Thank you for joining the weekly webinar!
We are admitting audience members from the waiting room.
Please allow a few moments for the webinar to begin.
HEALEY ALS Platform Trial:

Common Protocol and Shared Infrastructure

- Regimen A
- Regimen B
- Regimen C
- Regimen D
- Regimen E
- Regimen F
- Regimen G

Screen for eligibility → Randomization 3:1 → Active

- Placebo

Screening Period → Randomized Period 24 weeks → Open-Label Extension Period (Active Treatment Extension)

ENROLLMENT COMPLETE

ENROLLING

IN START-UP
36 Sites Currently Active for Regimen F

- Nova Southeastern University
- Essentia Health
- Texas Neurology
- Mass General Hospital
- University of Nebraska
- Hospital for Special Care
- Henry Ford Hospital
- Augusta University
- Beth Israel Deaconess
- University of Texas HSC
- University of Colorado
- Loma Linda University
- Ohio State University
- Cedars Sinai Medical Center
- Duke University
- Wake Forest University
- Saint Alphonsus
- UMass Worcester

(as of 4/20/23)

https://bit.ly/3g2NZr5

Site Map & Contacts:

- Lehigh Valley
- Thomas Jefferson
- University of South Florida
- University of Pennsylvania
- SUNY Upstate
- University of Iowa
- California Pacific Med Center
- Houston Methodist
- Vanderbilt University
- University of Minnesota
- Washington University
- Barrow Neurological Institute
- University of Miami
- Temple University
- University of Virginia
- Johns Hopkins University
- University of Southern CA
- Holy Cross Hospital
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 participants at this time.

<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>
</tbody>
</table>

[Contact a study team near you to discuss enrollment opportunities](https://bit.ly/3g2NZr5)
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.

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

Regimen F: A Phase 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 randomized fluid collection via the lumbar puncture to assess the effects of ABBV-CLS-7262.

3.5 Active Drug to Placebo Bellini: Participants who receive 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 24-week randomized controlled trial (RCT) period.

Active Treatment Extension (ATE): Participants have the option to enroll in the Active Treatment Extension (ATE) following completion of the 24-week RCT. 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/3WjGtV1

Printable Brochures!

Regimen F Brochure
Lumbar Puncture Brochure
General Platform Trial Brochure

ABBV-CLS-7262 is ready to be evaluated as a new potential treatment for ALS

**Problem**
- IDR is activated in ALS
- Aggregates of the protein TDP-43 are observed in most ALS cases
- Drugs tested in ALS clinical trials must have their intended biological effect in people
- The right dose needs to be administered in clinical trials
- Our understanding of ALS is incomplete

**Calico**
- ABBV-CLS-7262 is a potent inhibitor of the ISR by binding to, and activating, eIF2B
- ABBV-CLS-7262 dissolves stress granules containing TDP-43 which may reduce formation of new TDP-43 aggregates
- Blood cells from people given ABBV-CLS-7262 show increased eIF2B activity and reduced ISR
- ABBV-CLS-7262 was measured in the CSF at levels predicted to be pharmacologically active at tolerated doses
- CSF and blood samples will improve our understanding of the ISR in ALS and may identify people most likely to respond to ABBV-CLS-7262

**Topic:** Regimen F Drug Science and Mechanism of Action

**Recording Available:** [https://bit.ly/3mQy5qQ](https://bit.ly/3mQy5qQ)**
The ALS Association/Northeast ALS Consortium Educational Webinar

Why lumbar puncture and CSF biomarkers are important to ALS therapeutic development

*Monday, May 8th
1:00–2:00pm Eastern

Presenter: Nicholas J. Maragakis, M.D., Johns Hopkins University

Register Here:

https://bit.ly/3JTZqzN

Recording will later be available under “educational webinars” on neals.org
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

Upcoming Webinars:
April 27th- Guest speaker Judi Carey, RN (Research Access Nurse at MGH)
May 4th- Weekly Q&A
May 11th- Weekly Q&A