

HEALEY ALS Platform Trial

Weekly Q&A – Feb 9, 2023



Healey Center

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



Calico



THE ARTHUR M. BLANK
FAMILY FOUNDATION



The AMG Foundation



MASTER PROTOCOL

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

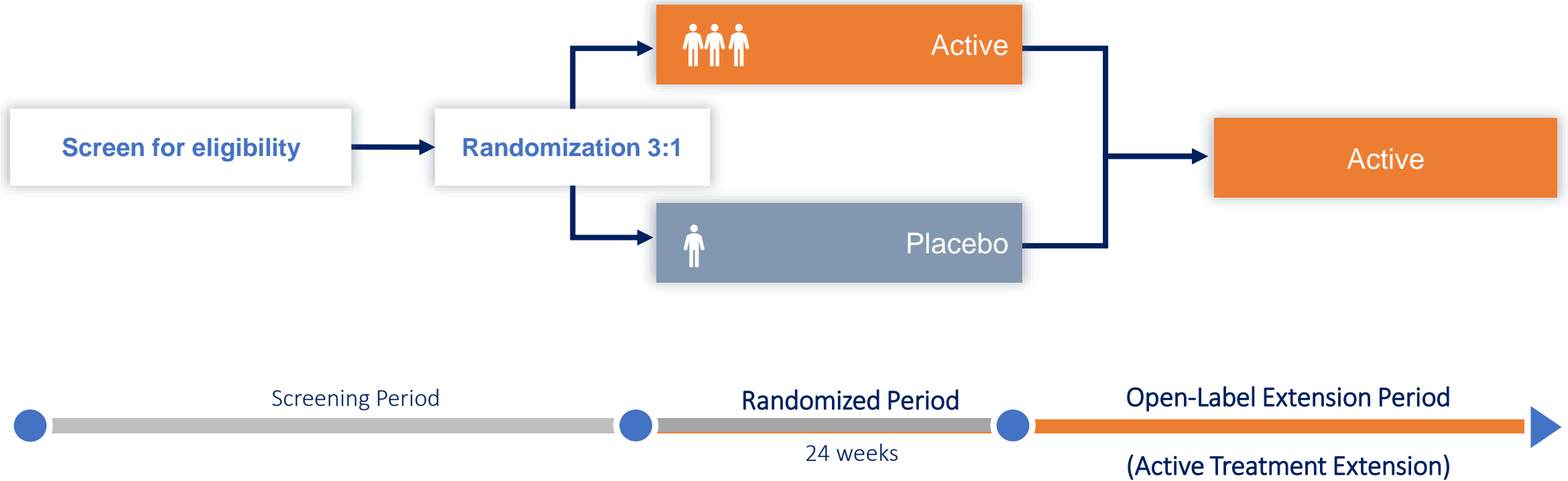


IN START-UP



IN START-UP

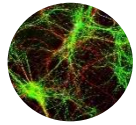
Schema for Each Regimen



Platform trials are a unique opportunity to advance science



DNA – whole genome sequencing



Neurofilaments –for all regimens



Biomarkers (Blood, Urine, CSF) – several drug-specific biomarkers

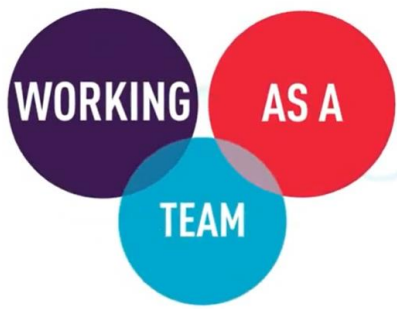


Speech Analysis – emerging digital biomarker



Home Spirometry – critical during the pandemic

**Additional biomarkers/outcome measures for upcoming regimens
(new patient-reported outcomes; PBMCs for stem cell generation)**



Therapy Evaluation Committee

- All investigational products in the Platform Trial were chosen by a committee of expert ALS scientists and clinicians
- Industry partners from selected companies work with the Healey Center Trial Design Team, the Northeast ALS Consortium (NEALS), Barrow Neurological Institute and Berry Consultants to tailor a new regimen to their experimental drug
- Each investigational product added to the Platform Trial is believed to have an equal chance of success for all forms of ALS based on available scientific evidence

Criteria for selection included:

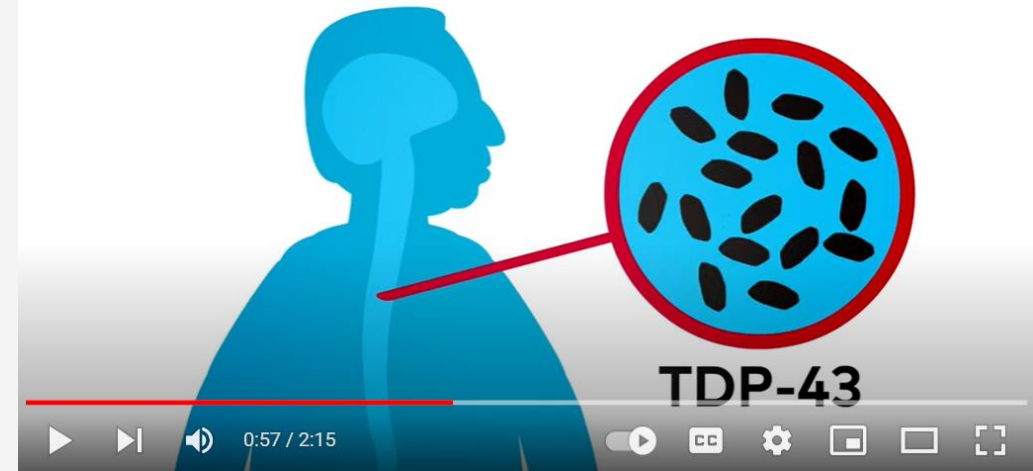
- Robust preclinical data (data from the lab that support the scientific rationale for testing these products in ALS)
- Previous human experience in ALS or other neurological diseases (to support the dose, safety and target engagement of the product and its inclusion in a late-stage trial such as the Platform Trial).

Regimen F

Integrated Stress Response (ISR)

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**
- 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.
- 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.**
- Targets eIF2B, a key regulator of the integrated stress response, to restore protein synthesis and dissolve pre-formed TDP-43 containing stress granules.



“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>

Weekly Recordings Available on MGH Website

Webinar Recordings

Science & Mechanism of Action Series +

Weekly & Monthly Updates: 2023 -

January 26, 2023: Weekly Q&A and Regimen C Update

Sabrina Paganoni, MD, PhD presented updates on the HEALEY ALS Platform Trial and answered questions from the audience. Guest speakers Michael Hotchkin (Chief Development Officer at Clene Nanomedicine, Inc) and James Berry, MD, MPH (Regimen C co-Lead, Mass General Hospital) joined the webinar again this week to recap the latest news and updates regarding Regimen C.

[Watch recording.](#) [Download slides \(PDF\).](#)

January 19, 2023: Weekly Q&A

Sabrina Paganoni, MD, PhD presented this week's updates on the HEALEY ALS Platform Trial and answered questions from the audience.

[Watch recording.](#) [Download slides \(PDF\).](#)

Visit the Website:



<https://bit.ly/3g4kzfv>

Patient Navigation

Central resource for people living with ALS



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Weekly webinar
registration:



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

ALS Link sign-up:



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

Upcoming Webinars:

February 16th- Weekly Q&A

February 23rd- Weekly Q&A



Allison Bulat