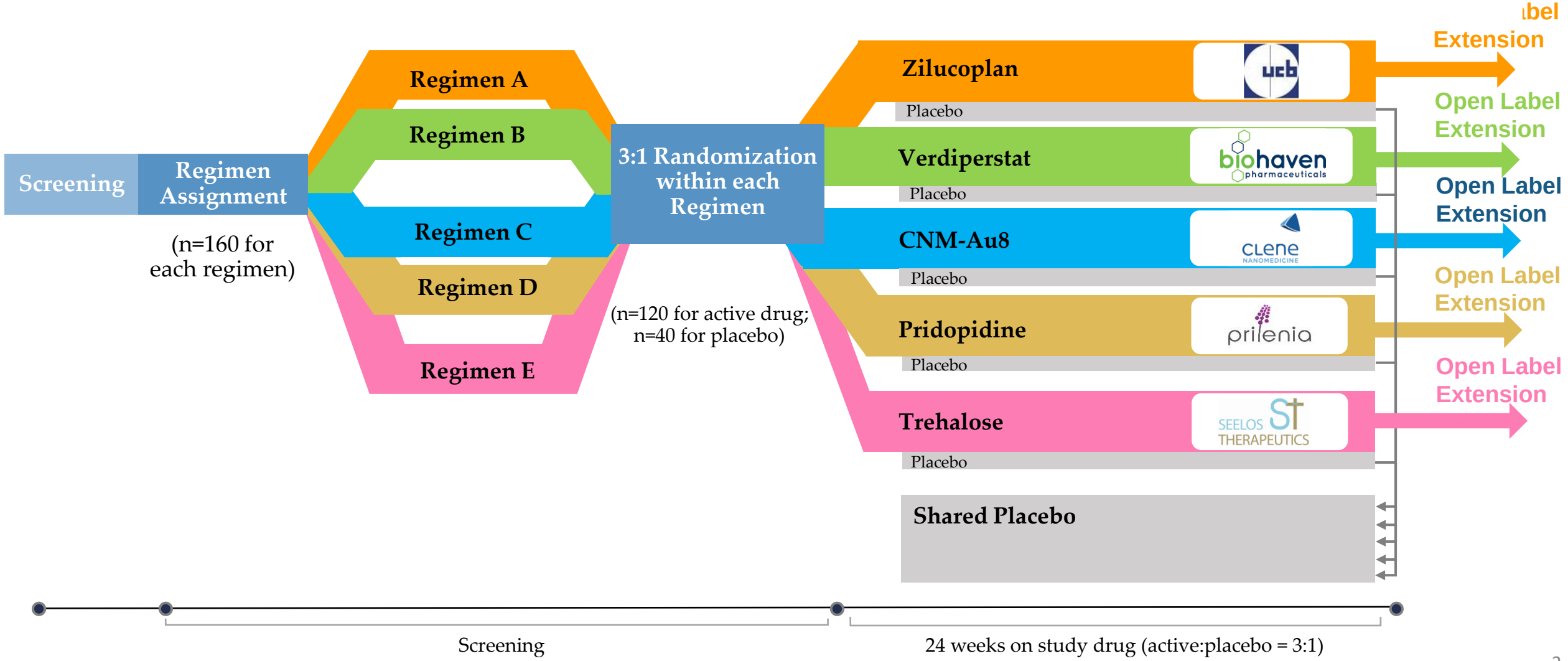
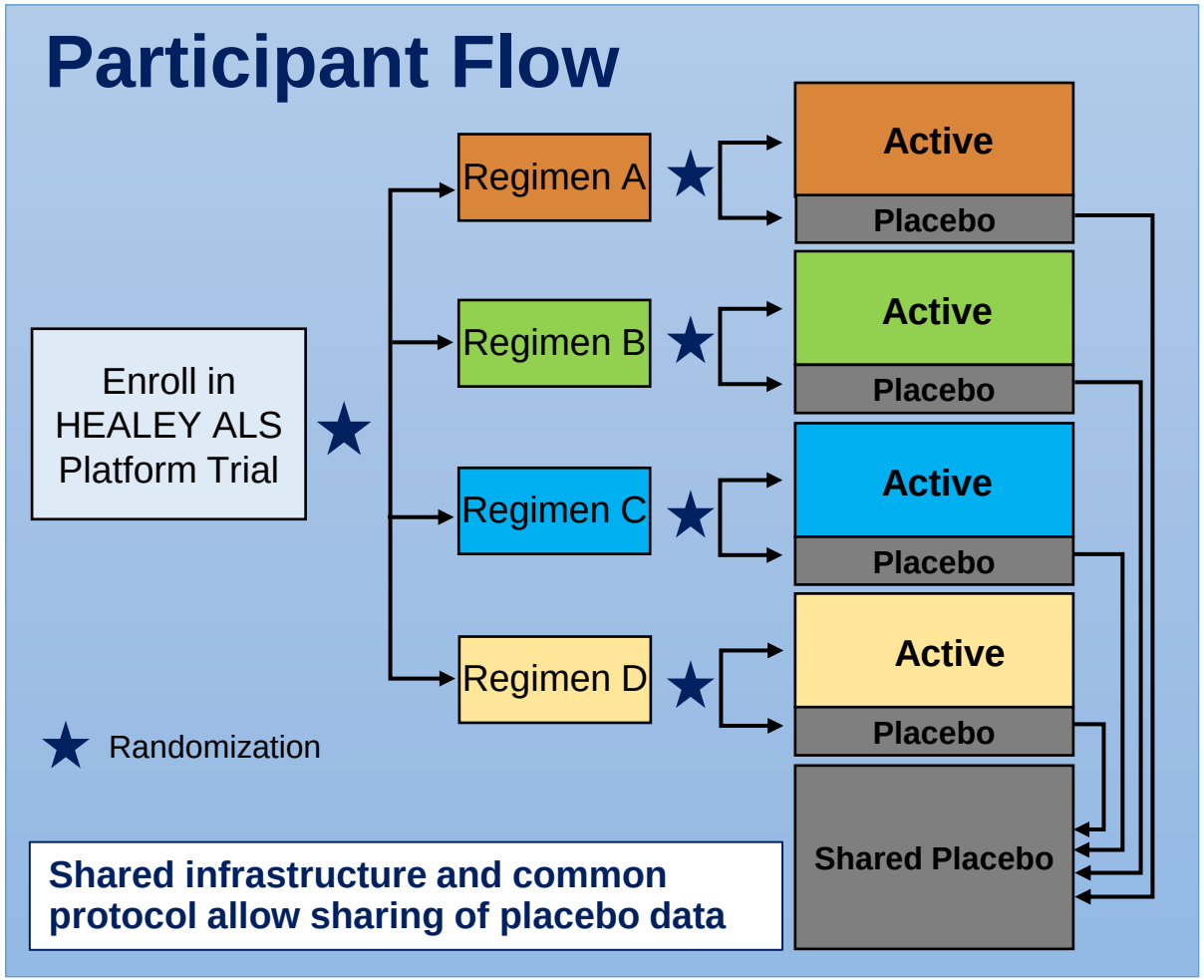
HEALEY ALS Platform Trial

Weekly Q&A – Oct 13, 2022

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



Shared Infrastructure and Common Protocol Allow for Operational and Scientific Efficiencies

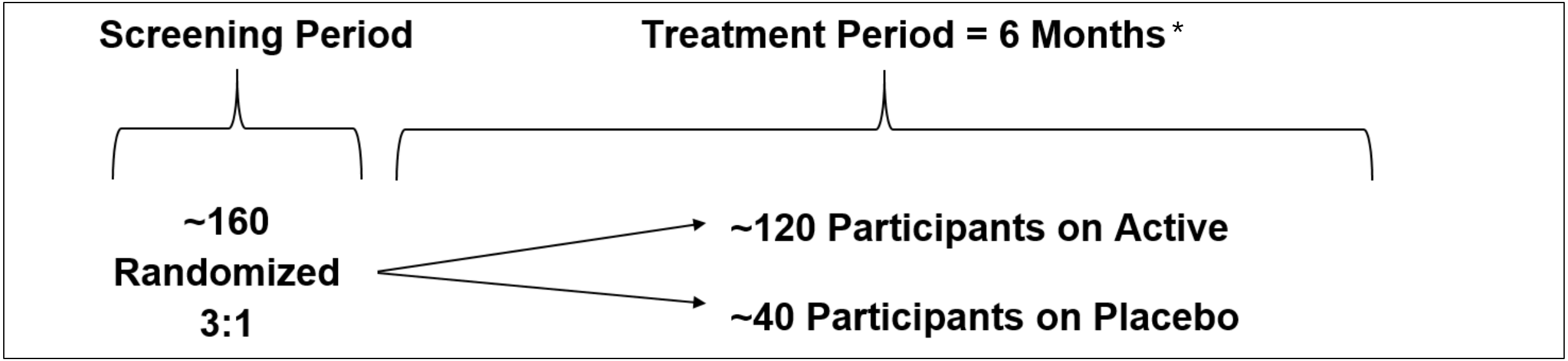


Cuts time in 1/2

Cuts costs by 1/3

Reduces placebo

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)

HEALEY ALS Platform Trial

Initial Regimen Updates – trial gave clear answers and direction, efficient execution (time, resources, less placebo)

- February 2022: **Regimen A** stopped early for futility
- September 2022: **Regimen B** top line results announced
  - Did not meet the prespecified primary endpoint and there were no statistically significant benefits on key secondary measures; full study results, including data on biomarkers and exploratory measures, are expected in the coming months
- October 2022: **Regimen C** top line results announced
  - While the primary endpoint was not met, a secondary endpoint analysis of survival demonstrated a significant reduction in risk of death or permanently assisted ventilation when adjusting for baseline risk imbalances in the CNM-Au8 regimen for the 30 mg dose; full study results, including data on biomarkers and exploratory measures, are expected in the coming months

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

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

Regimens D: ongoing

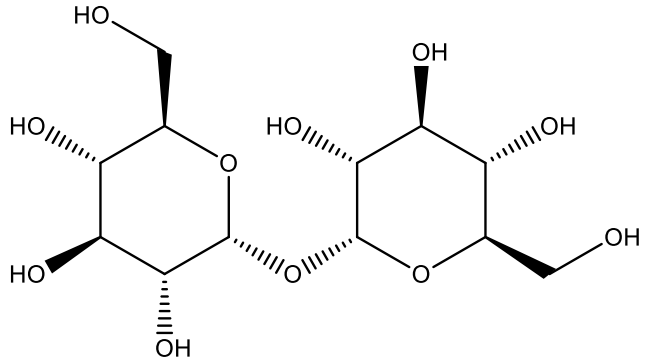
Regimen E enrolling new participants now

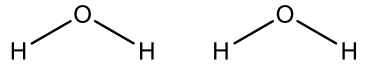
- **Regimens F&G in start-up** (Calico-AbbVie; Revalesio)
- **Three additional Regimens selected** for inclusion; working on contracts

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 ALS[1-3]





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

SEELOS THERAPEUTICS

The ALS Association/Northeast ALS Consortium Educational Webinar

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

Recording Available!

https://bit.ly/3dhQvff

Recording available under "educational webinars" on neals.org

Enrollment Updates (as of Oct 13, 2022)

- **148 individuals have signed informed consent**

- **107 individuals have been randomized within Regimen E**

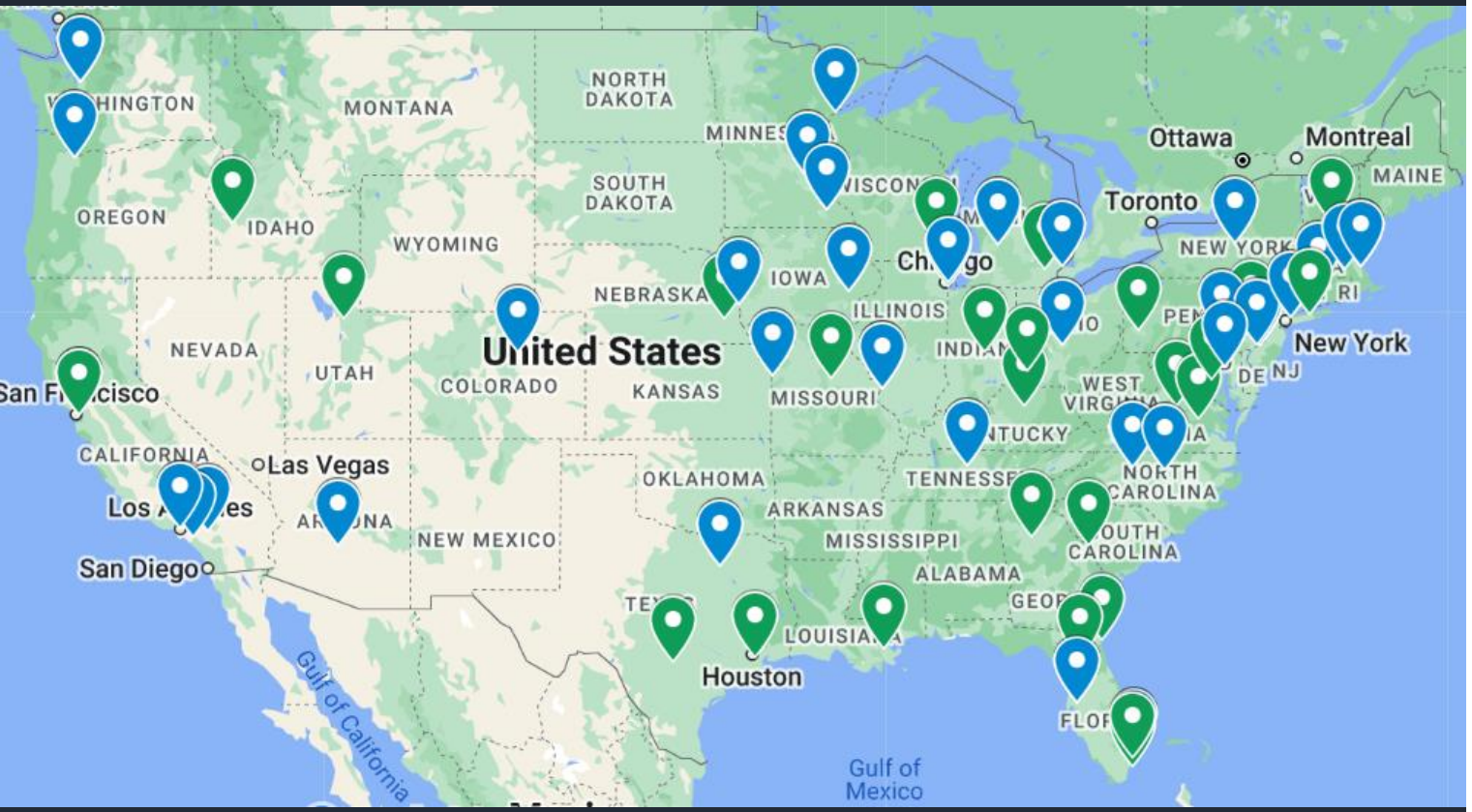
Thank You

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 10/13/22)

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

Only 10% of people living with ALS participate in clinical trials

Expanded Access

FDA Definition:

- Sometimes called “compassionate use”
- Potential pathway for a patient with an immediately life-threatening or serious disease or condition
- Allows access to an investigational medical product outside of clinical trials
- Used when no comparable or satisfactory alternative therapy available

https://www.fda.gov/news-events/public-health-focus/expanded-access

Categories of Expanded Access Protocols (EAPs)

Individual Patient, including emergency use

Intermediate-size Patient Populations

Treatment Protocol (large patient population)

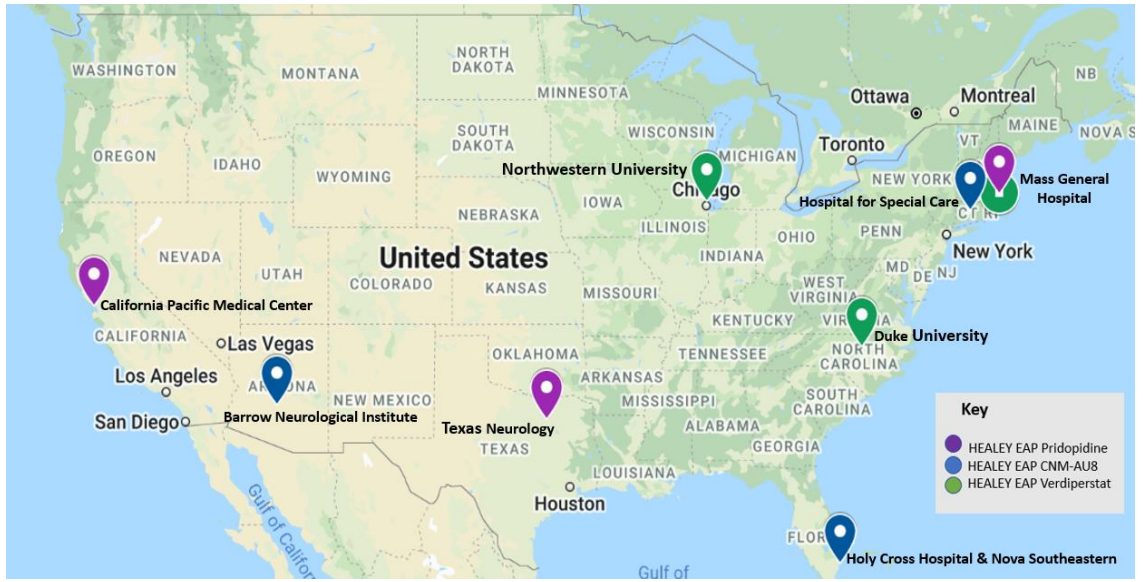
Requirements for All EAPs

- Patient has a **serious** or **immediately life-threatening** disease or condition; no comparable or satisfactory alternative therapy
- **Potential benefit justifies potential risk**; potential risk not unreasonable in context of disease or condition
- Providing drug will **not interfere with clinical trials** that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use

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



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

I AM ALS

biohaven pharmaceuticals

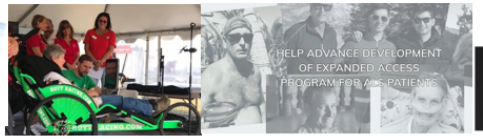
CLENE NANOMEDICINE

prilenia

Community Support to EAPs

EAP COMPANION PROGRAM SUPPORTERS

- Healey Center for ALS
- Clearing Corporation Charitable Foundation
- Eddie and Jo Allison Smith Family Foundation
- Richard Stravitz Foundation
- I AM ALS
- Biohaven
- Clene
- Prilenia
- Elliott & Frantz, Inc.
- **Community Fundraisers**
  - Tackle ALS – Team Change ALS
  - Ellen Corindia's Fundraiser
  - 2019 Olson Cornhole Tournament
  - 2019 Worthington Fore ALS
  - 2020 and 2021 Fishing for ALS Warriors
  - 2020 and 2021 sALSa For a Cure Pick Your Own Path Walk
  - 2020 and 2021 Lori's Shoes "Hope Is In the Bag"
  - 2021 and 2022 MLB Lou Gehrig Day 4-ALS
  - 2021 Russ Pallesen Fundraiser for EAP
  - 2021 Voices for ALS Golf Tournament
  - 2021 The Martha Olson-Fernandez Foundation Golf Tournament
  - 2021 Gwendolyn Strong Walk
  - TechVs.ALS
- **Big thanks to countless individual contributors**

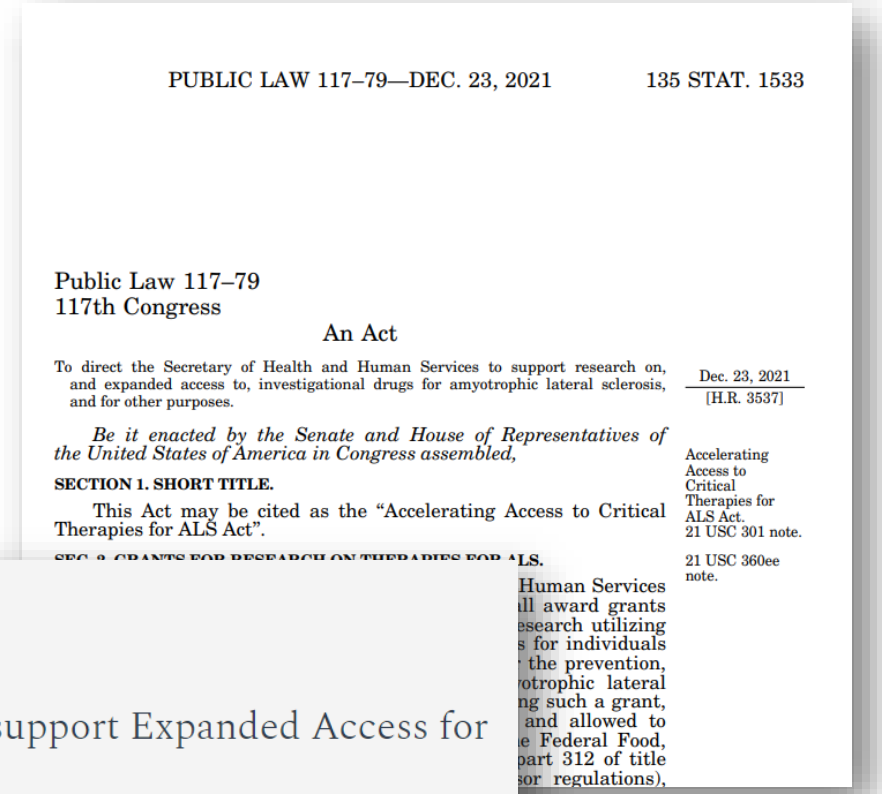


TechVsALS
Benefitting the Sean M. Healey and AMG Center for ALS

ACT for ALS

Signed into law on Dec 23, 2021

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



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.

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

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

21 USC 360ee note.

Human Services
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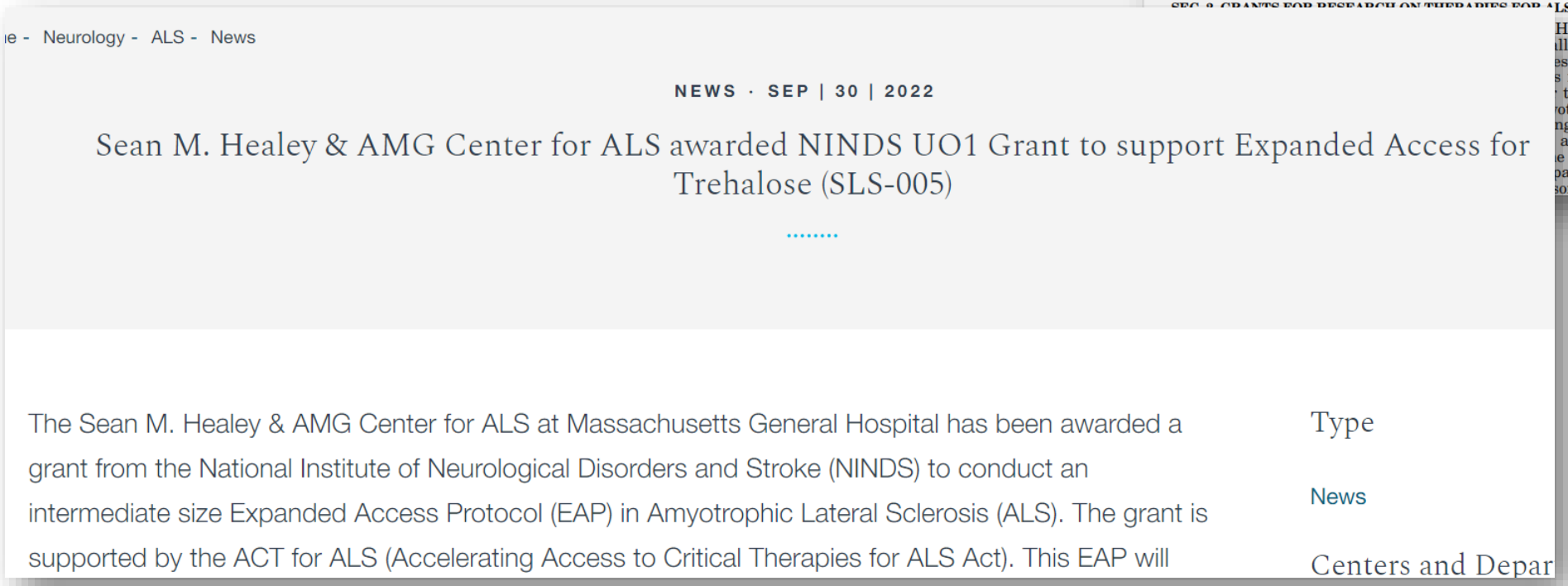

e - Neurology - ALS - News

NEWS · SEP | 30 | 2022

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

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

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

NIH National Institute of Neurological Disorders and Stroke

SEELOS THERAPEUTICS

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)

WORKING AS A TEAM

Summary

Clinical trials are **essential** to develop new treatments for all people living with ALS

Expanded Access Protocols (EAPs) provide access to new investigational products to people who are **not eligible** for clinical trials while clinical trials are ongoing

Data collected in EAPs can help **supplement** clinical development programs by providing **safety, clinical, and biomarker data** in **broad populations** that are typically not evaluated in clinical trials

The ALS community has created mechanisms to run EAPs in parallel to clinical trials