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

Weekly Q&A – April 13, 2023

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

Northeast Amyotrophic Lateral Sclerotic Consortium

Harvard Medical School
Massachusetts General Hospital
NEALS
NEurological Clinical Research Institute
BARROW Neurological Institute
Berry Consultants
SEELOS THERAPEUTICS
Calico
AMG
The AMG Foundation

TACKLE ALS
ALSASSOCIATION
MUDA
MUSCULAR DYSTROPHY ASSOCIATION
ALS Association
FINDINGACURE
I AM ALS
TAMBOURINE
ALS ONE
RUN2REVIVE
The Arthur M. Blank Family Foundation

BASEBALL: WINTER MEETINGS

CLINICAL NANOMEDICINE
prilenia

UCB
biohaven pharmaceuticals

The AMG Foundation
HEALEY ALS Platform Trial:

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

Common Protocol and Shared Infrastructure

- **Screen for eligibility**
- **Randomization 3:1**

ENROLLMENT COMPLETE

ENROLLING

IN START-UP
30 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

(as of 4/13/23)

Site Map & Contacts:
- Saint Alphonsus
- UMass Worcester
- 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

https://bit.ly/3g2NZr5
### 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>

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

[COVID-19 clinical trial website](https://bit.ly/3g2NZr5)
Regimen F: ABBV-CLS-7262, by Calico and AbbVie - Now Recruiting

Regimen F: 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 first-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: 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. The regimen involves biomarker analysis and cerebrospinal fluid collection via two lumbar punctures to assess the effects of ABBV-CLS-7262.

LUMBAR PUNCTURE

Lumbar puncture (LP) or spinal tap is a procedure to remove a small sample (LP fluid or a specimen) of cerebrospinal fluid (CSF) from the inner 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 lumbosacral vertebrae (Burstions) in the lower back and into the space in the spinal canal that contains CSF.

Sometimes, people feel twisted that a lumbar puncture could be risky or painful. In reality, this is safe and common procedure for a healthy individual of 30 years.

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.

Printable Brochures!

Regimen F Brochure
Lumbar Puncture Brochure
General Platform Trial Brochure

Regimen F Drug Science Q&A Webinar
Hosted: Monday, March 27th
Recording Available!
https://bit.ly/3r6Nd2L

Webinar Recordings

Science & Mechanism of Action Series

March 27, 2023: ABBV-CLS-7262 Mechanism of Action & Science
Merit Cudkowicz, MD, MSc and Sabrina Paganoni, MD, PhD, along with regimen co-lead Senda Ajroud-Driss, MD and research scientists from Calico Life Sciences, presented the rationale and science behind ABBV-CLS-7262, the investigational product being tested in Regimen F of the HEALEY ALS Platform Trial, and answered questions from the audience.
Watch recording | Download slides (PDF)
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

ALS Link sign-up:
https://bit.ly/3o2Ds3m

Upcoming Webinars:
April 20th- Weekly Q&A
April 27th- Weekly Q&A