Spirometry)

Assessing emerging biomarkers/outcome measures



DNA – genetic analysis in progress for all regimens



Neurofilaments – NfL analysis in progress for all regimens



Biomarkers (Blood, Urine, CSF) – several drug-specific and MOA biomarkers are being analyzed in each regimen



Speech Analysis – data collected for regimens A-D; results expected in the coming months



Home Spirometry – critical during the pandemic for regimens A-D

Additional biomarkers/outcome measures being considered for upcoming regimens (PBMCs, ROADS)

Weekly Recordings Available on Website

Webinar Recordings

Science & Mechanism of Action Series +

Weekly & Monthly Updates -

October 6, 2022: Weekly Q&A featuring discussion of Regimen C/CNM-Au8 results

Merit Cudkowicz, MD, MSc and Sabrina Paganoni, MD, PhD presented this week's updates on the HEALEY ALS Platform Trial and answered questions from the audience. We were joined by the co-lead investigators for Regimen C and representatives from Clene Nanomedicine, Inc. to discuss the trial results for CNM-Au8.

[Watch recording.](#)

September 29, 2022: Weekly Q&A featuring discussion of Regimen B/Verdiperstat results

Merit Cudkowicz, MD, MSc and Sabrina Paganoni, MD, PhD presented this week's updates on the HEALEY ALS Platform Trial and answered questions from the audience. We were joined by the co-lead investigators for Regimen B and representatives from Biohaven Pharmaceuticals to discuss the trial results for Verdiperstat.

[Watch recording.](#)

Visit the Website:



<https://bit.ly/3g4kzfv>

HEALEY ALS Platform Trial

Ongoing and Upcoming Regimens



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for ALS at Mass General

Regimens D: ongoing

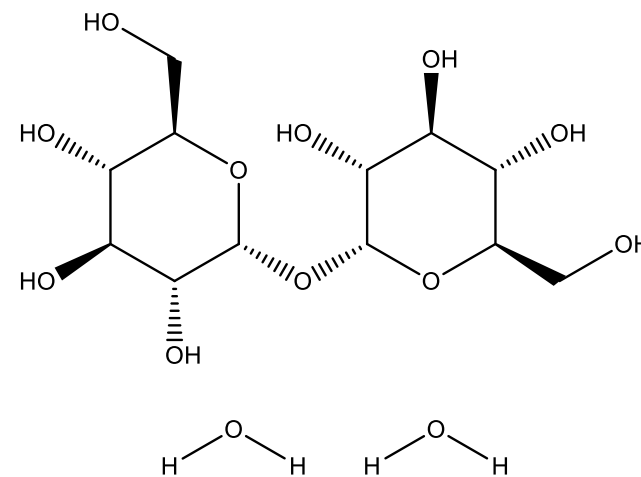
Regimen E enrolling new participants now

Additional Regimens in start-up or selected

Regimen E

TREHALOSE (SLS-005)

- Trehalose is a disaccharide composed of 2 glucose molecules
- Humans do not make trehalose, but can metabolize it
- Oral trehalose is not absorbed due to breakdown by gut trehalases (<0.5%)
- Therefore, it is administered IV to bypass the gut trehalase enzymes
- Trehalose penetrates muscle and brain
- When tested in vivo, treatment with trehalose resulted in preservation of motor neurons in the ventral horn of the spinal cord, improved muscle strength, and prolonged survival in SOD1 mouse models of ALS¹⁻³



1. Castillo et al, 2013
2. Zhang et al, 2014
3. Li et al, 2015



The ALS Association/Northeast ALS Consortium Educational Webinar

Update on Healey ALS Platform Trial Regimen E: Trehalose for ALS

**UPDATE ON
REGIMEN E**

TREHALOSE FOR ALS



Merit Cudkowicz, MD, MSc
SEAN M. HEALEY & AMG
CENTER FOR ALS AT MGH



Shafeeq Ladha, MD
BARROW NEUROLOGICAL
INSTITUTE

TUESDAY | 4 OCTOBER
3 PM EDT

Recording Available!



<https://bit.ly/3dhQvff>

*Recording available under
“educational webinars” on neals.org*

Enrollment Updates (as of Oct 27, 2022)

- **158** individuals have signed informed consent
- **116** individuals have been randomized within Regimen E

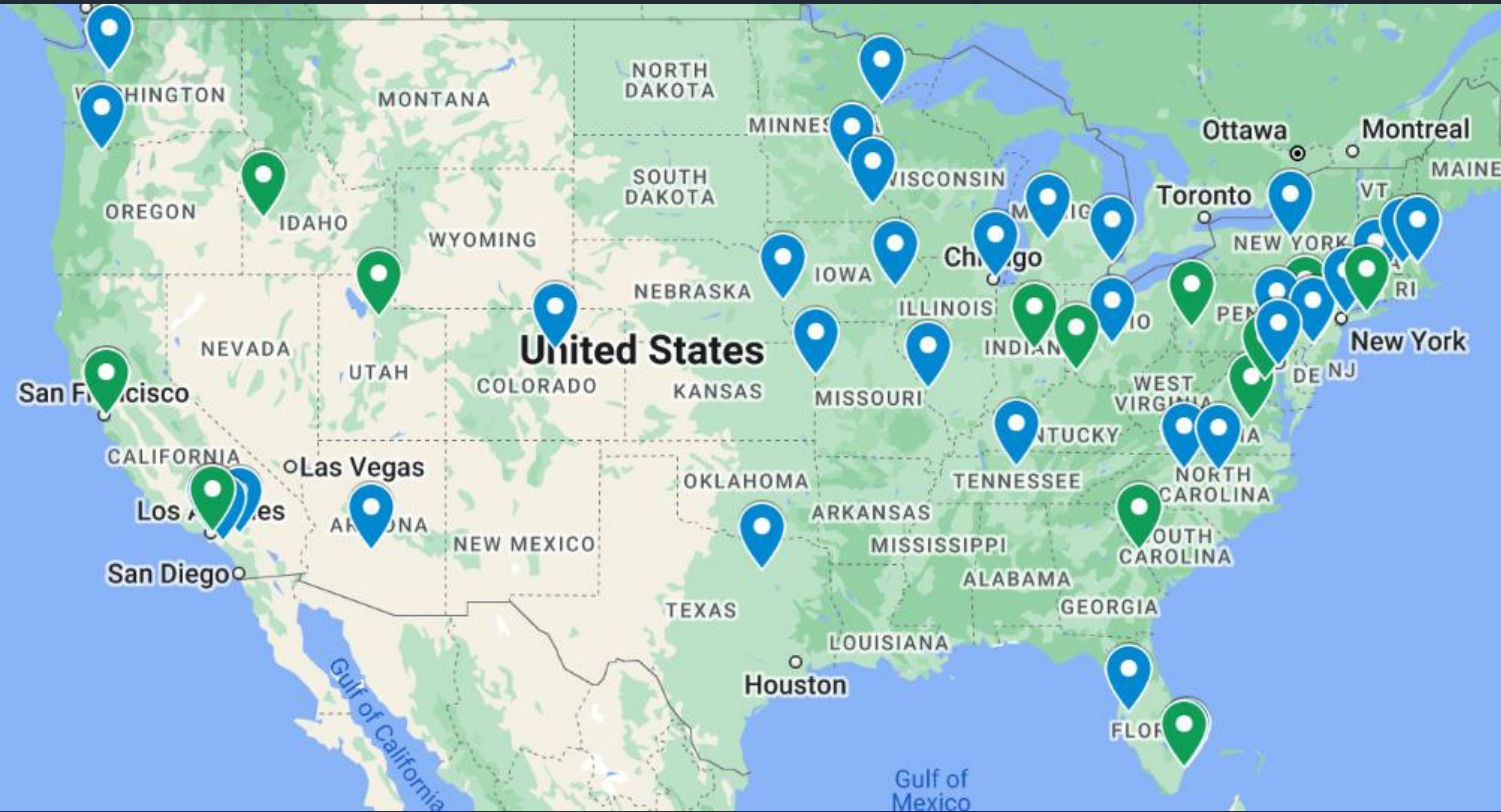
Thank You

This breakthrough trial would not be possible without your participation

Your **partnership** in research is what keeps us filled with passion, dedication, and the commitment to uncover new promising treatments for ALS

Every research participant, whether on the active drug or placebo, plays a critical role in making the hope of finding a cure for ALS a reality

51 Sites Currently Activated for Regimen E



(as of 10/27/22)

Sites in blue participated in previous regimens. Sites in green (underlined to the side) are new additions to the Platform Trial!

- Lehigh Valley Health Network
- Mass General Hospital
- University of Kansas
- University of Maryland
- California Pacific Medical Center
- Northwestern University
- Virginia Commonwealth University
- University of Nebraska
- Washington University
- Wake Forest University
- Hospital for Special Care
- Saint Alphonsus Regional
- University of Massachusetts
- Duke University
- Barrow Neurological Institute
- Georgetown University
- Texas Neurology
- Beth Israel Deaconess Medical Center
- SUNY Upstate
- Spectrum Health
- Henry Ford Hospital
- Essentia Health
- University of Southern California
- University of South Florida
- University of Colorado
- Providence Brain and Spine
- University of Minnesota
- Loma Linda University
- University of Iowa
- Swedish Medical Center
- Ohio State University
- University of Cincinnati
- Thomas Jefferson University
- UC San Francisco
- Mayo Rochester
- University of Washington
- Vanderbilt University
- UPMC
- Indiana University
- Augusta University
- University of Utah
- Holy Cross Hospital
- Penn State Hershey
- University of CA, Irvine
- Cedars Sinai Medical Center
- University of Pennsylvania
- Nova Southeastern University
- Johns Hopkins University
- Columbia University
- Stony Brook University
- Kaiser, Los Angeles

Site Map & Contacts:



<https://bit.ly/3g2NZr5>

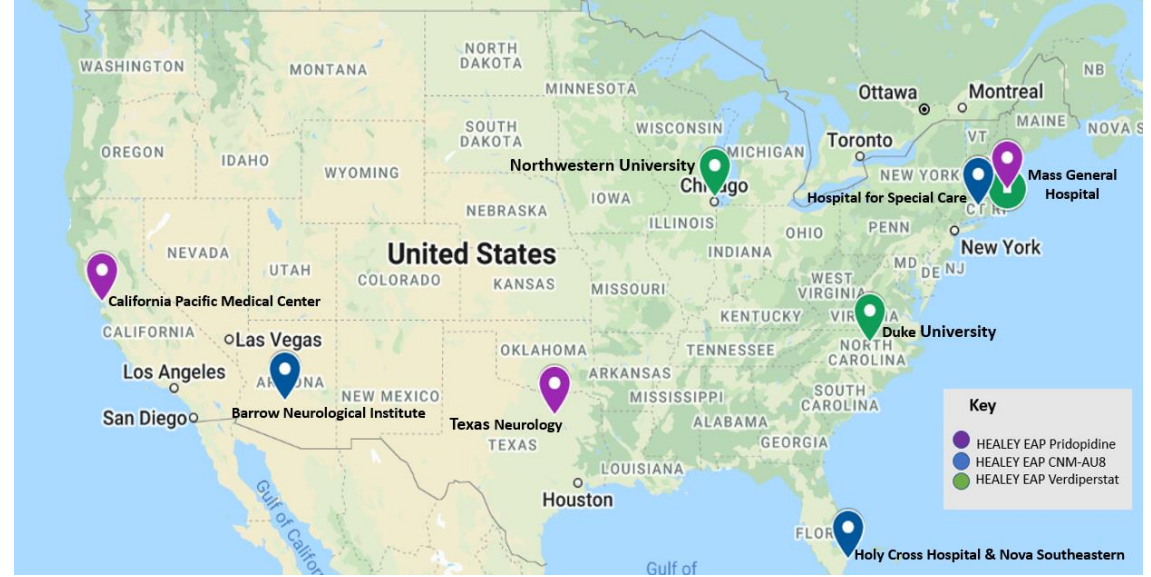
Requirements for EAPs

- Expanded Access Protocols (EAPs) are FDA regulated
- Providing drug via an EAP should **not interfere with clinical trials**
- EAPs are meant for ALS patients who are **not eligible for clinical trials**

EAP Companion To HEALEY ALS PLATFORM TRIAL

2021- present

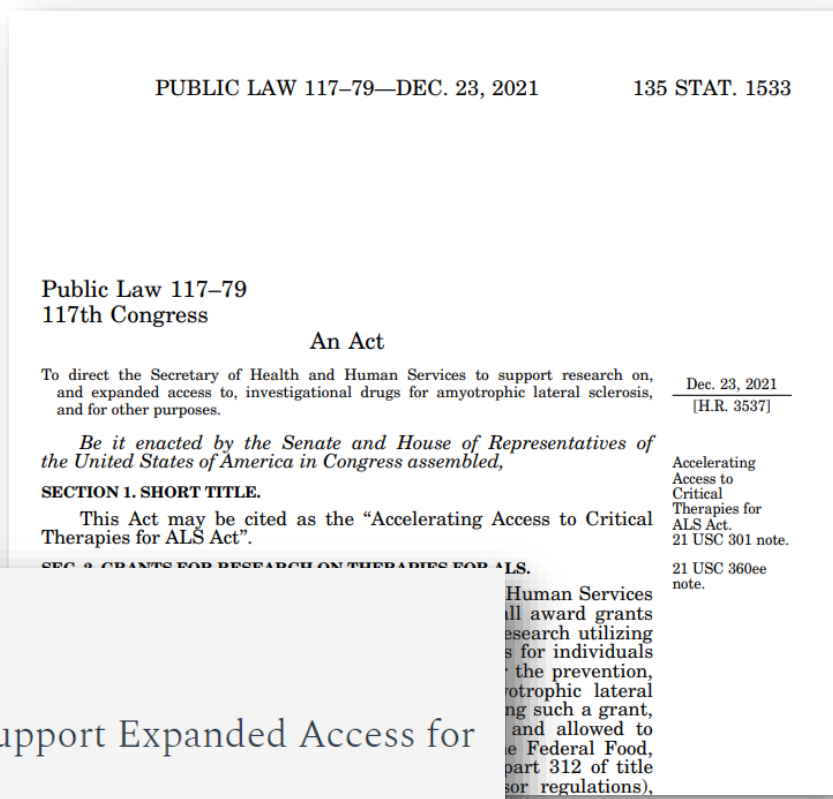
- 3 study drugs (Regimens B,C,D)
- 10 sites
- 85 participants
- Funded by philanthropy (study drug donated by manufacturers)
- Safety and clinical data; biomarker data



ACT for ALS

Signed into law on Dec 23, 2021

Section 2: Grants for Research on Therapies for ALS via Intermediate-Size EAPs



ie - Neurology - ALS - News

NEWS · SEP | 30 | 2022

Sean M. Healey & AMG Center for ALS awarded NINDS UO1 Grant to support Expanded Access for Trehalose (SLS-005)

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The Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital has been awarded a grant from the National Institute of Neurological Disorders and Stroke (NINDS) to conduct an intermediate size Expanded Access Protocol (EAP) in Amyotrophic Lateral Sclerosis (ALS). The grant is supported by the ACT for ALS (Accelerating Access to Critical Therapies for ALS Act). This EAP will

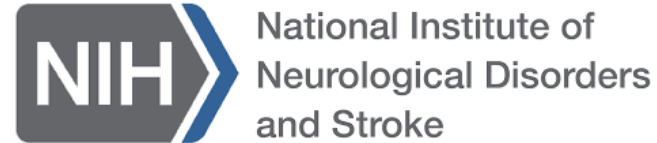
Type

News

Centers and Depar

Intermediate Size EAP - Trehalose

- In start up now
- Expected to enroll first participants in Q1 2023
- 25 sites
- 70 participants
- NIH-funded (PIs: Babu, Berry, Paganoni)
- Happening in parallel to Regimen E of the HEALEY ALS Platform Trial



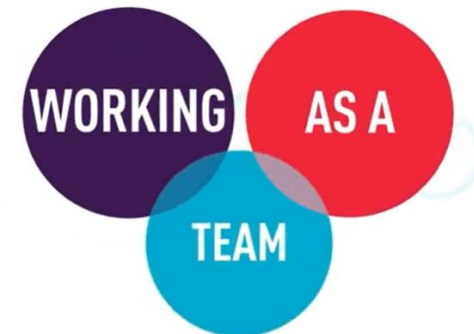
View Press Release:



<https://bit.ly/3S0a9eb>

Outcomes:

- Long-term safety in a broad population
- Biological impact (as measured by neurofilament light levels)
- Clinical efficacy signal (as compared to natural history cohorts)



Patient Navigation

Central resource for people living with ALS



Catherine Small

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E-mail: healeyalsplatform@mgh.harvard.edu

Weekly webinar
registration:



<https://bit.ly/3r6Nd2L>

ALS Link sign-up:



<https://bit.ly/3o2Ds3m>

Upcoming Cancelations:

November 3rd- Webinar canceled due to annual research conference

November 24th- Webinar canceled for holiday, Happy Thanksgiving!



Allison Bulat