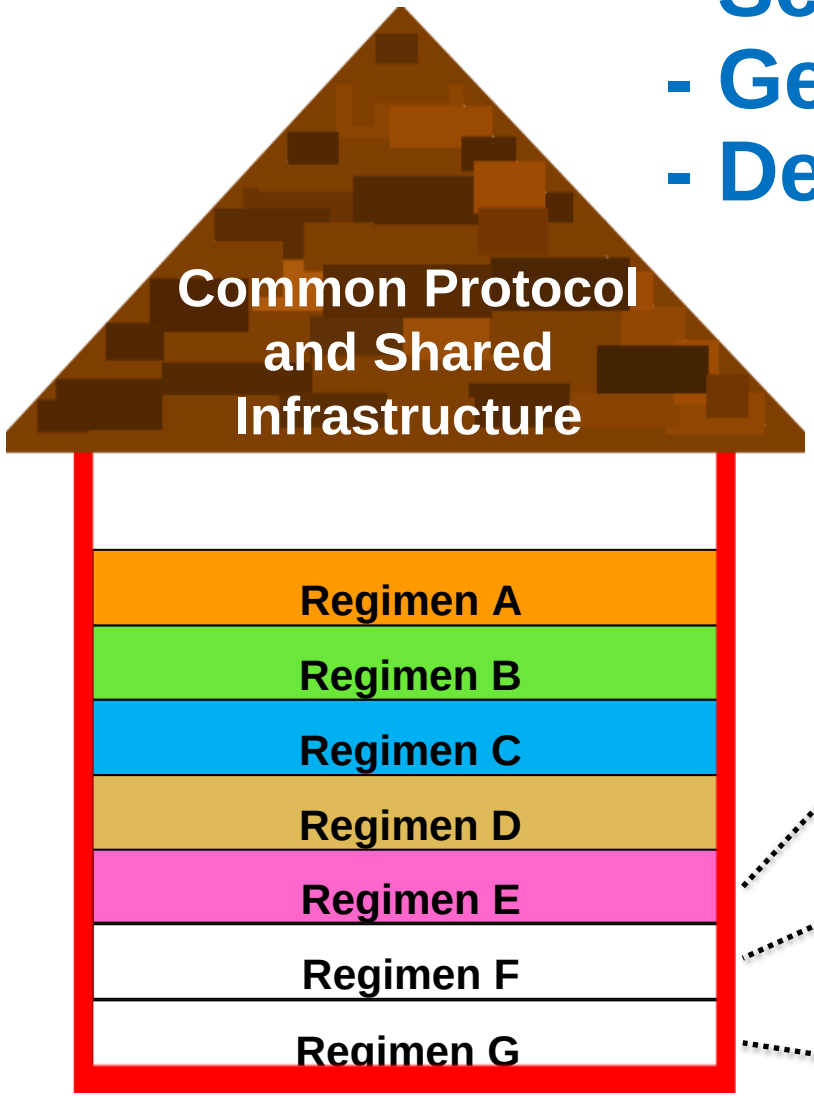
HEALEY ALS Platform Trial

Weekly Q&A – March 2, 2023

HEALEY ALS Platform Trial Goals:

- Screen new drugs rapidly and efficiently
- Get solid answers
- Determine next steps

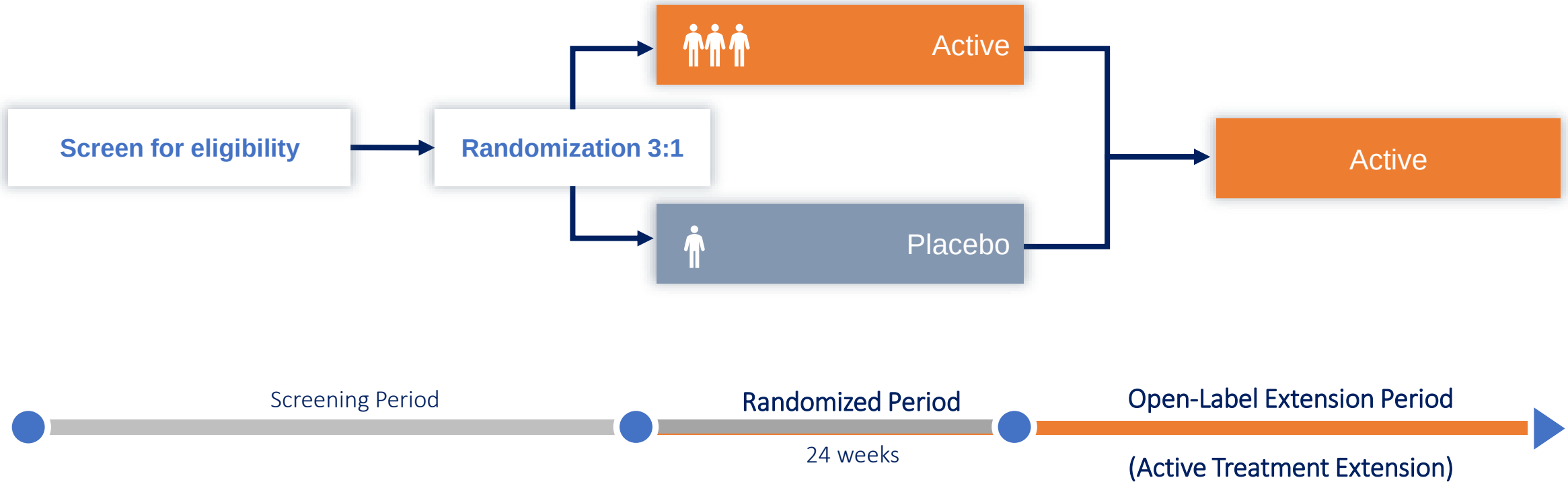


SEELOS THERAPEUTICS | ENROLLMENT COMPLETE

Calico | IN START-UP

DENALI THERAPEUTICS | IN START-UP

Schema for Each Regimen



The HEALEY ALS Platform Trial is a unique opportunity to advance science

DNA – whole genome sequencing

Neurofilaments –for all regimens

Biomarkers **(Blood, Urine, CSF)** – several drug-specific biomarkers

Speech Analysis – emerging digital biomarker

Home Spirometry – critical during the pandemic

Additional biomarkers/outcome measures are being considered for upcoming regimens (e.g., new patient-reported outcomes; PBMCs for stem cell generation)

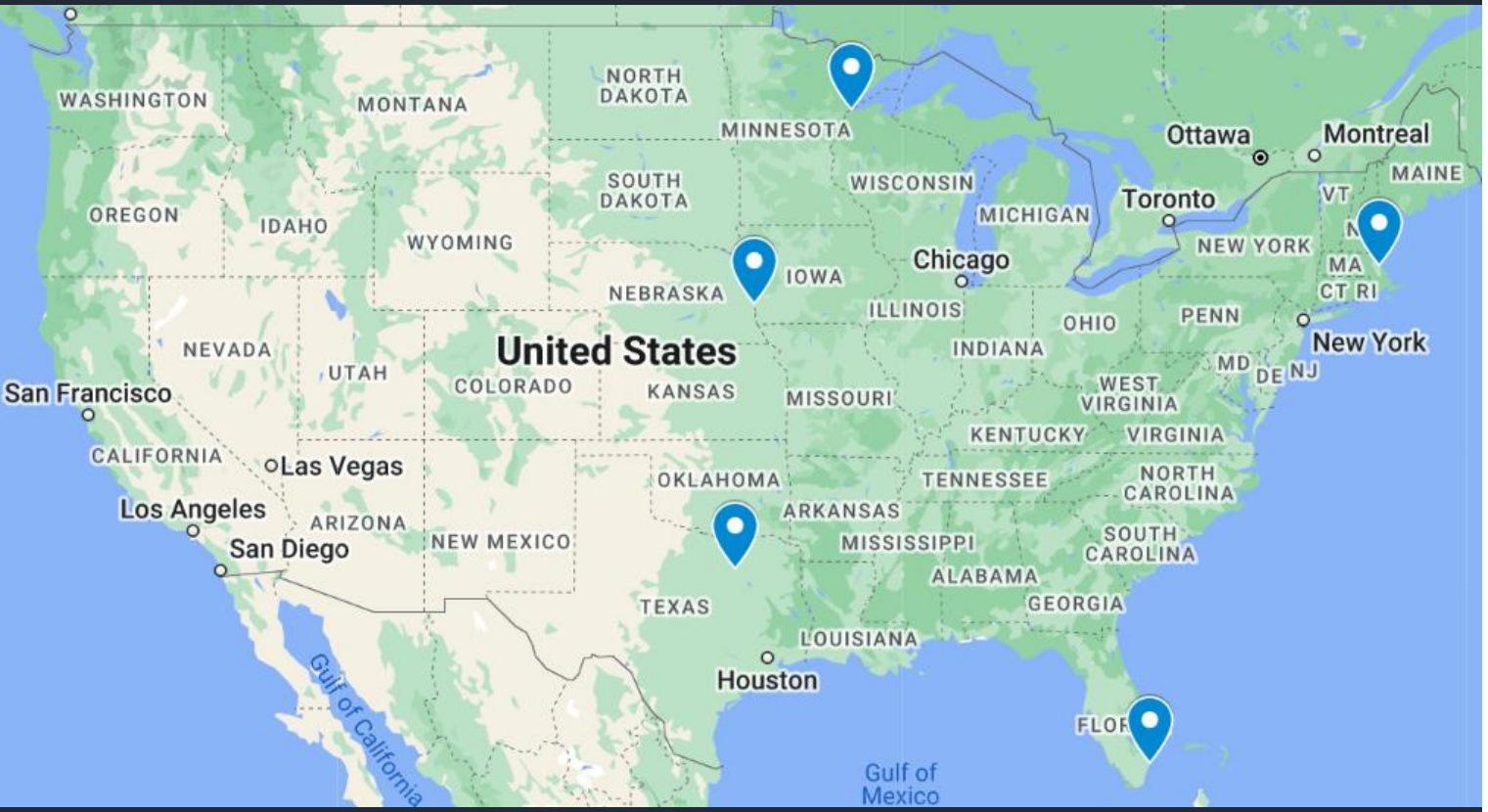
Platform Trial Enrollment

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

As of 02/23/2023

- Total # Consented Master Protocol 1098
- Total # Assigned to Regimen 880
- Total # Randomized within Regimen 814
  - ✓ RGA Total # Randomized 162
  - ✓ RGB Total # Randomized 167
  - ✓ RGC Total # Randomized 161
  - ✓ RGD Total # Randomized 163
  - ✓ RGE Total # Randomized 161
- Total # OLE Initiation 537

5 Sites Currently Active for Regimen F



(as of 3/2/23)

- ☑ Nova Southeastern University
- ☑ Essentia Health
- ☑ Texas Neurology
- ☑ Mass General Hospital
- ☑ University of Nebraska

Site Map & Contacts:

https://bit.ly/3g2NZr5

Checking Site Status Online

List of Participating Sites

Many sites are expected to start enrolling for Regimen F soon. Sites marked "Recruiting" are currently enrolling participants.

Sites marked "Active, Not recruiting" are active in the Platform Trial (for example, they are following participants in ongoing regimens that have already completed enrollment) but are not enrolling new

Site	State	Enrollment Status	Trial Contact Information
Mayo Clinic Florida	FL	Active, Not recruiting	Jany Paulett
Nova Southeastern University	**FL**	**Recruiting**	**Donovan Mott**
Phil Smith Neuroscience Institute, Holy Cross Hospital	FL	Active, Not recruiting	Ashley Stepler

https://bit.ly/3g2NZr5

as of 3/2/23

New Regimen F Resources on MGH Website

Regimen F: ABBV-CLS-7262, by Calico and AbbVie- Now Recruiting

ABBV-CLS-7262 is an investigational drug developed by Calico Life Sciences LLC in collaboration with AbbVie Inc. ABBV-CLS-7262 aims to restore function in cells affected by ALS by normalizing protein synthesis and preventing further sequestration and aggregation of TDP-43, thereby protecting neurons, and possibly slowing ALS progression.

The integrated stress response (ISR) is a fundamental transient process that regulates cell function during various stressful conditions. Tissue studies suggest that the ISR is chronically induced in people with ALS. It is proposed that TDP-43 aggregates, a hallmark feature in the motor neurons of people with ALS, could be formed by a chronically induced ISR. ABBV-CLS-7262 activates the protein complex eIF2B, which is a key regulator of the ISR. Binding of ABBV-CLS-7262 desensitizes eIF2B to stress and decreases the ISR. Reduction of the ISR restores normal protein synthesis, reduces TDP-43 sequestration in stress granules, and may decrease TDP-43 aggregation.

A prior first-in-human study of ABBV-CLS-7262 showed that this drug was well-tolerated by participants, demonstrated target engagement by increasing eIF2B enzymatic activity, and suppressed the ISR in blood cells. ABBV-CLS-7262 crossed the blood brain barrier at concentrations predicted to be efficacious in ALS. ABBV-CLS-7262 is currently being investigated in a Phase 1b study in people with ALS (NCT04948645), and will be studied further as part of the HEALEY ALS Platform Trial.

Watch this video for more information on the mechanism of action behind ABBV-CLS-7262.

Download brochure

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

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

HEALEY ALS Platform Trial

Regimen F

ABBV-CLS-7262

Developed by Calico Life Sciences LLC in collaboration with AbbVie Inc.

Investigational products included in the HEALEY ALS Platform Trial are selected by a team of experts after careful review of the study drug and the science supporting its treatment potential in Amyotrophic Lateral Sclerosis (ALS). Regimen F is testing an experimental medication called ABBV-CLS-7262, and the trial will involve in-person study visits every 4 to 8 weeks (about 6 visits total over the course of 24 weeks).

Please discuss the possible benefits and risks of this investigational product with your study team.

Visit our website to learn more about what to expect in the trial process:
https://bit.ly/3ExRal8

About Regimen F:

Regimen F is a Phase 2/3 trial enrolling approximately 240 participants to evaluate the safety and efficacy of ABBV-CLS-7262 as a potential treatment for ALS. This regimen involves biomarker analysis and cerebrospinal fluid collection via lumbar punctures to assess the effects of ABBV-CLS-7262.

3:1 Active Drug to Placebo Ratio: Participants who enroll in this trial have a 3 in 4 (75%) chance of being assigned to active study drug and a 1 in 4 (25%) chance of being assigned to placebo during the initial 24-week placebo-controlled trial (PCT) period.

Active Treatment Extension (ATE): Participants have the option to enroll in the ATE for ABBV-CLS-7262 upon completion of the 24-week PCT. During ATE, all participants will receive the active study drug.

To see if you may qualify, please review the list of eligibility criteria:
https://bit.ly/30ctynm

For general questions about the HEALEY ALS Platform Trial, **Contact the Patient Navigator:**
healeyalsplatform@mgh.harvard.edu
833-425-8257 (HALT ALS)

https://bit.ly/3SIwH4X

Printable Brochures!

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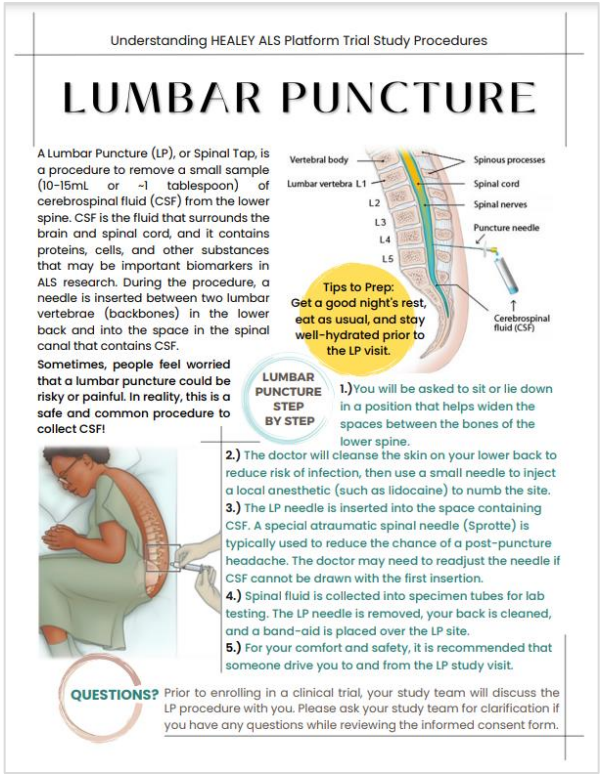
Regimen F Brochure

Lumbar Puncture Brochure

General Platform Trial Brochure



Upcoming Webinar- Regimen D Update

Community Webinar (Open to Public)

Monday, March 6th at 10:00 am Eastern Time

Register here: https://bit.ly/3KQ3q6L

Register:

PRESS RELEASE · FEB | 23 | 2023

Healey & AMG Center & the Northeast ALS Consortium announce results in platform trial with pridopidine

View Press Release:

https://bit.ly/3xSzBdG

"The positive results on speech and bulbar function, and on overall function and breathing in people earlier in disease course, are very encouraging and ***deserve further investigation*** *in a phase III trial."*

Merit Cudkowicz, MD, MSc

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

Patient Navigation
Central resource for people living with ALS

Catherine Small

Allison Bulat

Phone: 833-425-8257 (HALT ALS)

E-mail:healeyalsplatform@mgh.harvard.edu

Weekly webinar registration:

https://bit.ly/3r6Nd2L

ALS Link sign-up:

https://bit.ly/3o2Ds3m

Upcoming Webinars:

March 9th- Weekly Q&A

March 16th- Weekly Q&A

March 23rd- Weekly Q&A