

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 – May 11, 2023



## Healey Center

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



Calico



THE ARTHUR M. BLANK  
FAMILY FOUNDATION



The AMG Foundation

# Building Community & Partnership in ALS Research



## Patient Navigator: Central Resource

**2,614** Total emails/phone calls/zoom calls with ALS families  
**630** Uses of the Online Eligibility Checking Tool  
**39** Countries in contact about research



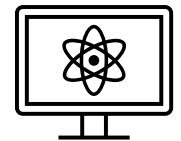
## Weekly Webinars: News & Updates

**115** Public Q&A webinars hosted to date  
**50+** Guest speakers featured  
**8,317** Total attendees, **71** Weekly average  
**40,553** Total views on YouTube



## Drug Science Q&A Webinars

**6** Webinars hosted (Regimens A,B,C,D,E,F)  
**8,481** Total views on YouTube  
**242** Questions answered live

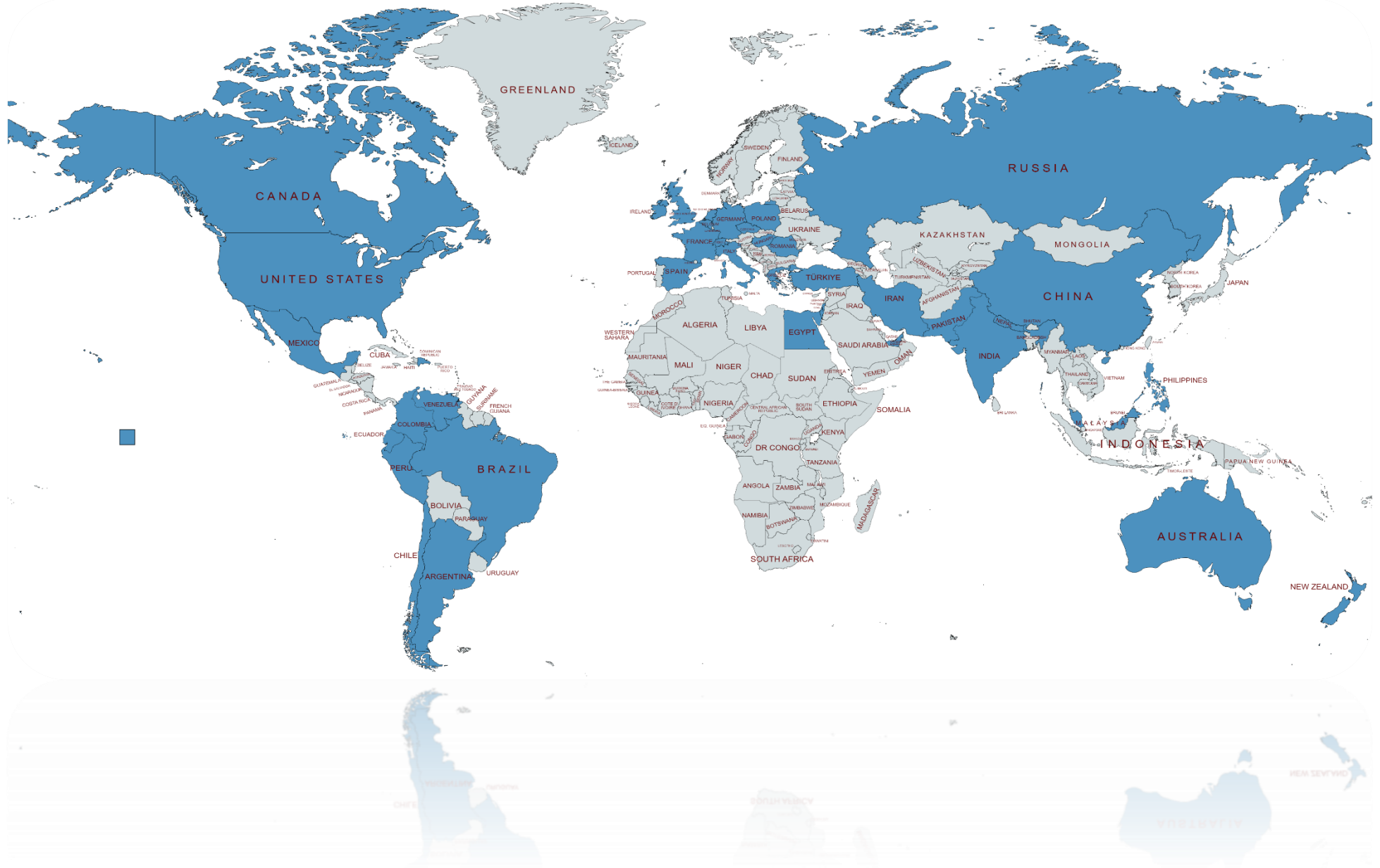


*(Data Collected Oct 2020-Mar 2023)*



# Global Reach of Patient Navigation: 39 Countries

- Argentina
- Australia
- Belgium
- Brazil
- Canada
- Chile
- China
- Columbia
- Czech Republic/ Czechia
- Dominican Republic
- Ecuador
- Egypt
- England/UK
- France
- Germany
- Greece
- Hungary
- India
- Iran
- Ireland
- Israel/Palestine
- Italy
- Malaysia
- Mexico
- Nepal
- Netherlands
- New Zealand
- Pakistan
- Peru
- Philippines
- Poland
- Romania
- Russia
- Spain
- Switzerland
- Turkey
- United Arab Emirates
- United States
- Venezuela



# Online Eligibility Checking Tool

## Find Out If You're Eligible

We've prepared a short list of questions to help you find out if you might be eligible to participate in the HEALEY ALS Platform Trial.

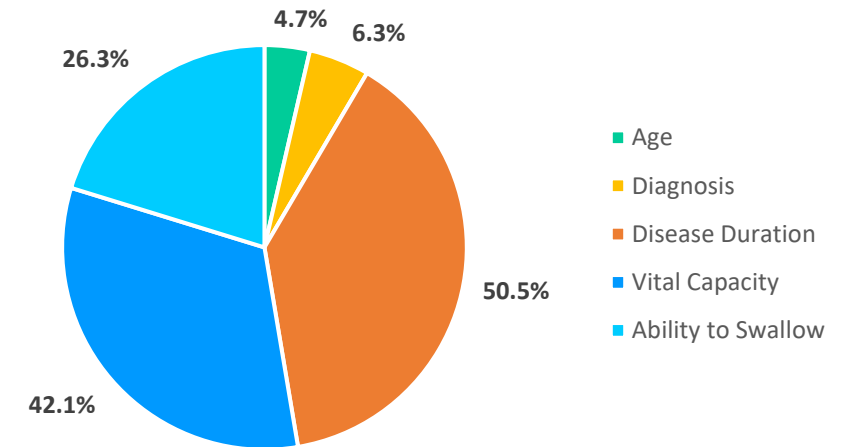
Please note that the result of this survey does not serve as official confirmation of your eligibility, as many factors are considered prior to study participation (view a full list of inclusion / exclusion criteria [here](#)). Determining eligibility for the Platform Trial will depend on a thorough assessment of your clinical symptoms, review of past medical history, and lab work that can only be performed by an investigator (doctor or nurse practitioner) on the trial.

[Eligibility questions](#)



<https://bit.ly/3ezu4Qx>

## Reasons for "Not Eligible" Survey Responses



Total survey responses generated between 5/10/21 and 4/18/23	650
How many total completed survey responses?	644
How many people were eligible based on survey (all yes)?	454
How many were ineligible (one or more no)?	190
Reasons for "No"	
18 or older?	9
Dx with ALS?	12
Symptom onset within 36mos?	96
VC at or above 50%?	80
Ability to swallow pills and liquids?	50

# Who are we?



**Catherine Small**  
Patient Navigator



**Allison Bulat**  
Community Engagement



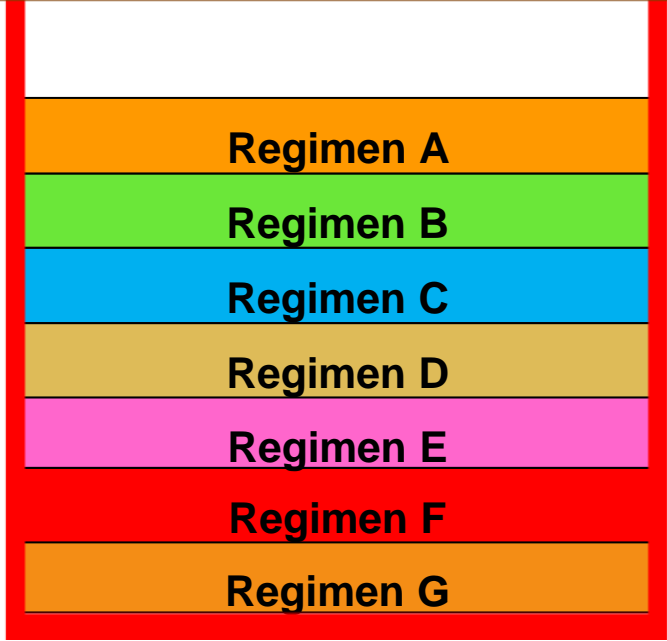
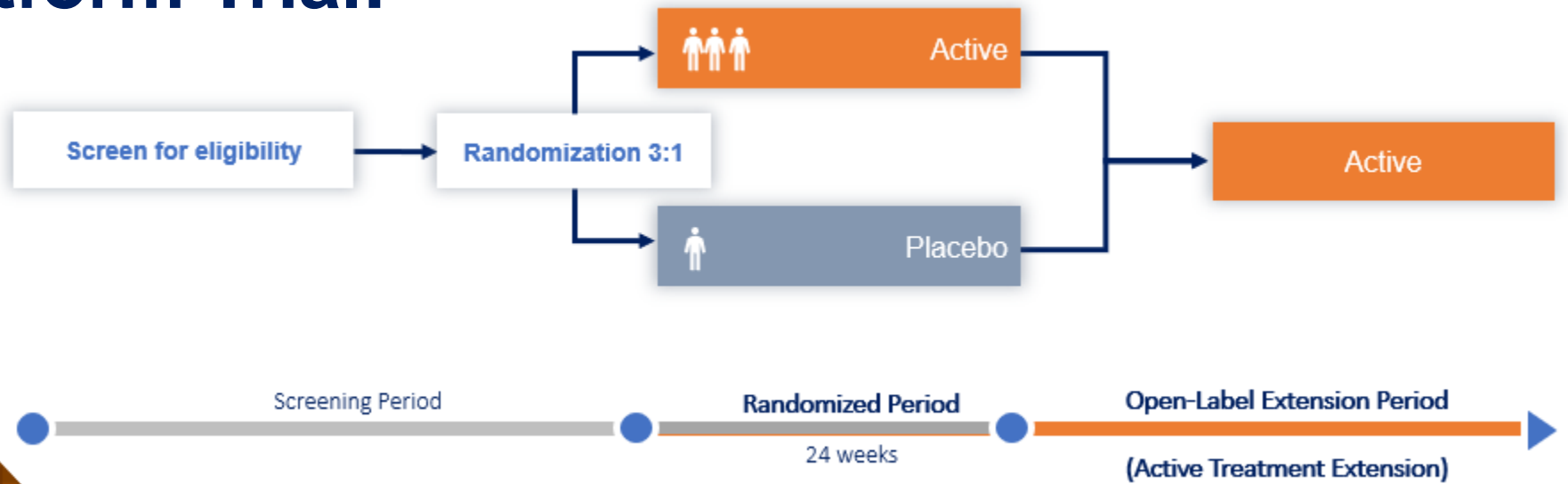
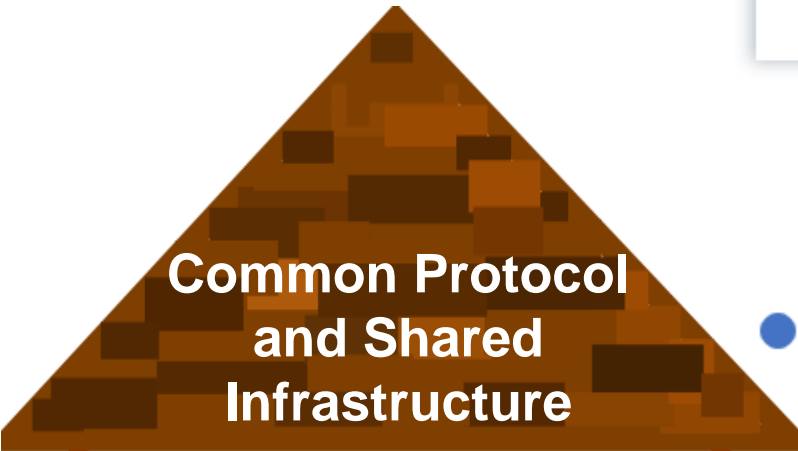
**Judi Carey, RN**  
Research Access Nurse

Contact the Patient Navigator  
HEALEYALSPlatform@mgh.harvard.edu  
833-425-8257 (HALT ALS)

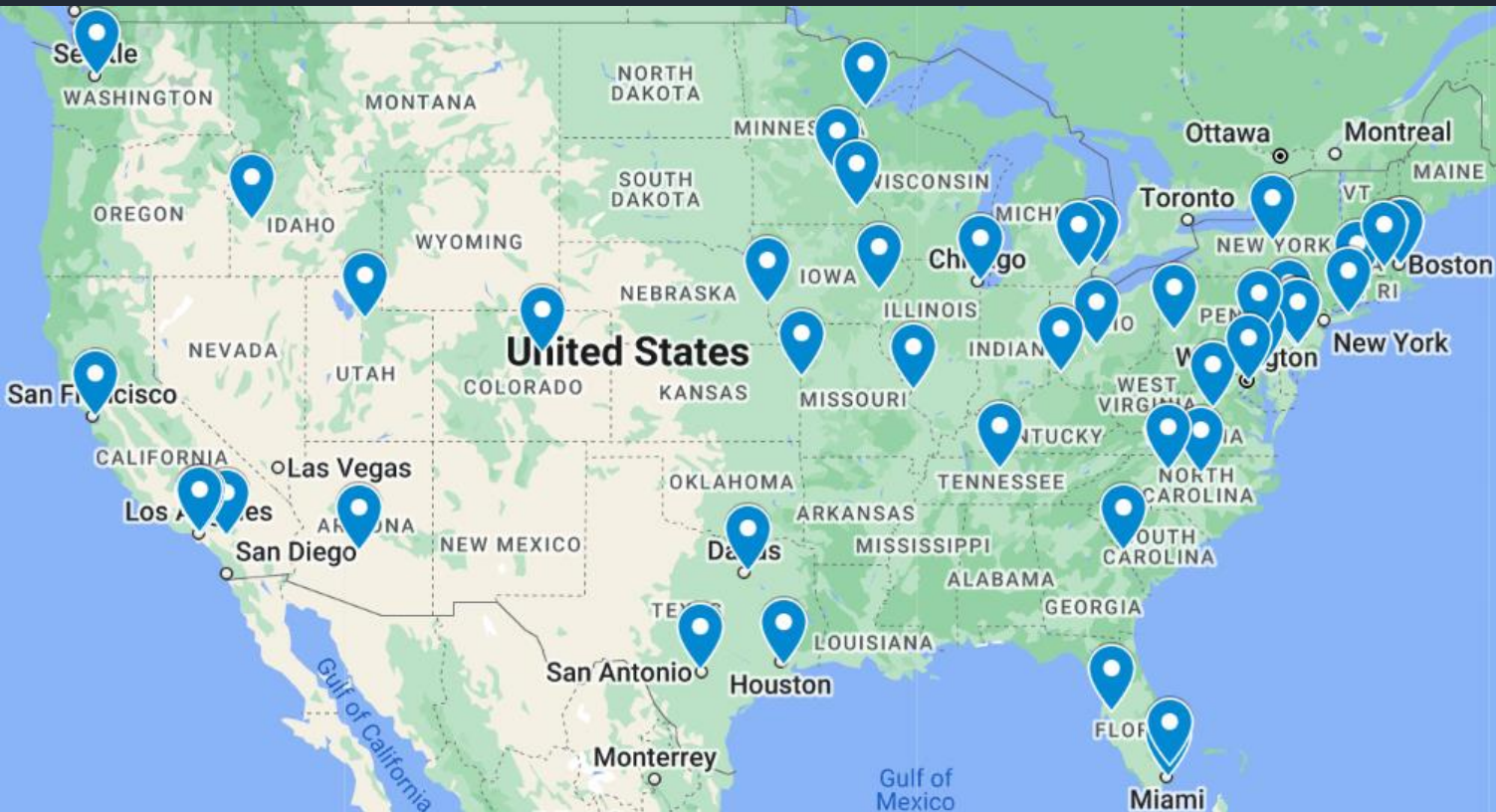


<https://bit.ly/3UPTzR9>

# HEALEY ALS Platform Trial:



# 48 Sites Currently Active for Regimen F



(as of 5/11/23)

- ✓ 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
- ✓ 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
- ✓ University of Washington
- ✓ University of Utah
- ✓ Penn State Hershey
- ✓ University of Michigan
- ✓ University of Kansas
- ✓ Stony Brook University
- ✓ University of Cincinnati
- ✓ Mayo Clinic Rochester
- ✓ Northwestern University
- ✓ Georgetown University
- ✓ Kaiser, Los Angeles
- ✓ UPMC

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 participants at this time.

Contact a study team near you to discuss enrollment opportunities

Site	State	Enrollment Status	Trial Contact Information
Mayo Clinic Florida	FL	Active, Not recruiting	<a href="#">Jany Paulett</a>
<b>Nova Southeastern University</b>	<b>FL</b>	<b>Recruiting</b>	<a href="#">Donovan Mott</a>



<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.

[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/3ExPa18>




**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 randomized controlled trial (RCT) period.

**Active Treatment Extension (ATE):**  
Participants have the option to enroll in the ATE for ABBV-CLS-7262 upon 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/3Dqatnm>



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



<https://bit.ly/3SIwH4X>

## Printable Brochures!



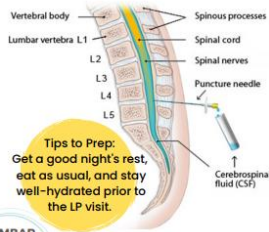
Regimen F Brochure  
Lumbar Puncture Brochure  
General Platform Trial Brochure

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.

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!



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

**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.

# Regimen F Drug Science Q&A Webinar



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

### Problem

### Calico

ISR is activated in ALS

ABBV-CLS-7262 is a potent inhibitor of the ISR by binding to, and activating, eIF2B

Aggregates of the protein TDP-43 are observed in most ALS cases

ABBV-CLS-7262 dissolves stress granules containing TDP-43 which may reduce formation of new TDP-43 aggregates

Drugs tested in ALS clinical trials must have their intended biological effect in people

Blood cells from people given ABBV-CLS-7262 show increased eIF2B activity and reduced ISR

The right dose needs to be administered in clinical trials

ABBV-CLS-7262 was measured in the CSF at levels predicted to be pharmacologically active at tolerated doses

Our understanding of ALS is incomplete

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



25

Topic: Regimen F Drug Science and Mechanism of Action

Recording Available: <https://bit.ly/3mQy5qQ>





The ALS Association/Northeast ALS Consortium Educational Webinar

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



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

**View Here:**



<https://bit.ly/3Mc1HZt>

*Recording are available under  
“educational webinars” on neals.org*

# Patient Navigation

## Central resource for people living with ALS



Catherine Small

Phone: 833-425-8257 (HALT ALS)

E-mail: [healeyalsplatform@mgh.harvard.edu](mailto:healeyalsplatform@mgh.harvard.edu)

Weekly webinar  
registration:



<https://bit.ly/3r6Nd2L>

ALS Link sign-up:



<https://bit.ly/3o2Ds3m>

### Upcoming Webinars:

**May 18th-** Weekly Q&A and overview of FDA approved medications for ALS

**May 25th-** Weekly Q&A and overview of Platform Trial progress to date

**June 1st-** Weekly Q&A



Allison Bulat