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.

The HEALEY ALS Platform Trial

A Multistakeholder Partnership to Accelerate ALS Drug Development

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

Design and Launch

Platform Level Learnings

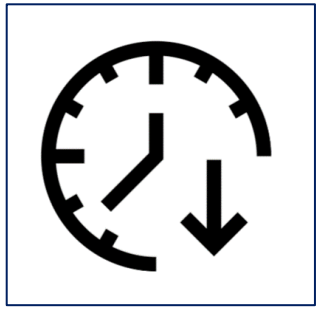
Regimen A-D Results

What's Next

Traditional Clinical Trial

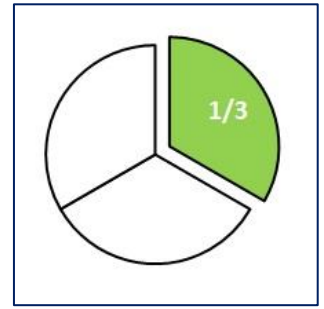
vs.

HEALEY ALS Platform Trial



Cuts time in 1/2

Cuts costs by 1/3



Reduces placebo

Platform trials have several advantages over traditional trials

Accelerating innovation for a cure

Merit Cudkowicz, MD, MSc
Sean M. Healey

"I lost the privilege of working on the human time clock on January 6, 2018
The ALS clock is a lot faster"

Sandy – Person with ALS

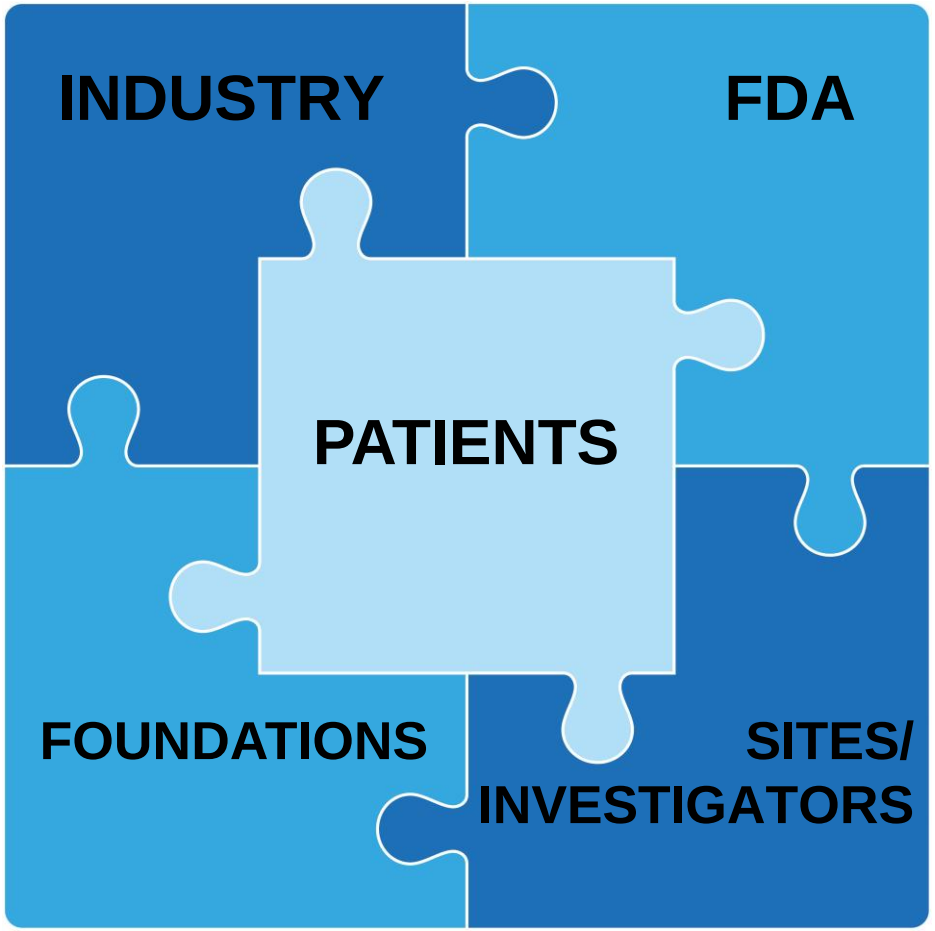
Worked with multiple stakeholders to launch the trial efficiently

ALS Platform Trial Industry Workshop

"Platform trials may possibly be the best thing I have seen since diagnosis!"

★★★★★

5-stars *Patient-Centric Trial Design (PaCTD) Rating*



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"I have not seen this level of patient interest since the 90's"
(Darah Heitzman; Texas Neurology site PI)

➢The HEALEY ALS Platform Trial is grounded in robust academia – industry partnerships

HARVARD MEDICAL SCHOOL

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

ALS ASSOCIATION

MDA Muscular Dystrophy Association

SALSA For a Cure

alsFINDINGaCURE

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

IAM ALS

TAMBOURINE

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BARROW Neurological Institute

ALS ONE

RUN2REVIVE MIND · BODY · POTENTIAL

Berry Consultants Statistical Innovation

1850 MELIORA

ucb

biohaven pharmaceuticals

CLene NANOMEDICINE

prilenia

THE ARTHUR M. BLANK FAMILY FOUNDATION

BASEBALL WINTER MEETINGS SAN DIEGO 2019

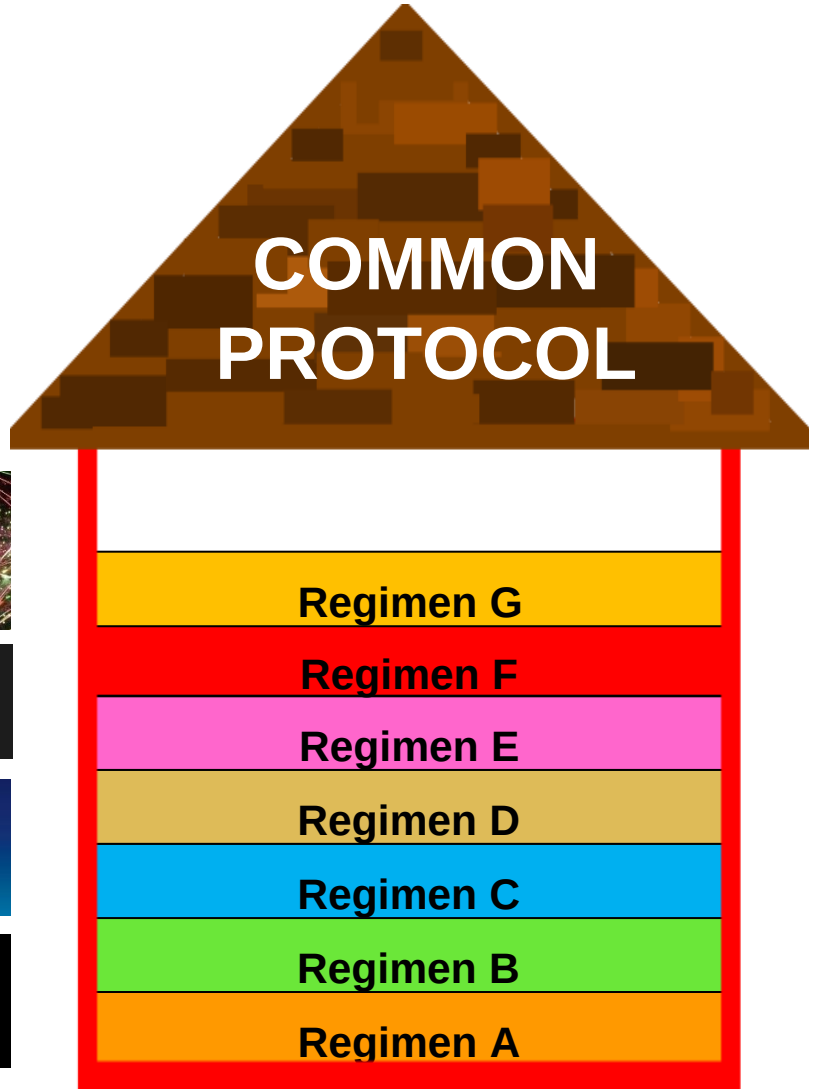
SEELOS THERAPEUTICS

Calico

DENALI THERAPEUTICS

AMG The AMG Foundation

➢Common Protocol and Shared Infrastructure Allow for Operational and Scientific Efficiencies



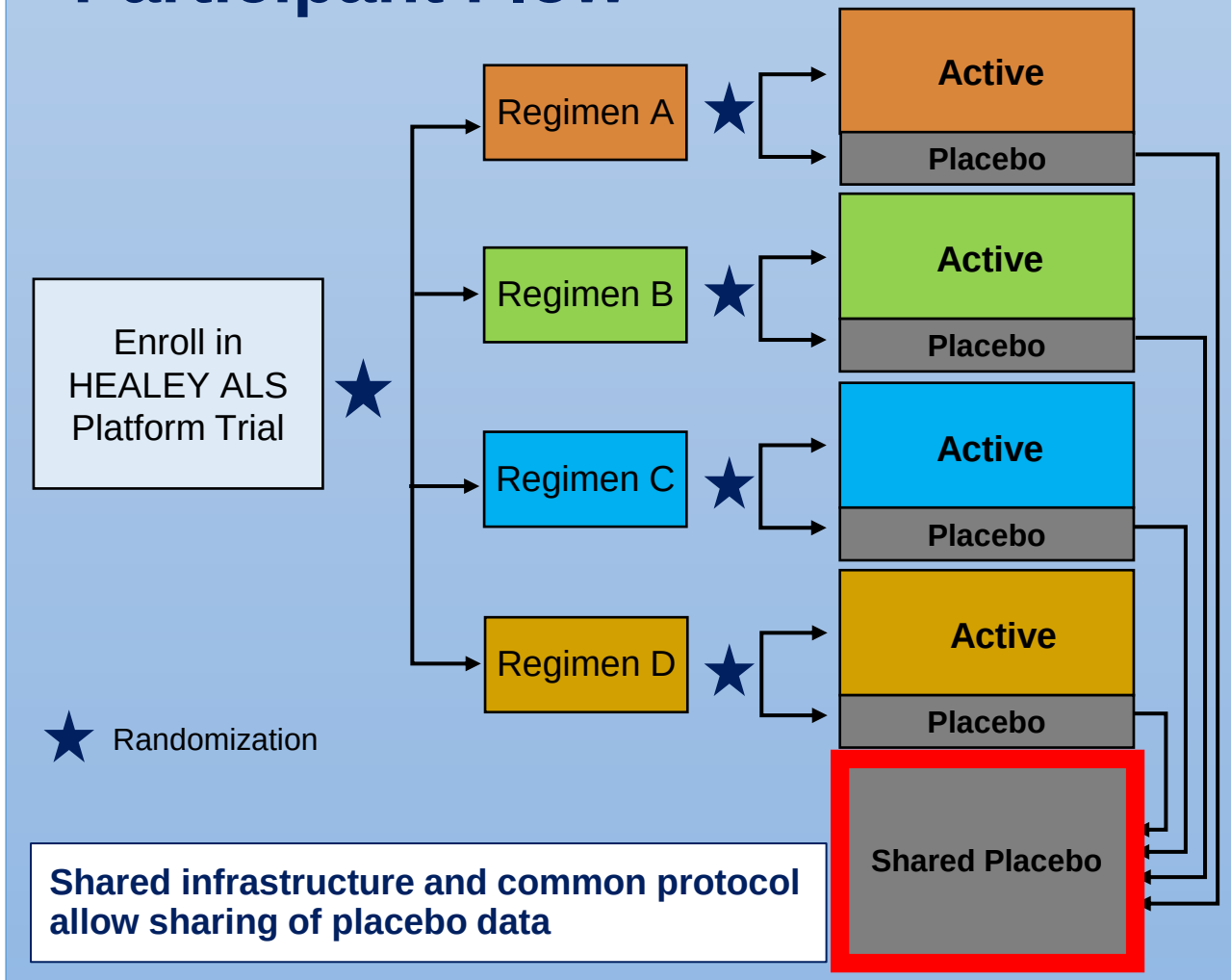
- ➢1 Protocol
- ➢(Phase 2/3)
- ➢1 single IRB
- ➢Central Governance

- ➢7 Regimens
- ➢70+ Enrolling Sites
- ➢~1300 Participants

Regimen: Active Study Drug + Matching Placebo

➢Each regimen is compared to the shared placebo dataset, which keeps growing as new regimens are added

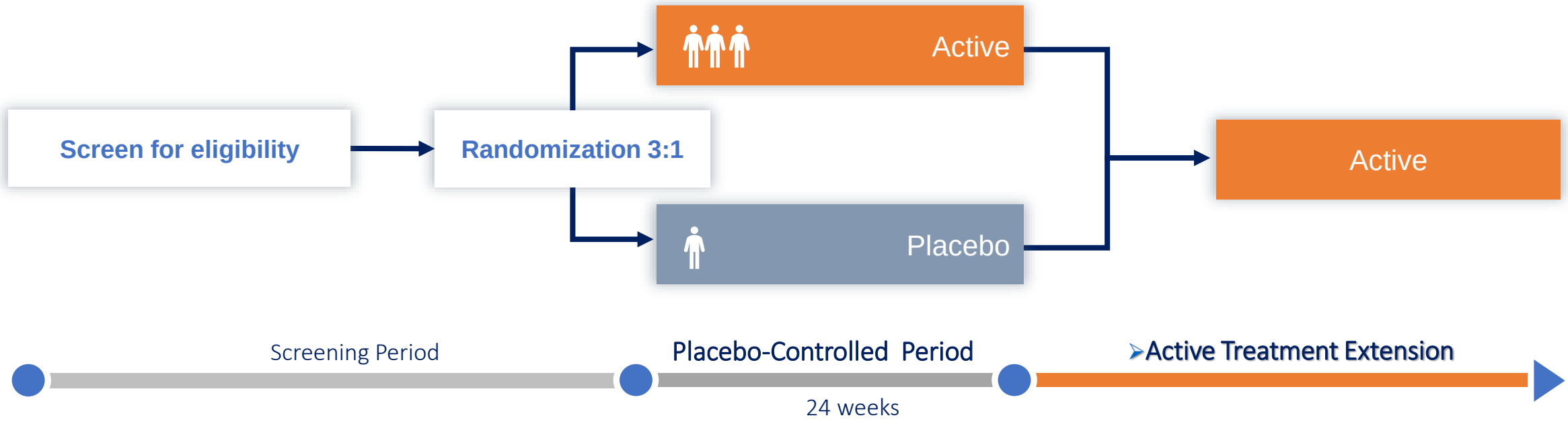
Participant Flow



➢KEY ELIGIBILITY CRITERIA

1. Sporadic or familial ALS
   - (possible, probable, lab-supported probable, or definite by revised EEC)
2. Time since weakness onset ≤ 3 years
3. Slow vital capacity ≥ 50% of predicted
4. Able to swallow
5. Either not take or be on stable dose of riluzole for ≥ 30 days
6. Either not take or have completed at least one cycle of edaravone
7. Either not take or have started Relyvrio/ Albrioza ≥ 30 days prior to screening

➢The objective of each regimen is to provide a go / no go decision to inform the clinical development program of the regimen study drug



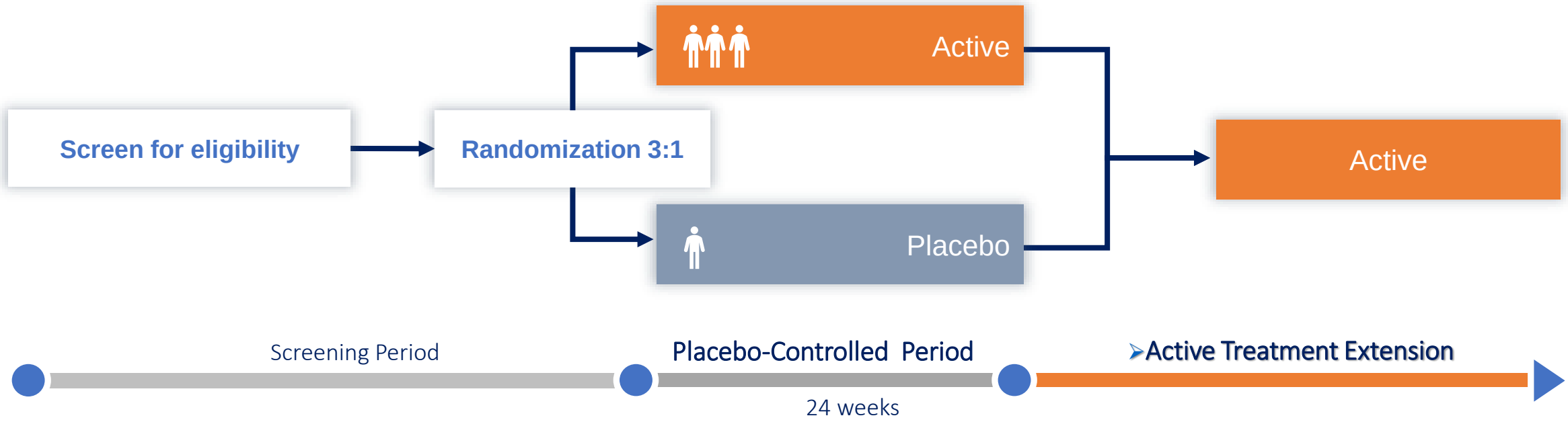
Primary Endpoint (Placebo-Controlled Period)

Change from baseline through week 24 in disease severity as measured by the ALSFRS-R total score and survival

Safety, Secondary, and Exploratory Endpoints

(respiratory function, muscle strength, survival, biomarkers + regimen-specific endpoints)

➢The objective of each regimen is to provide a go / no go decision to inform the clinical development program of the regimen study drug

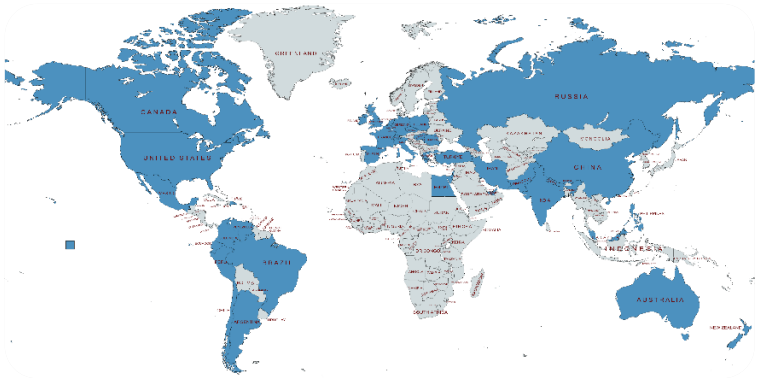


➢Interim analyses are planned to occur every 12 weeks and occur simultaneously for all actively enrolling regimens

➢Futility assessments for a regimen begin at the next interim analysis after the regimen had 40 randomized participants with the opportunity to complete at least 24 weeks of follow-up

Patients are eager to learn about and participate in innovative research

Patient Navigator Team
Building Community & Partnership in ALS Research



Catherine Small

Allison Bulat

Patient Navigator: Central Resource

2,602 Total emails/phone calls/zoom calls with ALS families
630 Uses of Online Eligibility Checking Tool
39 Countries in contact about research

Weekly Webinars: News & Updates

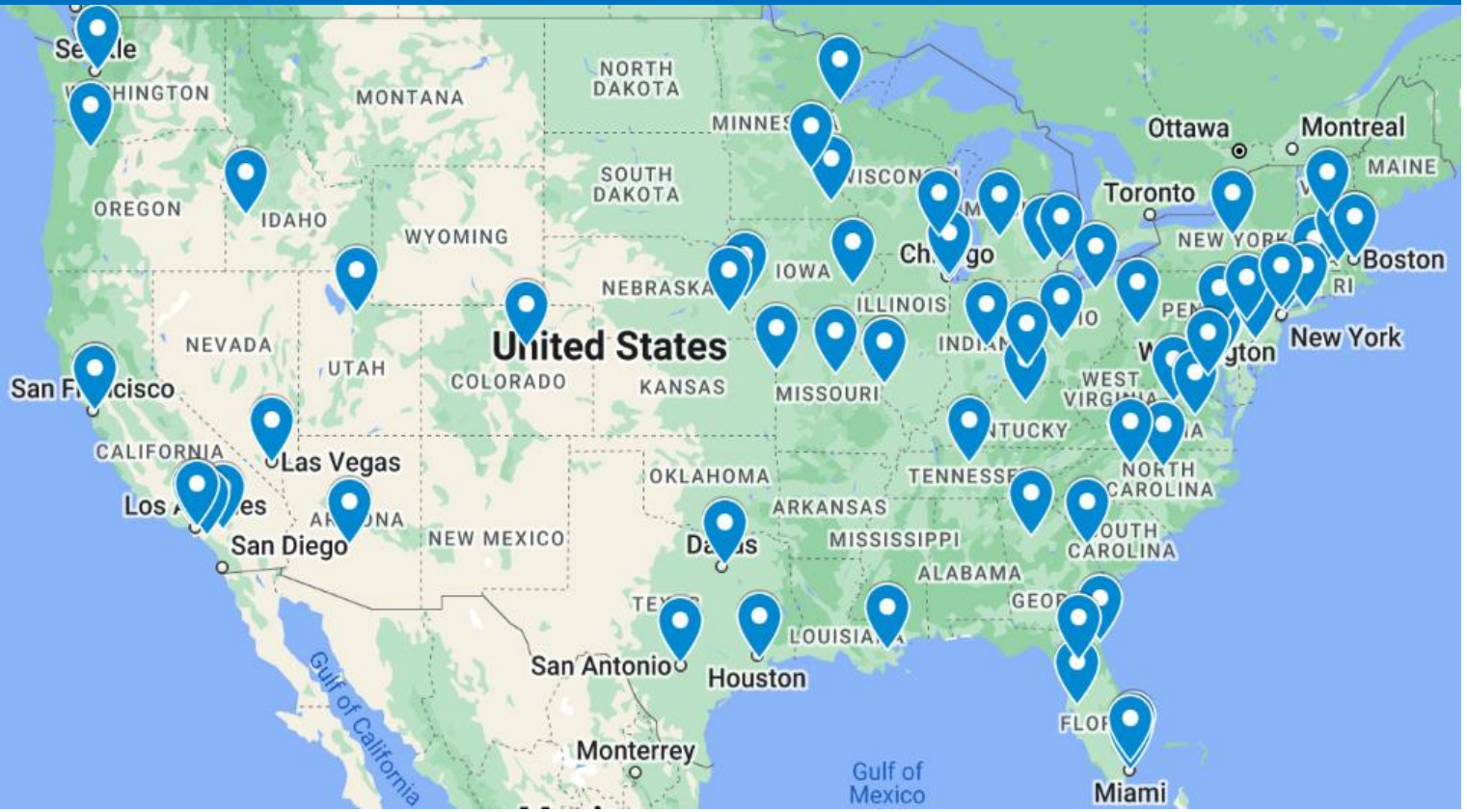
115 Public Q&A webinars hosted to date
50+ Guest speakers featured
8,317 Total attendees, **71** Weekly average
40,553 Total views on YouTube

Drug Science Q&A Webinars

6 Webinars hosted (Regimens A-F)
8,481 Total views on YouTube
242 Questions answered live

(Data Collected Oct 2020-Mar 2023)

Providing research access across a diverse network of 70+ NEALS sites

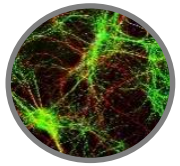


NEALS Northeast Amyotrophic Lateral Sclerosis Consortium®

- Texas Neurology
- Mass General Hospital
- UTHSCSA
- Hospital for Special Care
- Holy Cross Hospital
- Thomas Jefferson
- Houston Methodist
- Henry Ford Health System
- Barrow Neurological Institute
- Ohio State University
- Northwestern University
- University of Chicago
- Wake Forest
- University of Nebraska
- Loma Linda University
- University of Washington
- University of Iowa
- Washington University
- University of Pennsylvania
- University of Michigan
- California Pacific Medical Center
- Penn State Hershey
- UMass Worcester
- University of Miami
- University of Colorado
- Cedars-Sinai
- University of Florida
- University of South Florida
- Columbia University
- University of Virginia
- Emory University
- University of Maryland
- SUNY Upstate
- Beth Israel Deaconess
- Temple University
- Dartmouth-Hitchcock
- Medical College of Wisconsin
- Spectrum Health
- University of Missouri
- University of Minnesota
- Johns Hopkins University
- University of CA Irvine
- University of Kansas
- Vanderbilt University
- University of Kentucky
- Mayo Rochester
- Duke University
- Neurology Associates
- Ochsner Health System
- Mayo Clinic Florida
- St. Louis University
- Providence Brain and Spine
- Georgetown University
- University of Southern California
- Cleveland Clinic
- George Washington University
- University of California, San Francisco
- Indiana University
- Stony Brook University
- University of Pittsburgh
- University of Utah
- Augusta University
- University of Cincinnati
- Virginia Commonwealth University
- Swedish Medical Center
- Las Vegas Clinic
- Kaiser, Los Angeles
- Lehigh Valley Health Network
- St. Alphonsus Regional Medical Center
- Hackensack University
- Essentia Health
- Nova Southeastern University

The platform trial is a unique opportunity to move ALS biomarkers and new outcome measures forward

DNA – whole genome sequencing



Neurofilaments – for all regimens + regimen-specific biomarkers based on MOA

Home Spirometry – critical during the pandemic

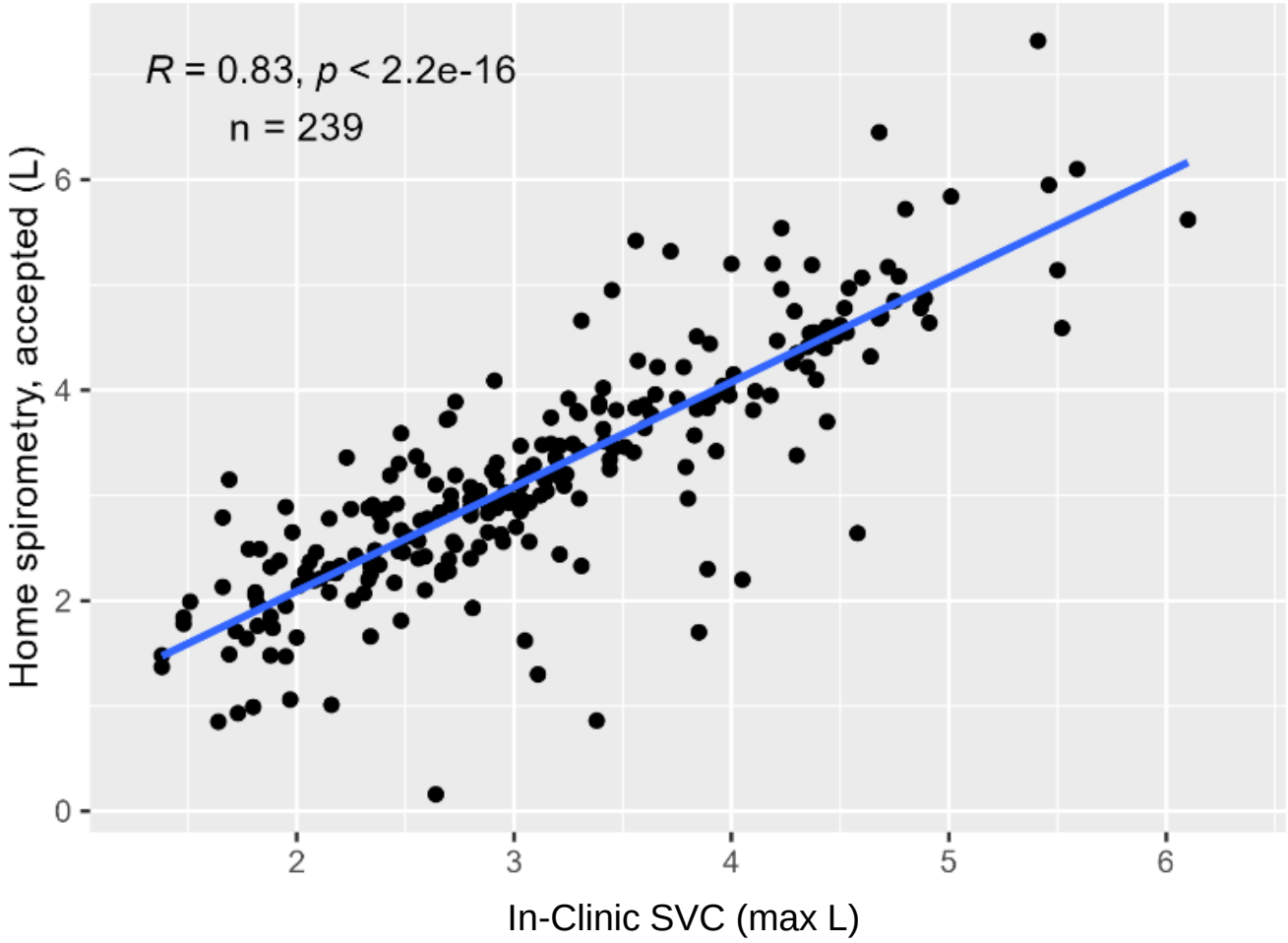
Speech Analysis – emerging digital biomarker

Additional biomarkers/outcome measures considered for upcoming and future regimens (e.g., new patient-reported outcomes- ROADS; PBMCs for stem cell generation)

Home spirometry correlated with in-clinic spirometry

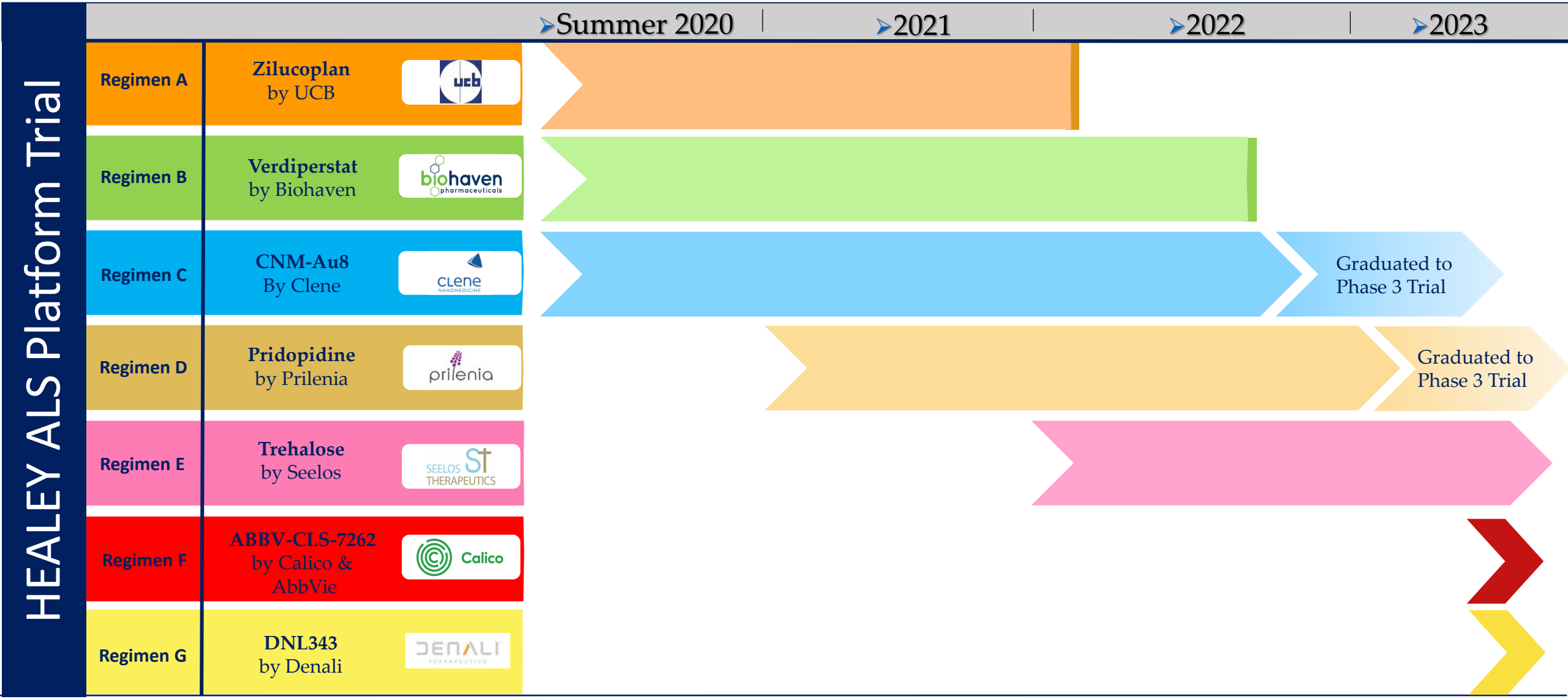
➢Home spirometer: MIR / ZephyRx

- Home Forced Vital Capacity (FVC) performed by participants with trained examiner on videoconference
- Home recordings reviewed centrally
- Clinic Slow Vital Capacity (SVC) performed by trained examiners
- Estimates of vital capacity are very similar by either method



Data include all participants with both in-clinic and home VC

The HEALEY ALS Platform Trial is a perpetual trial to provide decisive answers and direction with efficient execution



The HEALEY ALS Platform Trial

A Multistakeholder Partnership to Accelerate ALS Drug Development

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium®

- Platform trials are becoming popular in the Neurosciences due to operational and scientific advantages over traditional trials

  (faster, more efficient use of resources, embedded natural history study, biomarker/endpoint development engine)

- The HEALEY ALS Platform Trial is an adaptive, perpetual phase 2/3 trial – the trial launched in 2020, has included 70+ enrolling sites, 7 investigational drugs, and hundreds of participants so far. Additional regimens are ongoing, in start-up, or in the planning stages
- Initial learnings from the trial included go/no go decisions for the first 4 regimens, thus meeting the primary goal of the trial.
- We continue to learn about novel biomarkers and endpoints collected in the trial, and plan to share data and samples with the scientific community as they become available

Sharing our experience

Meetings with disease-specific networks both in the US and globally

Disease Areas

1. ALS
2. Alzheimer Disease
3. Duchenne Muscular Dystrophy
4. FSHD
5. Myotonic Dystrophy
6. Frontotemporal Dementia
7. Parkinson Disease
8. Progressive Supranuclear Palsy (PSP)
9. Traumatic Brain Injury
10. Spinal Cord Injury
11. Vanishing White Matter Disease
12. Depression
13. Neurofibromatosis (NF)
14. Scleroderma
15. Idiopathic Pulmonary Fibrosis
16. Fibrodysplasia Ossificans Progressiva (FOP)
17. Vascular Malformations

Master Protocol, Publications, and Other Documents Available at:
https://www.massgeneral.org/neurology/als/research/research-partners

New Regimen Application Form:

E-mail:
Merit Cudkowicz:
mcudkowicz@mgh.harvard.edu
Sabrina Paganoni:
spaganoni@mgh.harvard.edu

This trial is **dedicated to all people living with ALS**, their families, and friends

We are immensely grateful to the NEALS sites, researchers, funders, foundations, industry partners, and all stakeholders who provided and continue to provide thoughtful feedback and invaluable support

Your **partnership** in research is what keeps us filled with passion, dedication, and the commitment to develop new treatments for ALS

HEALEY ALS Platform Trial Updates

Wed, May 31 | Zoom call

4:00PM PT / 7:00PM ET

Register Here:

https://bit.ly/3OyjUlG

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 1st- Weekly Q&A and discussion of “what’s next” for the Platform Trial

June 8th- Weekly Q&A

June 15th- Weekly Q&A