

HEALEY ALS Platform Trial

Weekly Q&A – Jan 5, 2023



Healey Center

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



Calico



The AMG Foundation



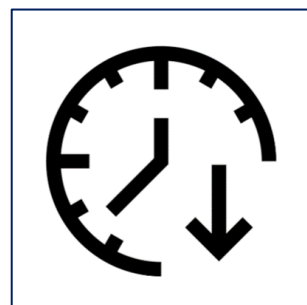
Accelerating innovation for a cure

*Merit Cudkowicz, MD, MSc
Sean M. Healey*

Traditional Clinical Trial

vs.

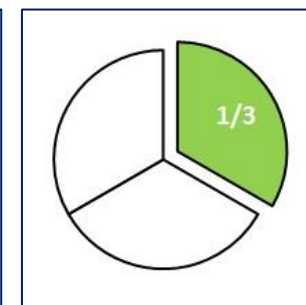
HEALEY ALS Platform Trial



**Cuts time
in 1/2**



**Cuts costs
by 1/3**



**Reduces
placebo**

The **1ST** Ever
ALS PLATFORM TRIAL

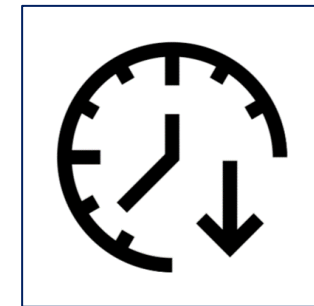
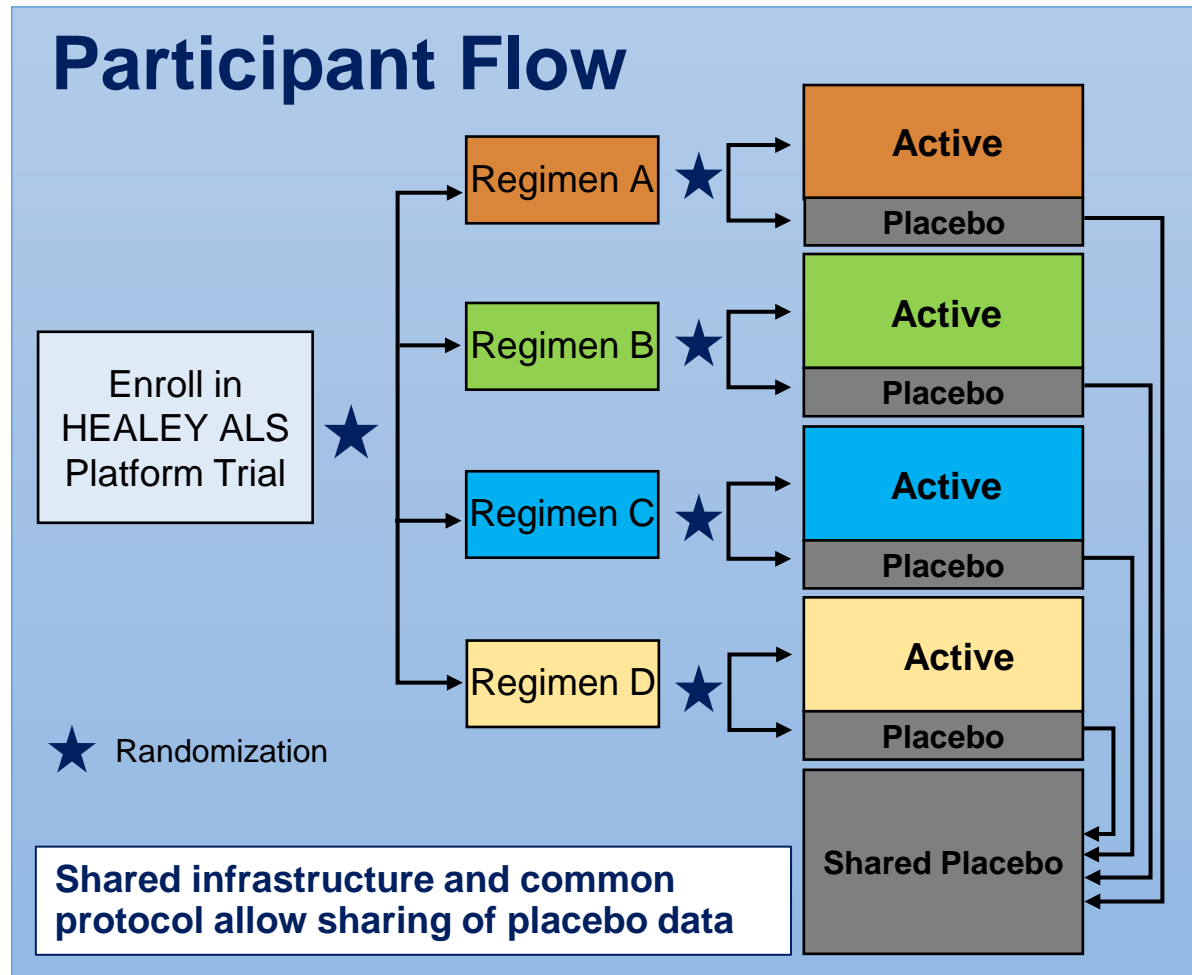
Video Link:



<https://bit.ly/3N9eTx6>

<https://www.youtube.com/watch?v=AkUVI-KsUfU>

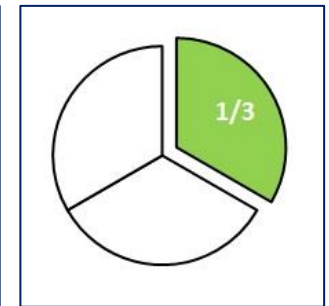
Shared Infrastructure and Master Protocol Allow for Operational and Scientific Efficiencies



Cuts time
in 1/2


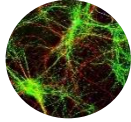





Cuts costs
by 1/3



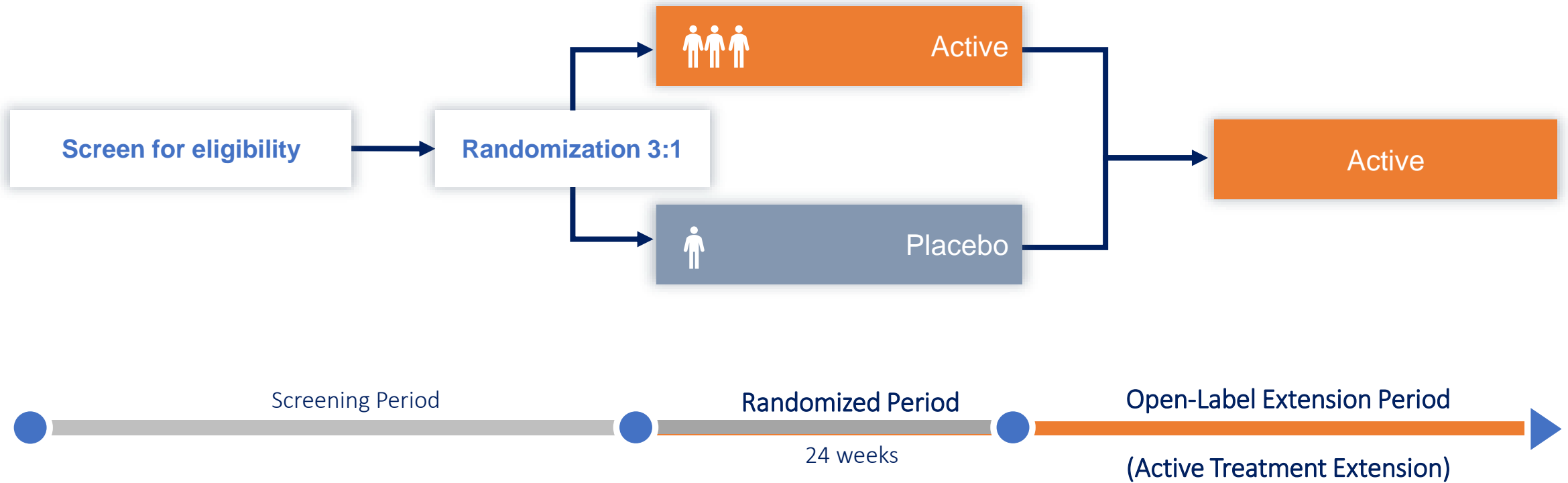
Reduces
placebo

Assessing emerging biomarkers/outcome measures

-  **DNA** – genetic analysis for all regimens
-  **Neurofilaments** – NfL analysis for all regimens
-  **Biomarkers** (Blood, Urine, CSF) – several drug-specific biomarkers in each regimen
-  **Speech Analysis** – data collected for regimens A-D
-  **Home Spirometry** – critical during the pandemic for regimens A-D

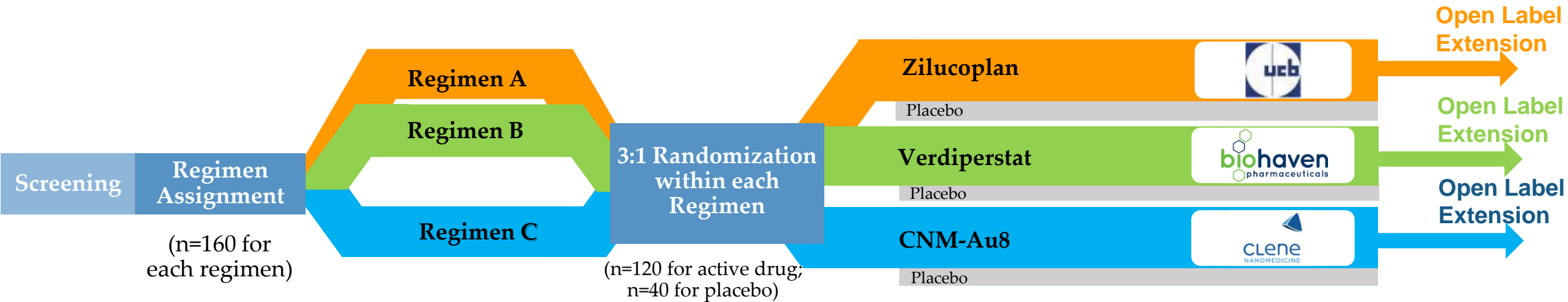
Additional biomarkers/outcome measures being considered for upcoming regimens (PBMCs, ROADS)

Schema for Each Regimen



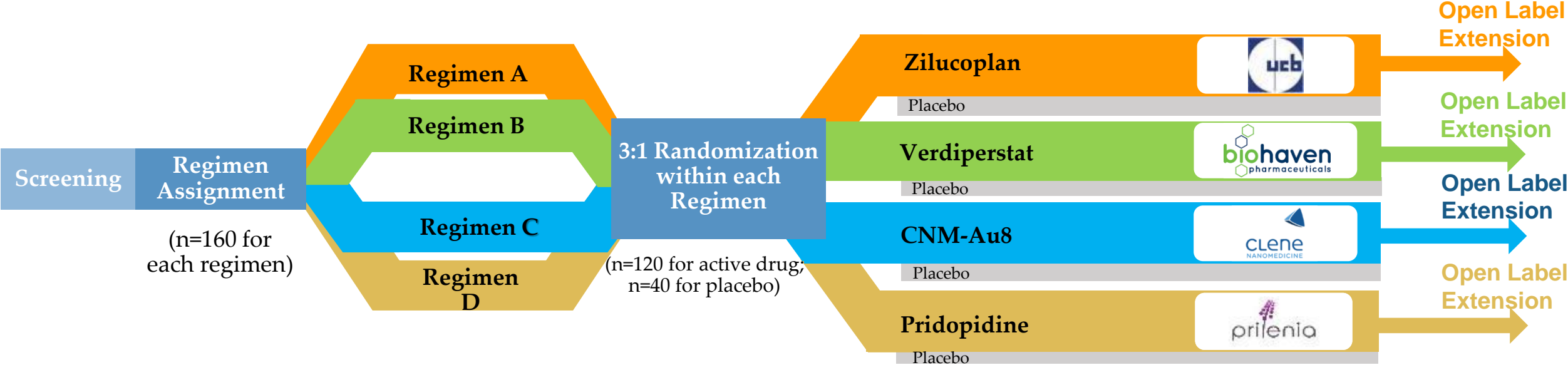


The HEALEY ALS Platform Trial is a Perpetual Adaptive Trial



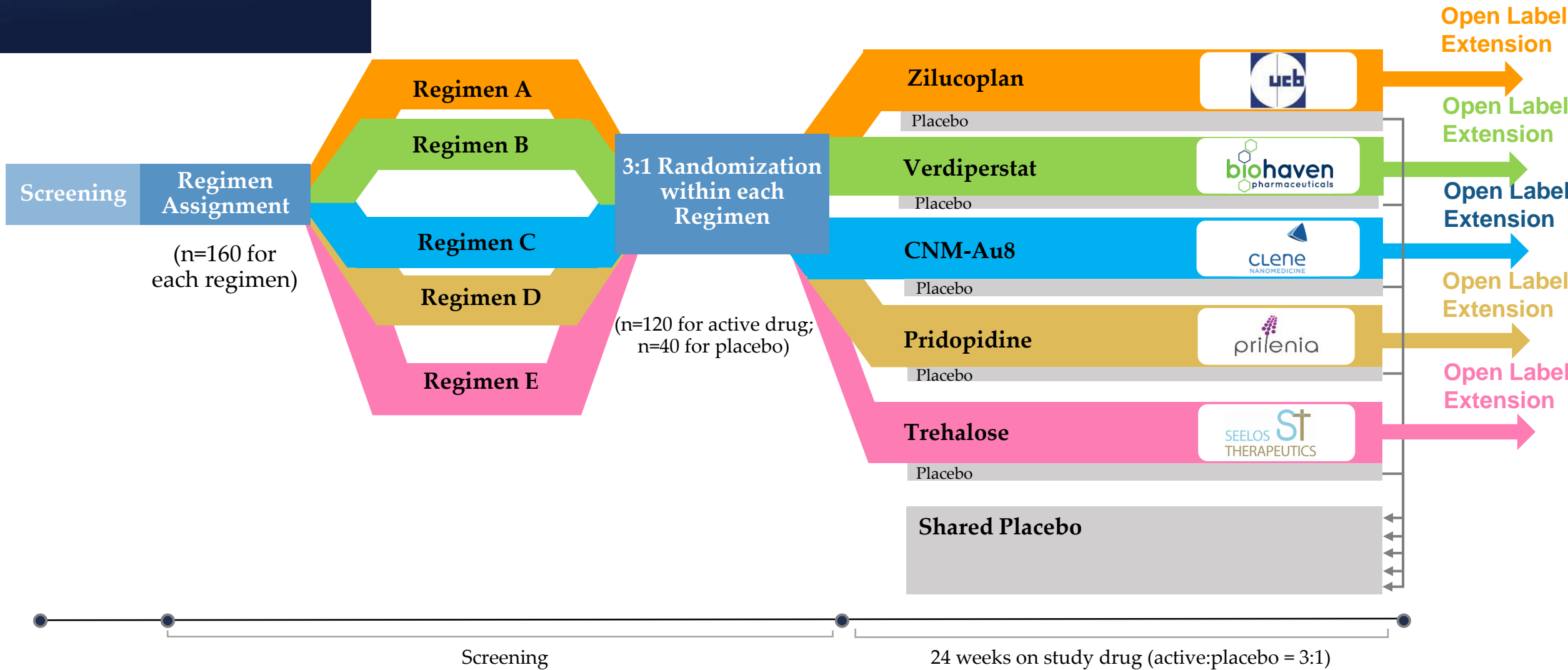


The HEALEY ALS Platform Trial is a Perpetual Adaptive Trial





The goal of the HEALEY ALS Platform Trial is to screen drugs rapidly and efficiently, get solid answers, and determine next steps



Initial Regimen Updates – trial gave clear answers and direction, efficient execution (time, resources, less placebo)

- February 2022: **Regimen A** stopped early for futility
- September 2022: **Regimen B** top line results announced
 - * Did not meet the prespecified primary endpoint and there were no statistically significant benefits on key secondary measures; full study results, including data on biomarkers and exploratory measures, are expected in the coming months
- October 2022: **Regimen C** top line results announced
 - * While the primary endpoint was not met, a secondary endpoint analysis of survival demonstrated a significant reduction in risk of death or permanently assisted ventilation when adjusting for baseline risk imbalances in the CNM-Au8 regimen for the 30 mg dose; full study results, including data on biomarkers and exploratory measures, are expected in the coming months



MASTER PROTOCOL

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



ENROLLING

IN START-UP

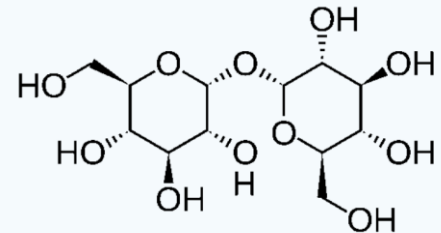
Informational Webinars about **Regimen E**

Trehalose/SLS-005 Drug Science and Mechanism of Action Q&A Webinar

Hosted by Seelos Therapeutics on 10 March 2022

Recording Available!

SEELOS **St**
THERAPEUTICS



<https://bit.ly/3L4hrdB>

Recording available under “science and mechanism of action series”

The ALS Association/Northeast ALS Consortium Educational Webinar

Update on Healey ALS Platform Trial Regimen E: Trehalose for ALS

UPDATE ON REGIMEN E

TREHALOSE FOR ALS



Merit Cudkowicz, MD, MSc

SEAN M. HEALEY & AMG
CENTER FOR ALS AT MGH



Shafeeq Ladha, MD

BARROW NEUROLOGICAL
INSTITUTE

TUESDAY | 4 OCTOBER
3 PM EDT

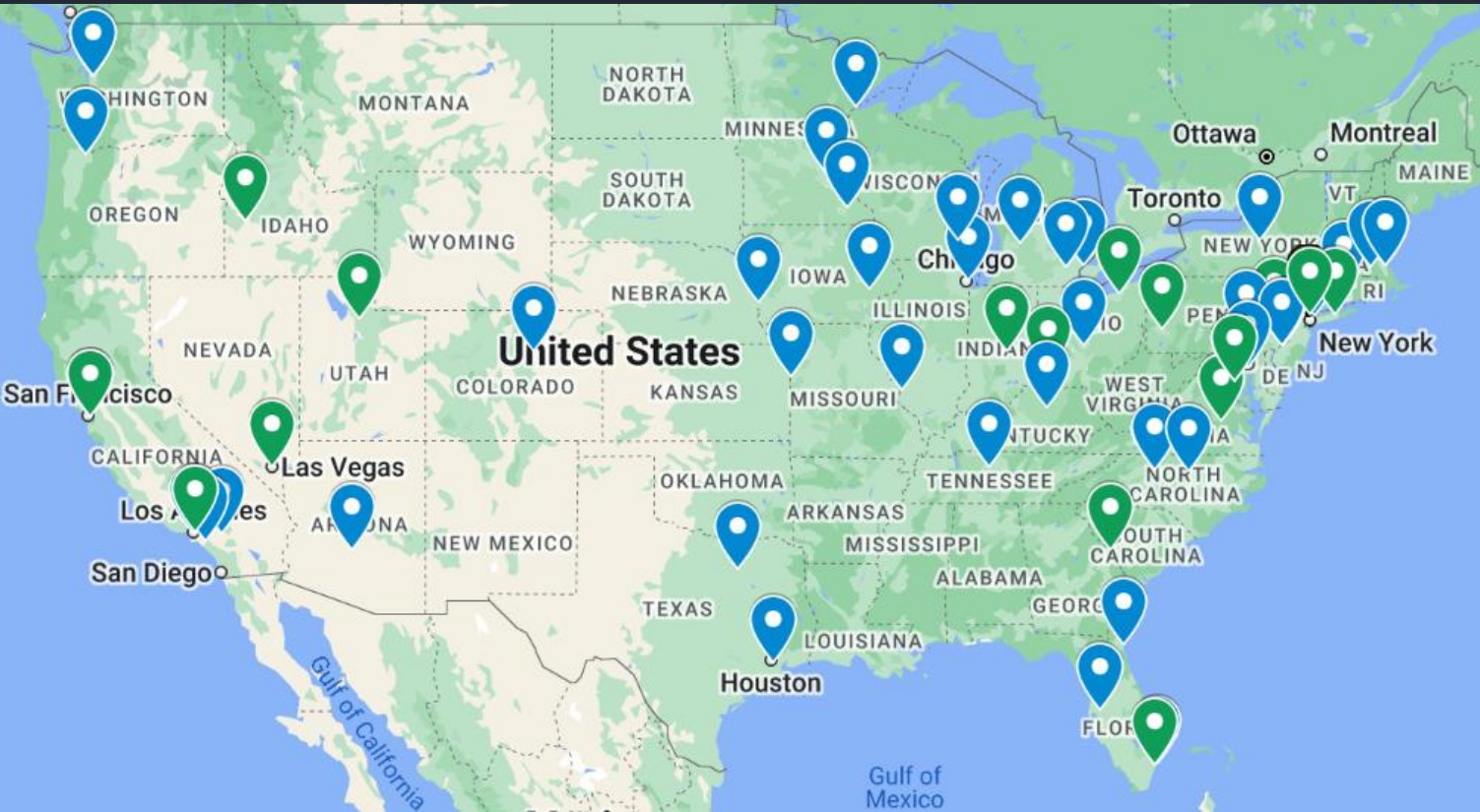
Recording Available!



<https://bit.ly/3X2u004>

Recording available under “educational webinars” on neals.org

60 Sites Currently Activated for Regimen E



(as of 1/5/23)

Sites in blue participated in previous regimens. Sites in green (underlined to the side) are new additions to the Platform Trial!

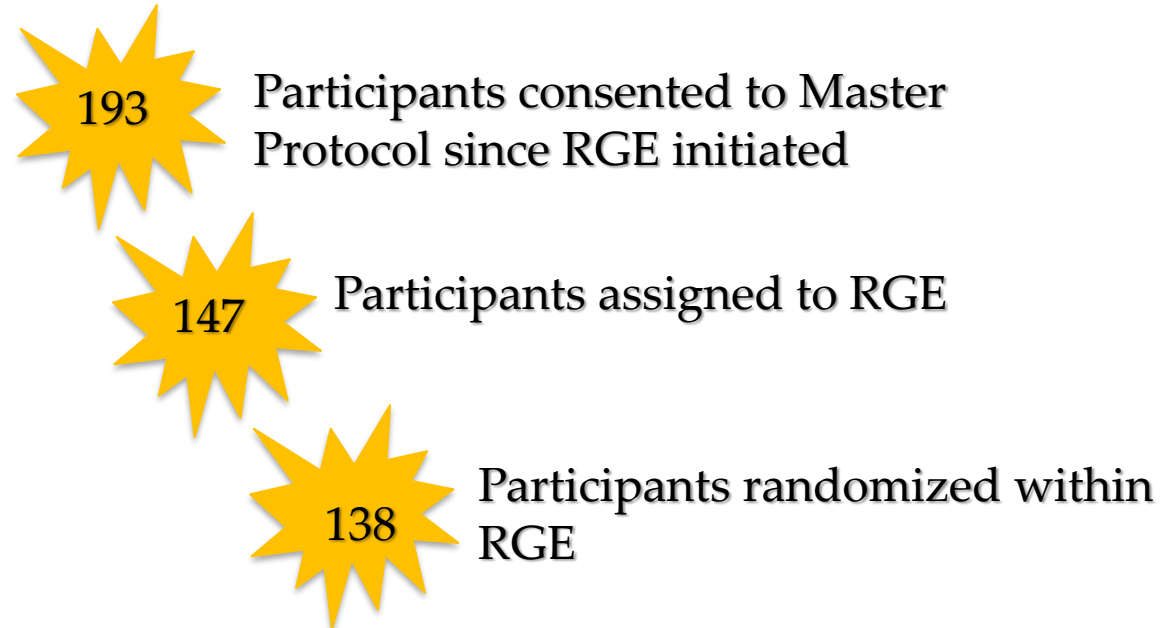
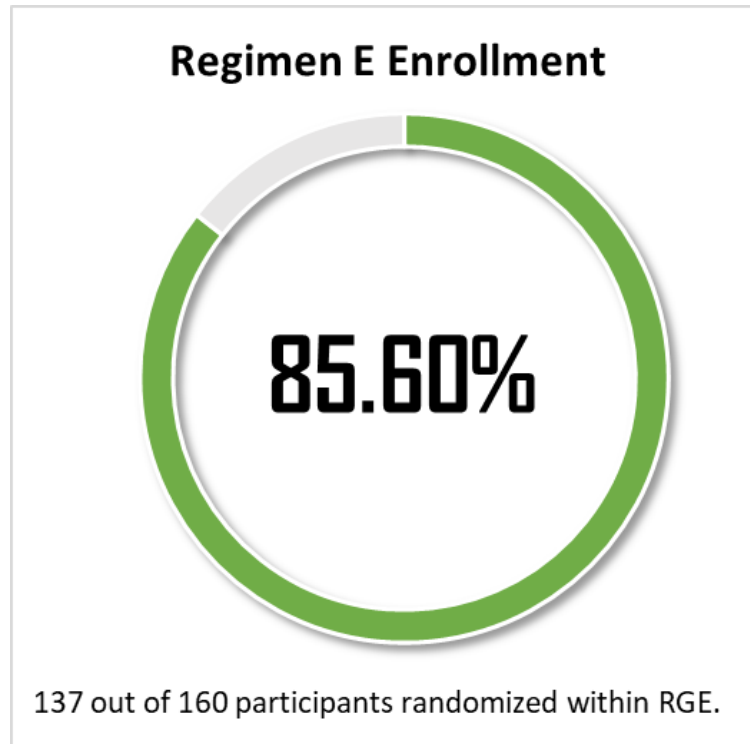
- Lehigh Valley Health Network
- Mass General Hospital
- University of Kansas
- University of Maryland
- California Pacific Medical Center
- Northwestern University
- Virginia Commonwealth University
- University of Nebraska
- Washington University
- Wake Forest University
- Hospital for Special Care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

Site Map & Contacts:



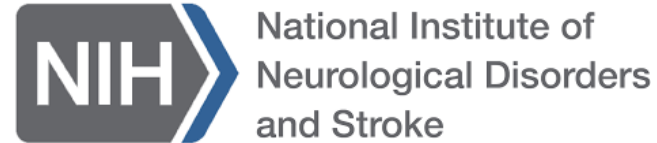
<https://bit.ly/3g2NZr5>

Regimen E Updates (as of Jan 5, 2023)



Intermediate Size EAP - Trehalose

- In start up now
- Expected to enroll first participants in Q1 2023
- 25 sites
- 70 participants
- NIH-funded (PIs: Babu, Berry, Paganoni)
- Happening in parallel to Regimen E of the HEALEY ALS Platform Trial



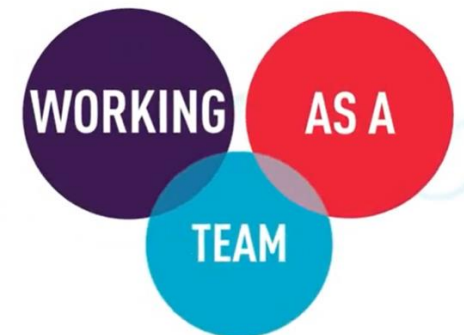
View Press Release:



<https://bit.ly/3S0a9eb>

Outcomes:

- Long-term safety in a broad population
- Biological impact (as measured by neurofilament light levels)
- Clinical efficacy signal (as compared to natural history cohorts)



Regimen F

PRESS RELEASE · 5 MINUTE READ · JUL | 12 | 2022

Investigational drug ABBV-CLS-7262 initiates design phase for entry into the HEALEY ALS Platform Trial



- **ABBV-CLS-7262 is being developed by AbbVie Inc and Calico Life Sciences**
- It targets eIF2B, a key regulator of the integrated stress response (ISR). In neurons exposed to cellular stressors, inhibition of the ISR by ABBV-CLS-7262 restores protein synthesis and dissolves pre-formed TDP-43 containing stress granules. This effect of ABBV-CLS-7262 is of clinical interest because TDP-43 containing stress granules are thought to lead to TDP-43 inclusions, a hallmark of ALS pathology.



Calico



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

Regimen G

PRESS RELEASE · DEC | 5 | 2022

Healey & AMG Center for ALS announces new drug regimen for testing DNL343 in HEALEY ALS Platform Trial

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- **DNL343 is being developed by Denali Therapeutics.**
- It targets eIF2B, a key regulator of the integrated stress response, to restore protein synthesis and dissolve pre-formed TDP-43 containing stress granules which are thought to lead to TDP-43 inclusions, a hallmark of ALS pathology.

“By adding one more drug to the platform, we continue to push research forward in hopes of soon finding many more effective treatments for ALS.”

Merit Cudkowicz, MD, MSc

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



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

Patient Navigation

Central resource for people living with ALS



Catherine Small

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:

January 12- Weekly Q&A

January 19- Weekly Q&A

January 26- Weekly Q&A



Allison Bulat