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

Common Protocol and Shared Infrastructure

Regimen A
Regimen B
Regimen C
Regimen D
Regimen E
Regimen F
Regimen G
Schema for Each Regimen

- Screen for eligibility
- Randomization 3:1
- Placebo
- Active

Screening Period

Randomized Period 24 weeks

Open-Label Extension Period (Active Treatment Extension)
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)
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

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

(as of 3/2/23)

https://bit.ly/3g2NZr5

Site Map & Contacts:
# Checking Site Status Online

As of 3/2/23

## 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 participants.

<table>
<thead>
<tr>
<th>Site</th>
<th>State</th>
<th>Enrollment Status</th>
<th>Trial Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo Clinic Florida</td>
<td>FL</td>
<td>Active, Not recruiting</td>
<td>Jany Paulett</td>
</tr>
<tr>
<td>Nova Southeastern University</td>
<td>FL</td>
<td>Recruiting</td>
<td>Donovan Mott</td>
</tr>
<tr>
<td>Phil Smith Neuroscience Institute, Holy Cross Hospital</td>
<td>FL</td>
<td>Active, Not recruiting</td>
<td>Ashley Stepler</td>
</tr>
</tbody>
</table>
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 elf2B, which is a key regulator of the ISR. Binding of ABBV-CLS-7262 desensitizes elf2B 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 in-human study of ABBV-CLS-7262 showed that this drug was well-tolerated by participants, demonstrated target engagement by increasing elf2B 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.

Visit our website to learn more about what to expect in the trial process.

Regimen F is a Phase 2/3 trial enrolling approximately 345 participants to evaluate the safety and efficacy of ABBV-CLS-7262 as a potential treatment for ALS. This regimen involves biomarker analysis and a covariate flow collection of blood samples to assess the effects of ABBV-CLS-7262.

3.5 Active Drug to Placebo Ratio: Participants who enter this trial have a 3:4 (75%) chance of being assigned to active study drug and a 1:4 (25%) chance of being assigned to placebo during the Initial 13-week placebo-controlled trial (PCT) period.

To see if you may qualify, please review the list of eligibility criteria:

Download 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

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

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