

HEALEY ALS Platform Trial

Weekly Q&A – March 2, 2023



Healey Center

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



als FINDING a CURE



Calico



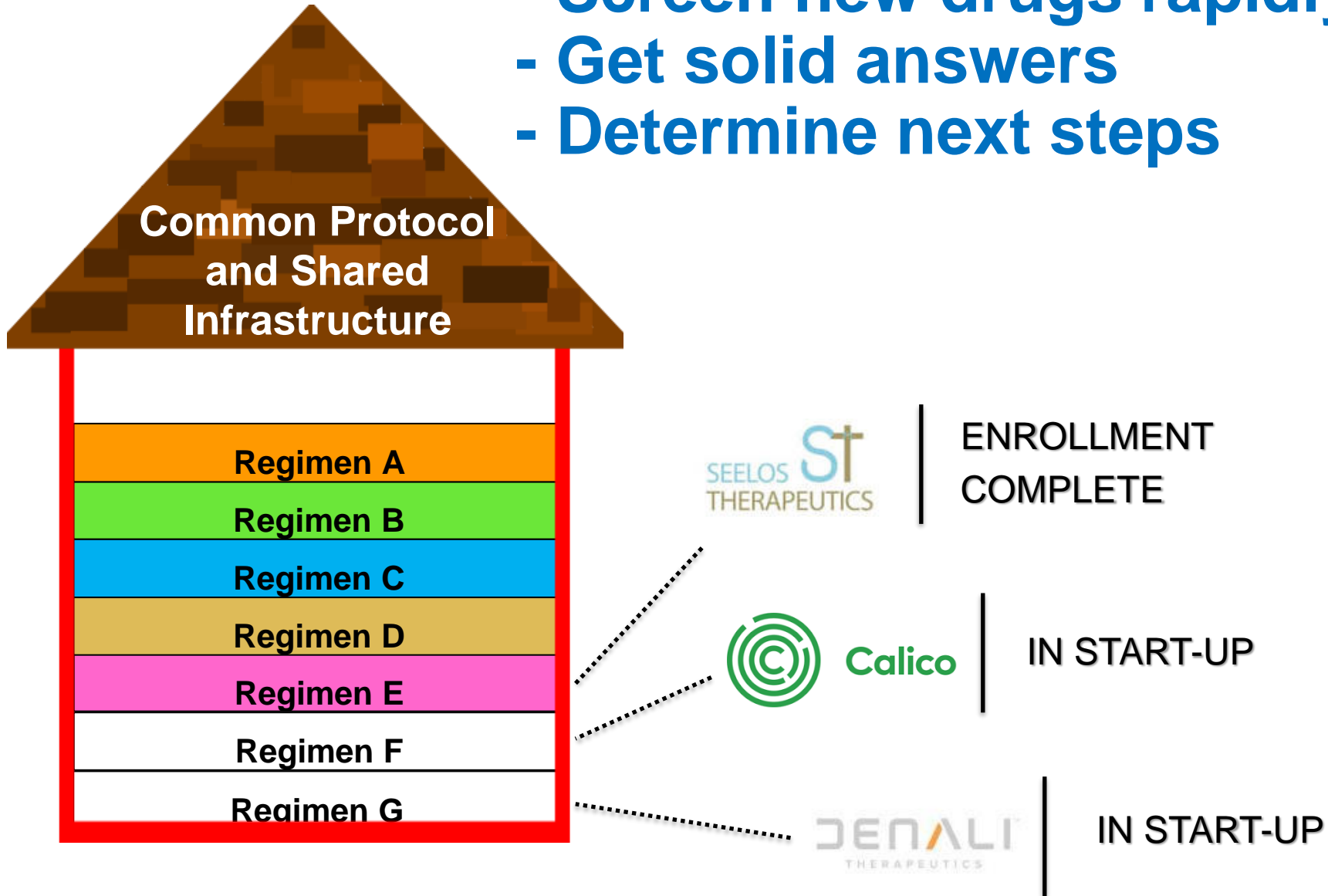
THE ARTHUR M. BLANK
FAMILY FOUNDATION



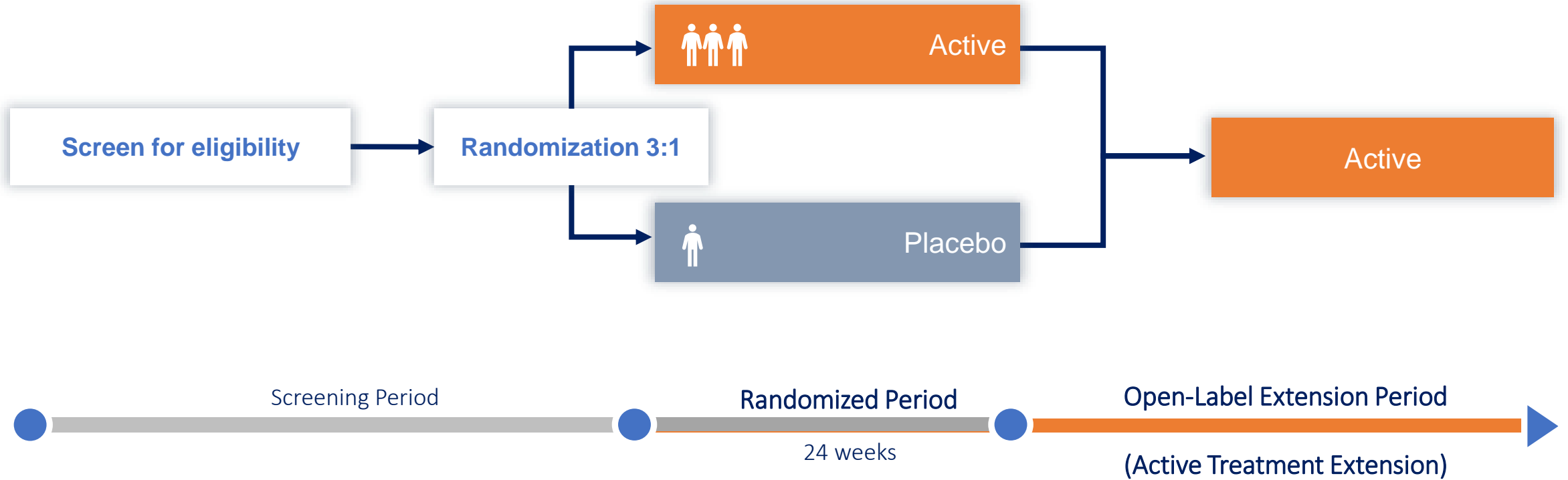
The AMG Foundation

HEALEY ALS Platform Trial Goals:

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



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

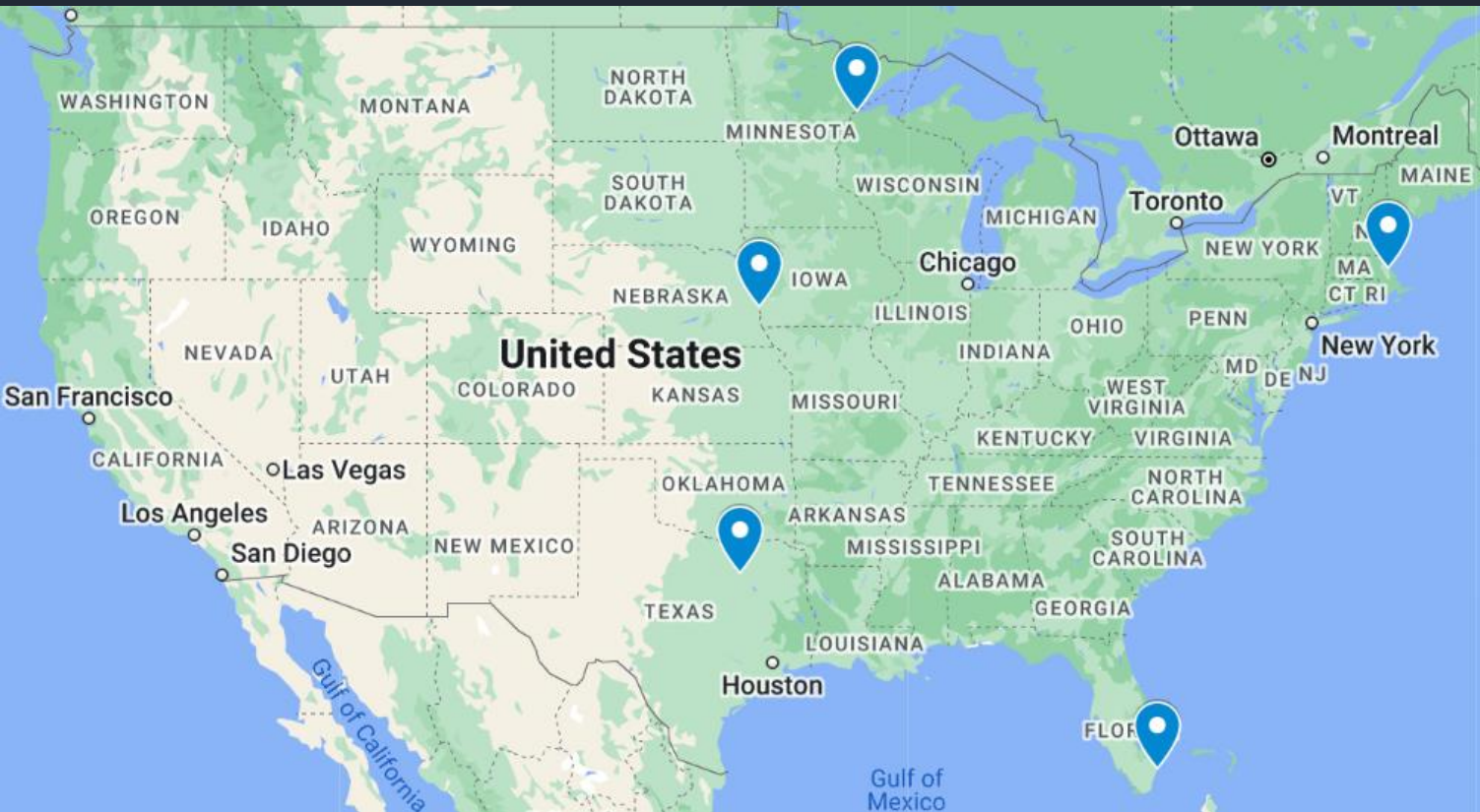
Additional biomarkers/outcome measures are being considered for upcoming regimens (e.g., new patient-reported outcomes; PBMCs for stem cell generation)

Platform Trial Enrollment

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>

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 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/3ExRel8>



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/30stvmn>



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!

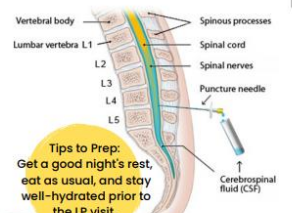


Regimen F Brochure
Lumbar Puncture Brochure
General Platform Trial Brochure

Understanding HEALEY ALS Platform Trial Study Procedures

LUMBAR PUNCTURE

A Lumbar Puncture (LP), or Spinal Tap, is a procedure to remove a small sample (10-15mL or ~1 tablespoon) of cerebrospinal fluid (CSF) from the lower spine. CSF is the fluid that surrounds the brain and spinal cord, and it contains proteins, cells, and other substances that may be important biomarkers in ALS research. During the procedure, a needle is inserted between two lumbar vertebrae (backbones) in the lower back and into the space in the spinal canal that contains CSF.



Tips to Prep:
Get a good night's rest, eat as usual, and stay well-hydrated prior to the LP visit.

- Sometimes, people feel worried that a lumbar puncture could be risky or painful. In reality, this is a safe and common procedure to collect CSF!**
- LUMBAR PUNCTURE STEP BY STEP**
- 1.) You will be asked to sit or lie down in a position that helps widen the spaces between the bones of the lower spine.
 - 2.) The doctor will cleanse the skin on your lower back to reduce risk of infection, then use a small needle to inject a local anesthetic (such as lidocaine) to numb the site.
 - 3.) The LP needle is inserted into the space containing CSF. A special atraumatic spinal needle (Sprotte) is typically used to reduce the chance of a post-puncture headache. The doctor may need to readjust the needle if CSF cannot be drawn with the first insertion.
 - 4.) Spinal fluid is collected into specimen tubes for lab testing. The LP needle is removed, your back is cleaned, and a band-aid is placed over the LP site.
 - 5.) For your comfort and safety, it is recommended that someone drive you to and from the LP study visit.



QUESTIONS?

Prior to enrolling in a clinical trial, your study team will discuss the LP procedure with you. Please ask your study team for clarification if you have any questions while reviewing the informed consent form.

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>

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*“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

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



Allison Bulat