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 – June 15, 2023

Massachusetts General Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL

Healey & AMG Center

Sean M. Healey & AMG Center for ALS
at Massachusetts General Hospital

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

NCRI NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BARROW Neurological Institute

Berry Consultants Statistical Innovation

1850 MELIORA

ucb

biohaven pharmaceuticals

CLene NANOMEDICINE

prilenia

SEELOS THERAPEUTICS

Calico

DENALI THERAPEUTICS

TACKLE ALS "DON'T BE SORRY LETS BEAT THIS"

ALS ASSOCIATION

MDA Muscular Dystrophy Association

SALSA For a Cure

alsFINDINGaCURE

IAM ALS

TAMBOURINE

ALS ONE

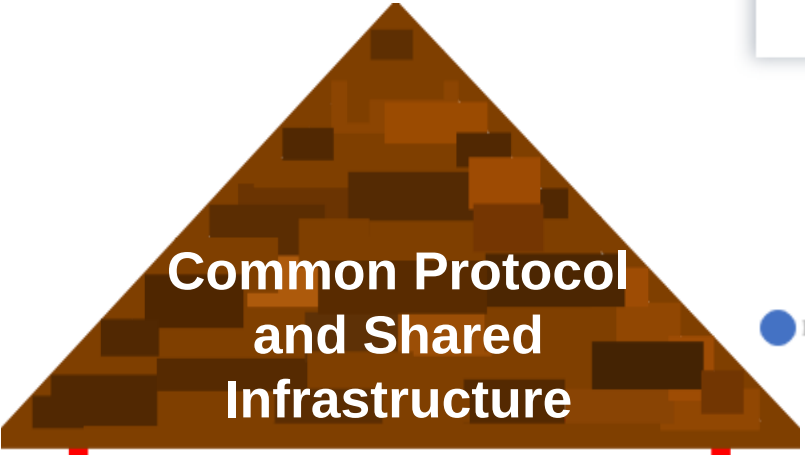
RUN2REVIVE MIND · BODY · POTENTIAL

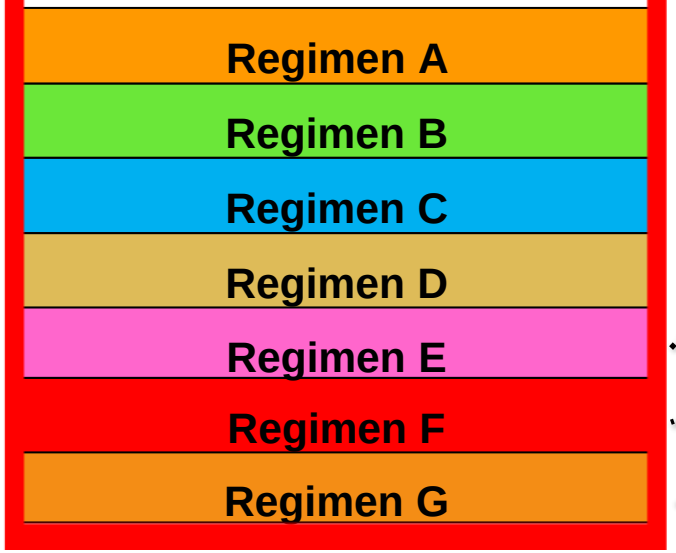
THE ARTHUR M. BLANK FAMILY FOUNDATION

BASEBALL WINTER MEETINGS SAN DIEGO 2019

AMG The AMG Foundation

HEALEY ALS Platform Trial:



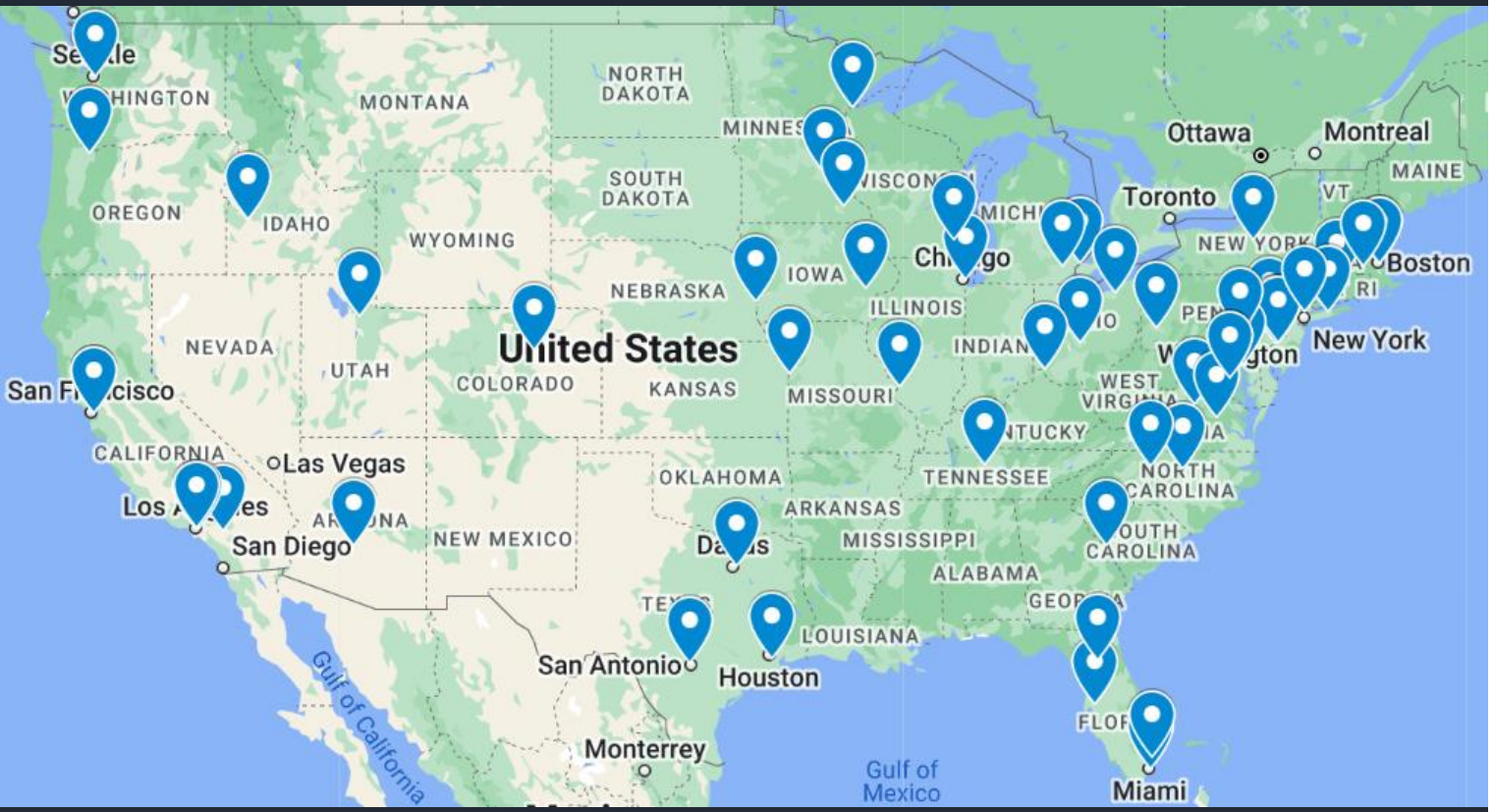


SEELOS THERAPEUTICS | ENROLLMENT COMPLETE

Calico | ENROLLING

DENALI THERAPEUTICS | ENROLLING

56 Sites Currently Active for Regimen F



(as of 6/15/23)

- 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
- University of Pittsburgh
- Virginia Commonwealth
- Med College Wisconsin
- University of CA, San Fran
- University of Florida, Gainesville
- Providence Brain and Spine
- Cleveland Clinic
- George Washington University
- Hackensack University

Site Map & Contacts:

https://bit.ly/3g2NZr5

Enrollment Update: Regimen F (as of 6/15/23)

119

Participants consented to Master Protocol since RGF initiated

76

Participants assigned to RGF

64

Participants randomized within RGF (enrollment goal ≈240)

Thank You

for your partnership in ALS research

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.

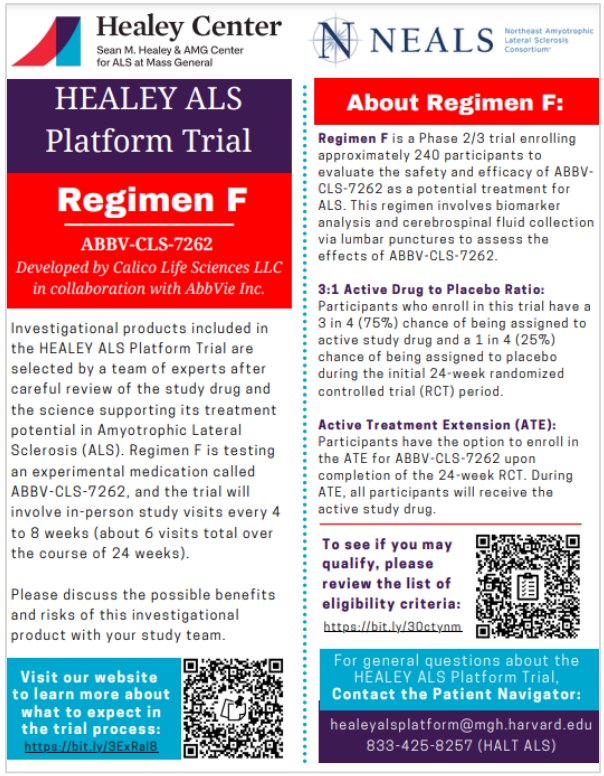
The integrated stress response (ISR) is a fundamental transient process that regulates cell function during various stressful conditions. Tissue studies suggest that the ISR is chronically induced in people with ALS. It is proposed that TDP-43 aggregates, a hallmark feature in the motor neurons of people 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 a webinar about the science behind ABBV-CLS-7262

Watch this video for more information on the mechanism of action behind ABBV-CLS-7262.

Download Regimen F Brochure
Download Lumbar Puncture Brochure



https://bit.ly/3SIwH4X

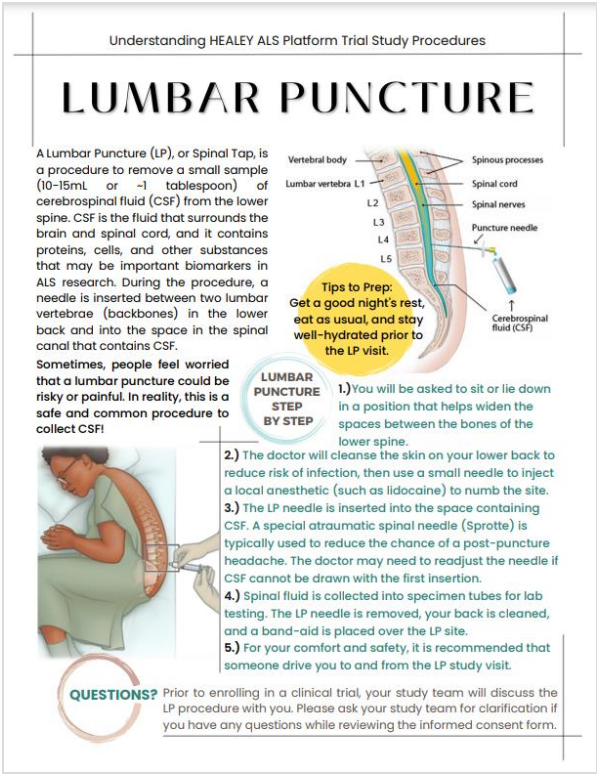
Printable Brochures!

↓

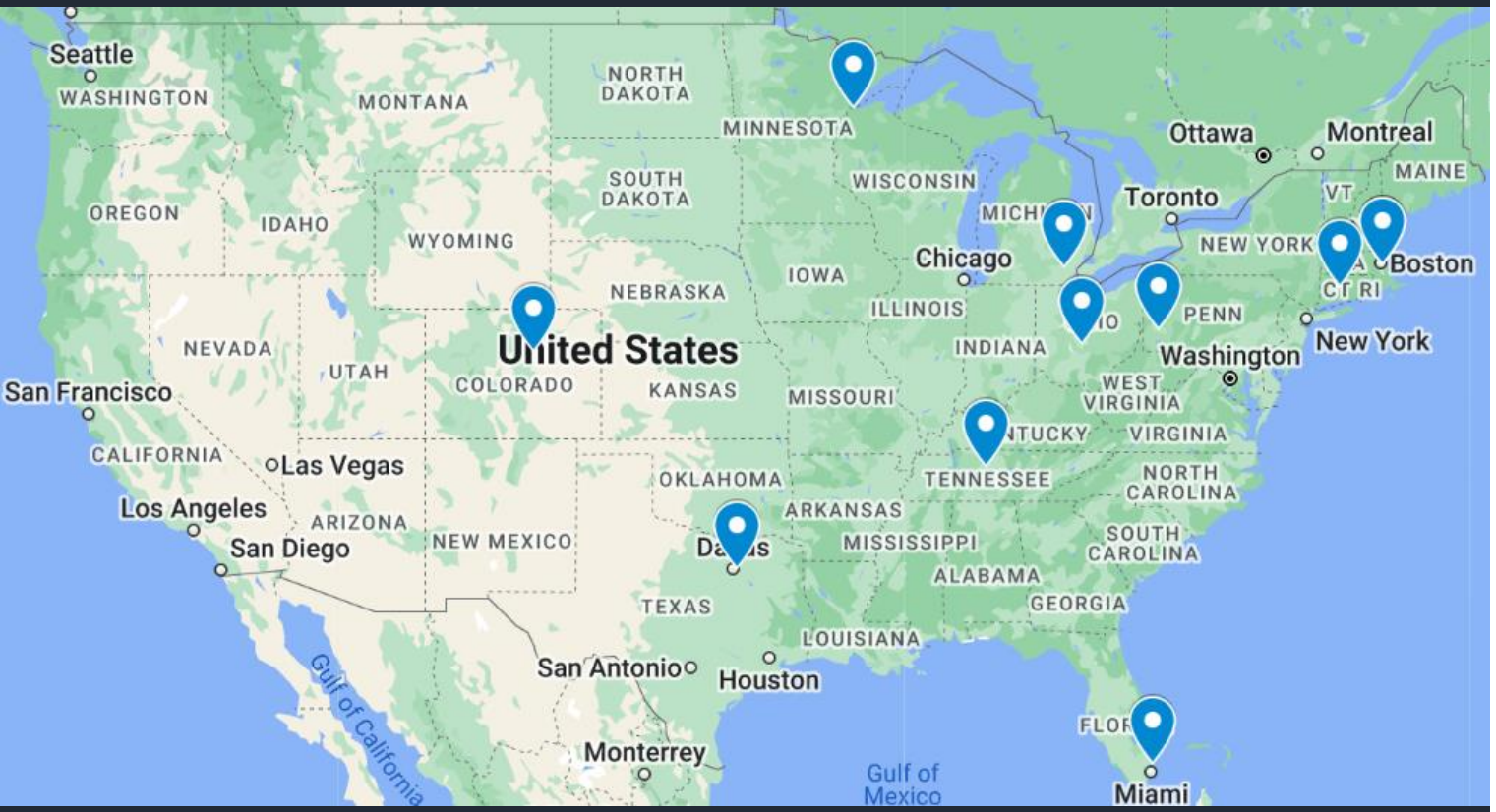
Regimen F Brochure

Lumbar Puncture Brochure

General Platform Trial Brochure



11 Sites Currently Active for Regimen G



(as of 6/15/23)

- ☑ Nova Southeastern University
- ☑ Texas Neurology
- ☑ University of Colorado
- ☑ Essentia Health
- ☑ University of Pittsburgh
- ☑ Beth Israel Deaconess
- ☑ Mass General Hospital
- ☑ Ohio State University
- ☑ University of Michigan
- ☑ Hospital for Special Care
- ☑ Vanderbilt University

Site Map & Contacts:

https://bit.ly/3g2NZr5

Regimen G Resources on MGH Website

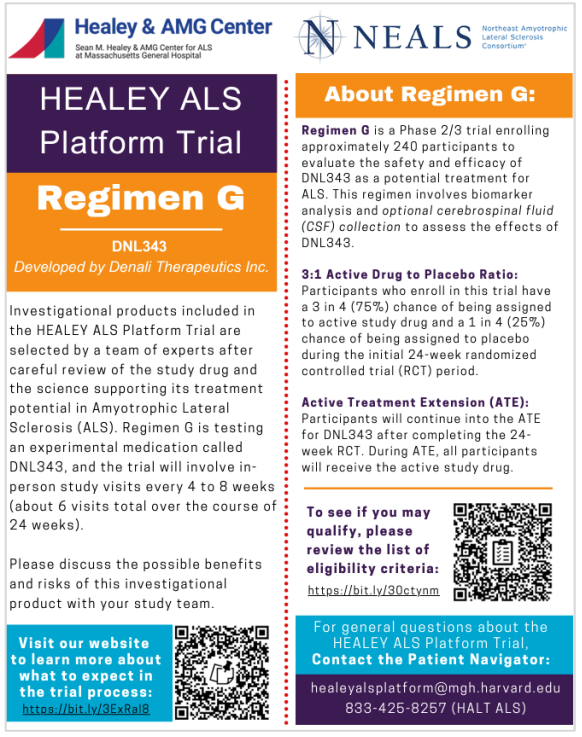
Regimen G: DNL343, by Denali Therapeutics

DNL343 is an investigational drug developed by Denali Therapeutics Inc. DNL343 aims to improve survival of nerve cells and slow ALS progression by restoring normal protein production and decreasing potentially harmful buildup of TDP-43 in cells affected by ALS. Abnormal TDP-43 buildup in nerve cells is found in >95% of individuals living with ALS.

The integrated stress response (ISR) appears to be overactive in ALS, and chronic activation of the ISR can lead to cellular dysfunction. In stressed cells, eIF2B activity is suppressed by the ISR, which leads to impaired protein synthesis and the formation of stress granules containing TDP-43. TDP-43 containing stress granules are thought to lead to TDP-43 inclusions, a hallmark of ALS pathology. DNL343 is a drug that is designed to inhibit the ISR, restore normal protein synthesis, and prevent the formation of TDP-43 containing stress granules as well as dissolve existing ones; the effects of which may be beneficial in the treatment of ALS.

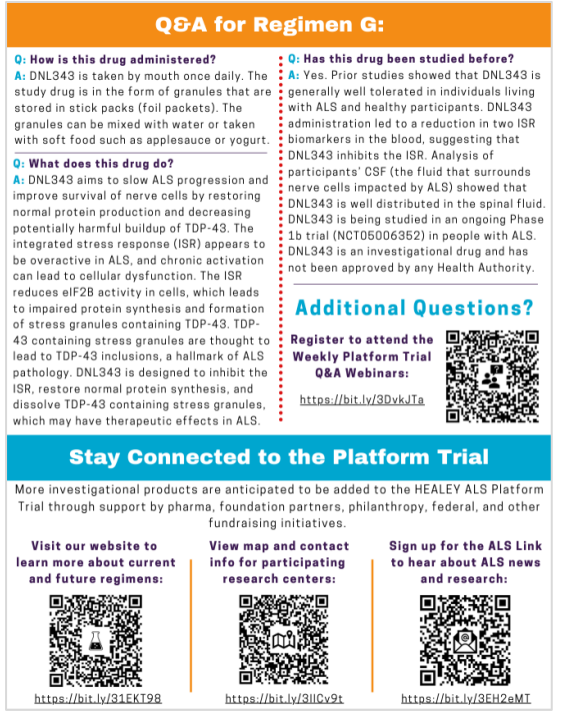
Prior studies of DNL343 showed that this drug is generally well tolerated in healthy participants and individuals living with ALS. Experimental treatment with DNL343 showed a reduction in ISR biomarkers measured in the blood, suggesting that DNL343 inhibits the ISR. Analysis of cerebrospinal fluid (the fluid that surrounds the brain, spinal cord, and nerve cells impacted by ALS) obtained from participants in these studies showed that DNL343 is well distributed in the spinal fluid. Results from previous studies support continued evaluation of DNL343 as a potential treatment for ALS in the HEALEY ALS Platform Trial. DNL343 is also being studied in an ongoing Phase 1b trial (NCT05006352) in people with ALS.

Download Regimen G Brochure



https://bit.ly/3SIwH4X

Printable Brochure Available!



Regimen G Drug Science Q&A Webinar

Open to everyone!

Thursday, July 20th

5:00-6:00pm Eastern

Topic: DNL343 Drug Science and Mechanism of Action

Link to Register: https://bit.ly/3NqJU1j

DENALI

Checking Site Status Online

Contact a study team near you to discuss enrollment opportunities

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.

Site	State	Enrollment Status	Trial Contact Information
Mayo Clinic Florida	FL	Active, Not recruiting	Jany Paulett
Nova Southeastern University	**FL**	**Recruiting**	**Donovan Mott**

https://bit.ly/3g2NZr5

THE ALS ASSOCIATION/NORTHEAST ALS CONSORTIUM

Educational Webinar

UNDERSTANDING STATISTICAL AND CLINICAL SIGNIFICANCE

SPEAKERS

JINSY ANDREWS, MD, MSC
COLUMBIA UNIVERSITY

CHRISTINA FOURNIER, MD, MSC
EMORY UNIVERSITY

ERIC MACKLIN, PhD
HARVARD MEDICAL SCHOOL

~~THURSDAY | 15 JUNE~~
~~4:00 - 5:00 PM ET~~

What do researchers and scientists mean when they describe a study as “statistically significant?” How do people with ALS and clinicians understand whether or not a treatment option is “clinically significant?” This webinar and panel discussion will provide a framework for understanding the results of ALS clinical trials, using several recent studies as examples.

Rescheduled!
WED, JUN 21
1:00-2:00pm ET

Register Here:

https://bit.ly/3oubqBo

Patient Navigation
Central resource for people living with ALS

Catherine Small

Allison Bulat

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:

June 22nd- Weekly Q&A **and Lumbar Puncture Discussion with Shafeeq Ladha, MD**

June 29th- Weekly Q&A **with Hilda Gutierrez from Beth Israel Deaconess (Boston)**

July 6th- Weekly Q&A **with Bill Cho MD, PhD from Calico Life Sciences (Regimen F)**