The HEALEY ALS Platform Trial

Working together to develop new treatments for ALS

HARVARD MEDICAL SCHOOL

MASSACHUSETTS GENERAL HOSPITAL

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BARROW Neurological Institute

Berry Consultants Statistical Innovation

MELIORA

Healey Center

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

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

IAMALS

TAMBOURINE

ALS ONE

RUN2REVIVE MIND · BODY · POTENTIAL

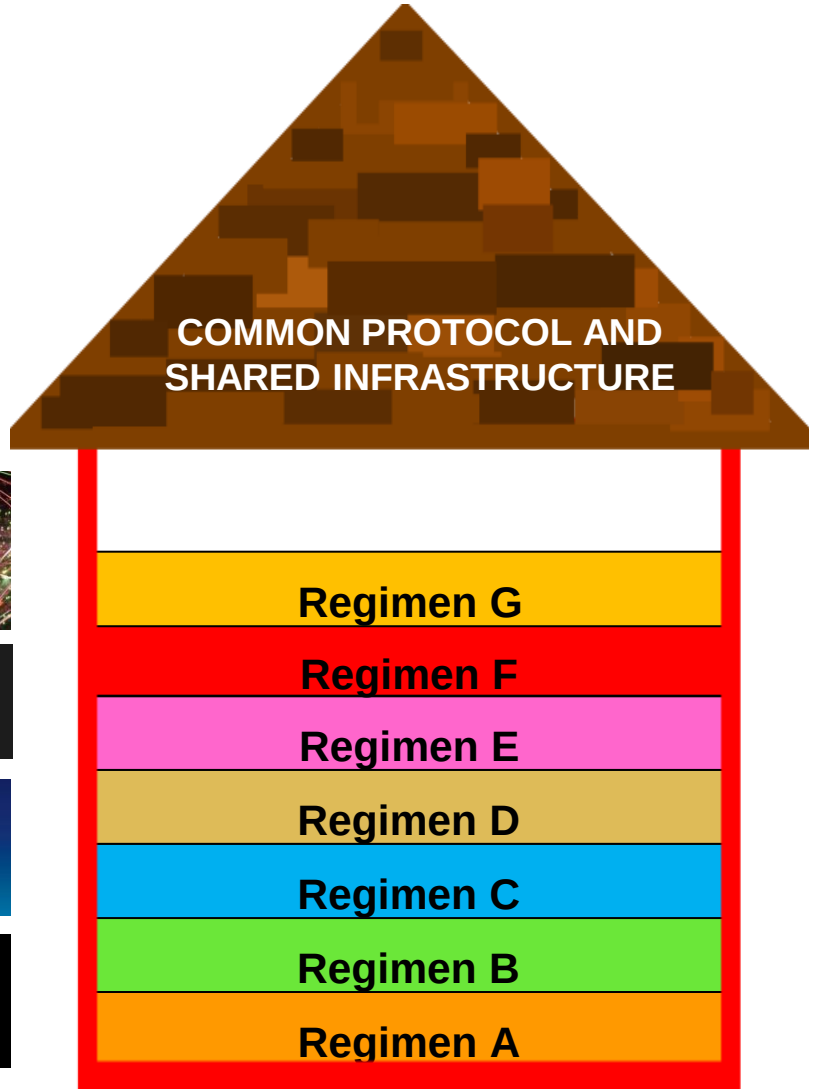
THE ARTHUR M. BLANK FAMILY FOUNDATION

BASEBALL WINTER MEETINGS SAN DIEGO 2019

AMG The AMG Foundation


SOMETHING
NEW
IS HERE

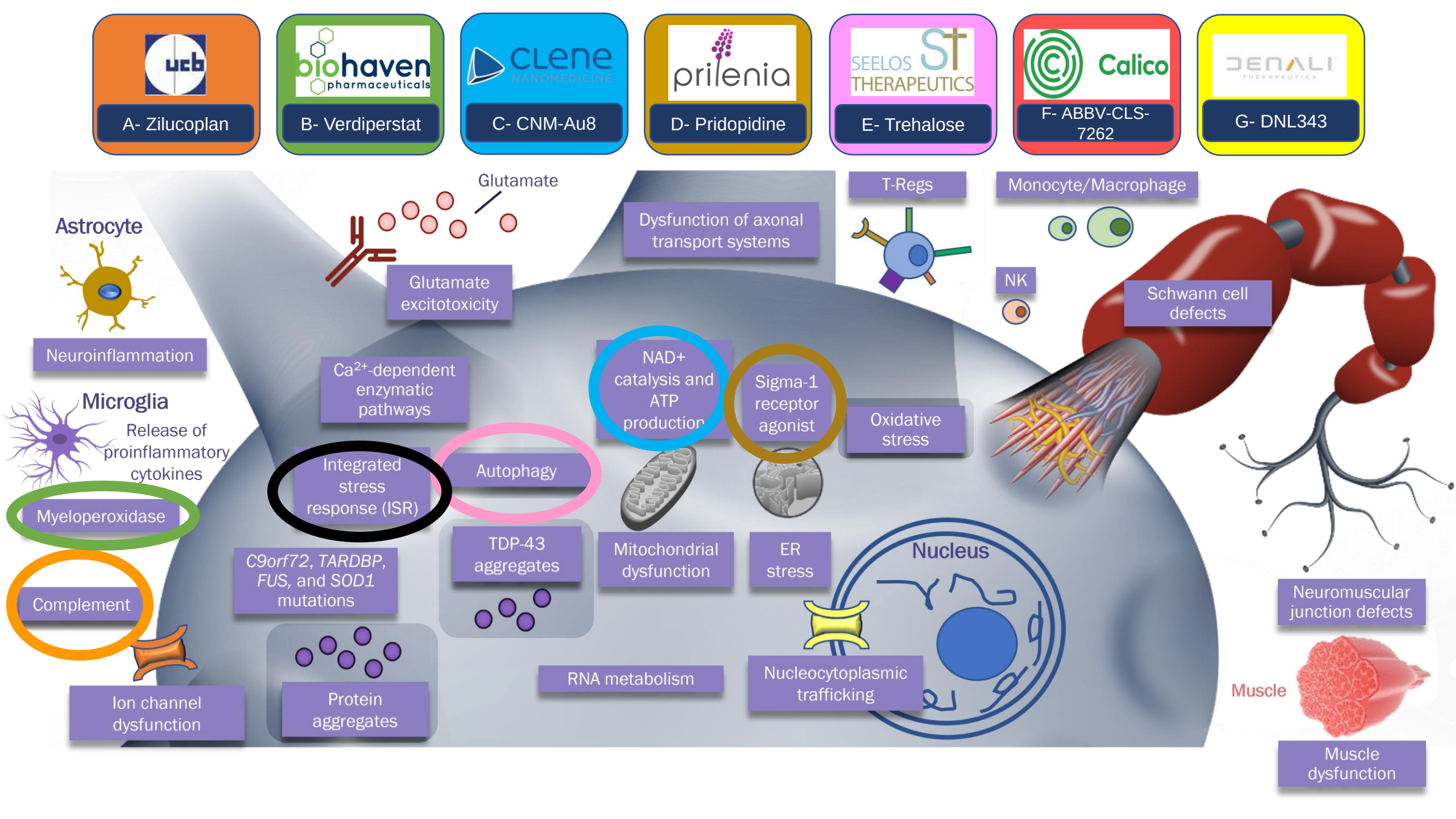
The platform trial continues to grow to test more drugs



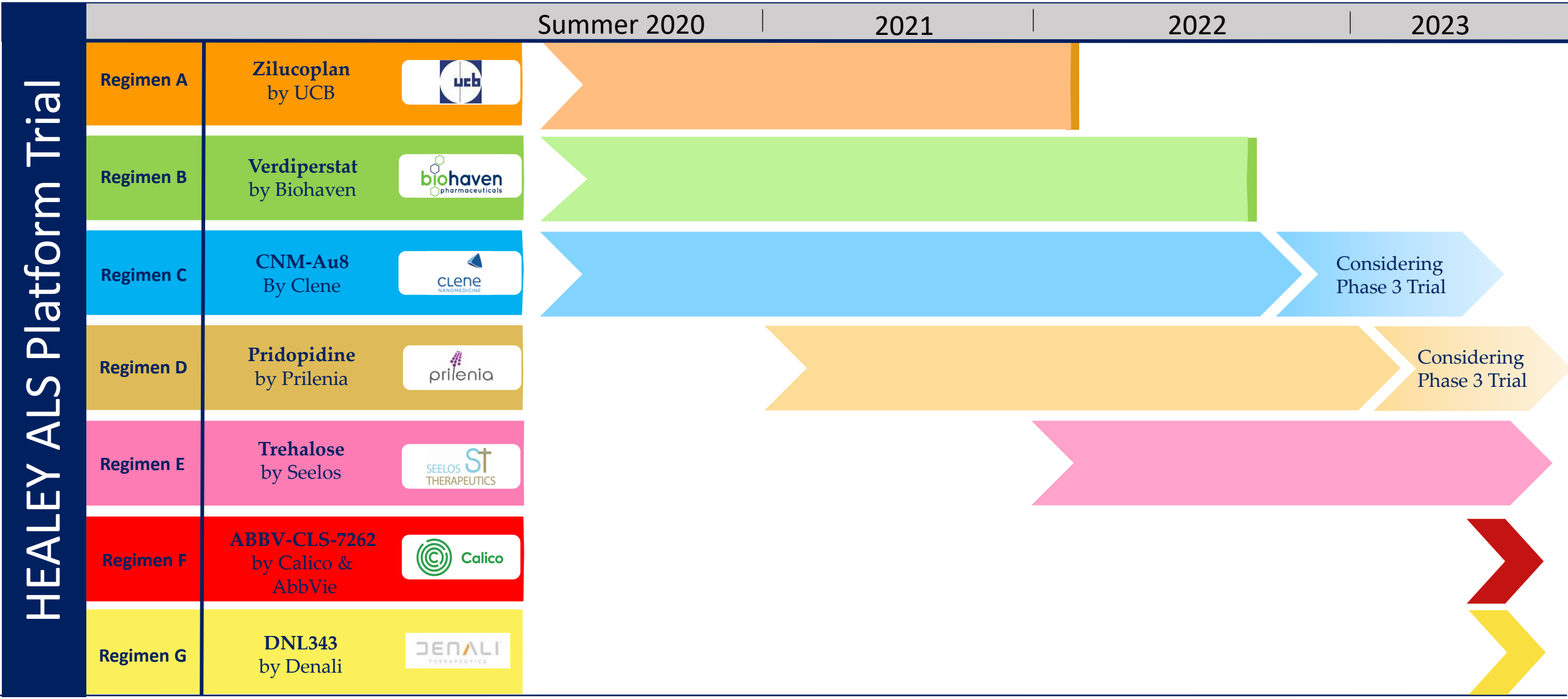
1 Protocol
(Phase 2/3)
1 single IRB
Central Governance

7 Regimens
70+ Enrolling Sites
~1300 Participants

Regimen: Active Study Drug + Matching Placebo

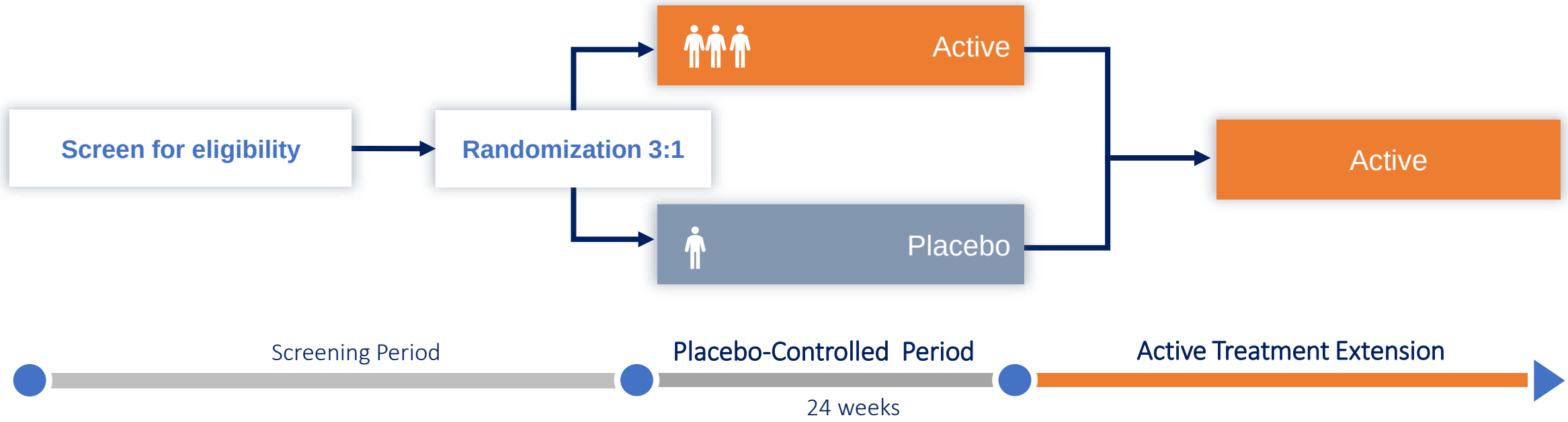

A- Zilucoplan
B- Verdiperstat
C- CNM-Au8
D- Pridopidine
E- Trehalose
F- ABBV-CLS-7262
G- DNL343
Glutamate
Astrocyte
Glutamate excitotoxicity
Dysfunction of axonal transport systems
T-Regs
Monocyte/Macrophage
NK
Schwann cell defects
Neuroinflammation
Microglia
Release of proinflammatory cytokines
Ca2+-dependent enzymatic pathways
NAD+ catalysis and ATP production
Sigma-1 receptor agonist
Oxidative stress
Integrated stress response (ISR)
Autophagy
Myeloperoxidase
Complement
C9orf72, TARDBP, FUS, and SOD1 mutations
TDP-43 aggregates
Mitochondrial dysfunction
ER stress
Nucleus
Neuromuscular junction defects
Ion channel dysfunction
Protein aggregates
RNA metabolism
Nucleocytoplasmic trafficking
Muscle
Muscle dysfunction

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



2023 Regimens – F and G

Placebo Controlled Period followed by Active Period Extension



Primary Endpoint (Placebo-Controlled Period)

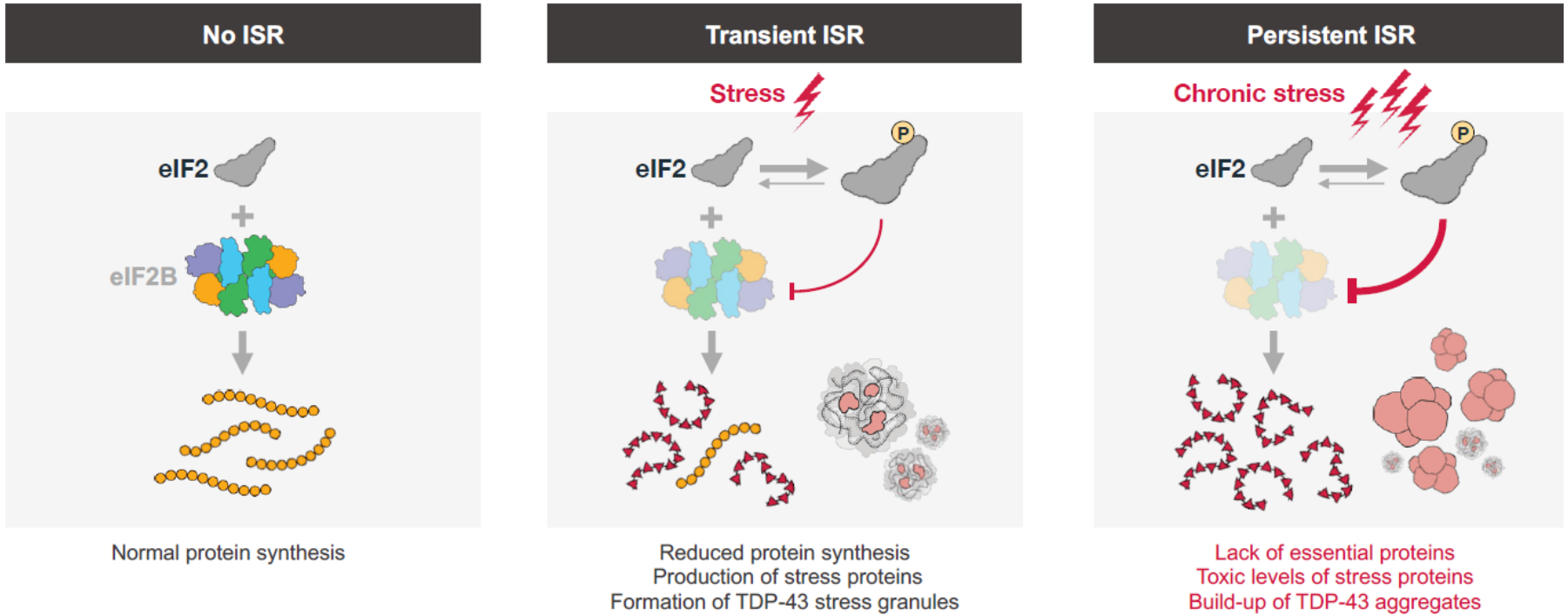
Change in disease severity

Safety, Secondary, and Exploratory Endpoints

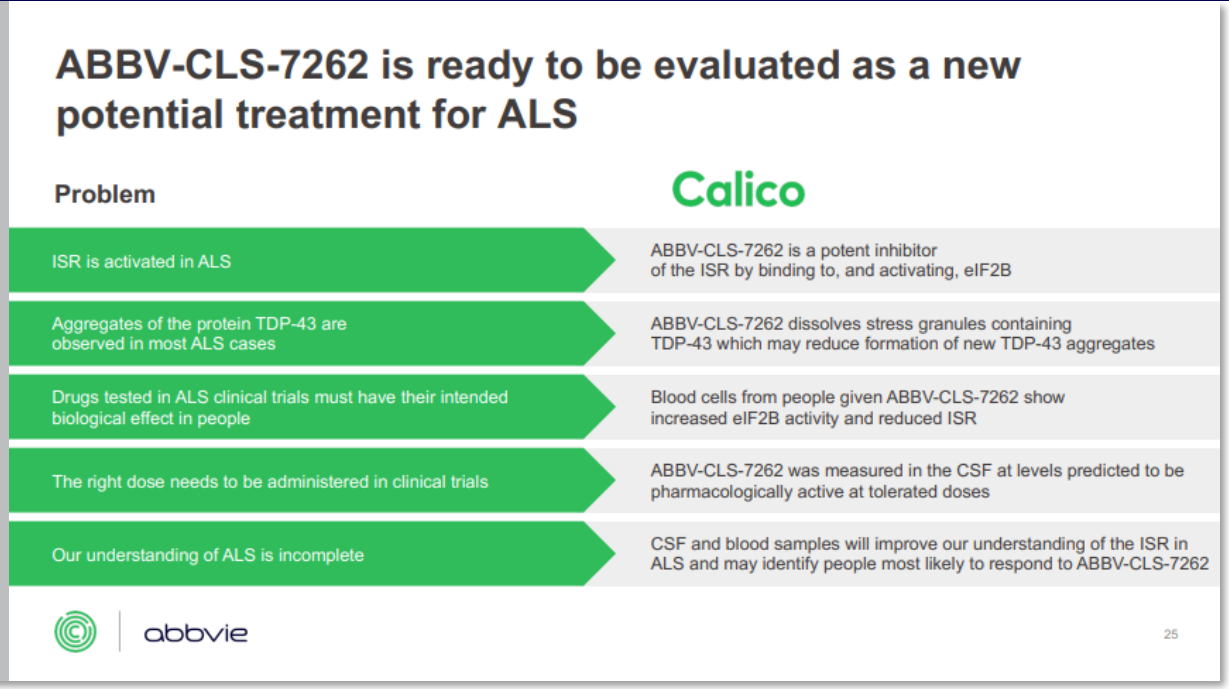
Including respiratory function, muscle strength, biomarkers

Regimen F – Enrolling now

The Integrated Stress Response (ISR)



Regimen F Drug Science Q&A Webinar



Topic: Regimen F Drug Science and Mechanism of Action

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

Calico

Regimen G – Enrolling now

- News - Press Release

PRESS RELEASE · 5 MINUTE READ · MAY | 30 | 2023

Sean M. Healey & AMG Center for ALS Announces First Participant Dosed in Regimen G of the HEALEY ALS Platform Trial Evaluating DNL343 by Denali Therapeutics

Brandon Chase · bchase7@mgb.org

BOSTON -- The Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital in conjunction with Denali Therapeutics have announced the first participant-dosing in Regimen G of the HEALEY ALS Platform Trial testing DNL343.

Type

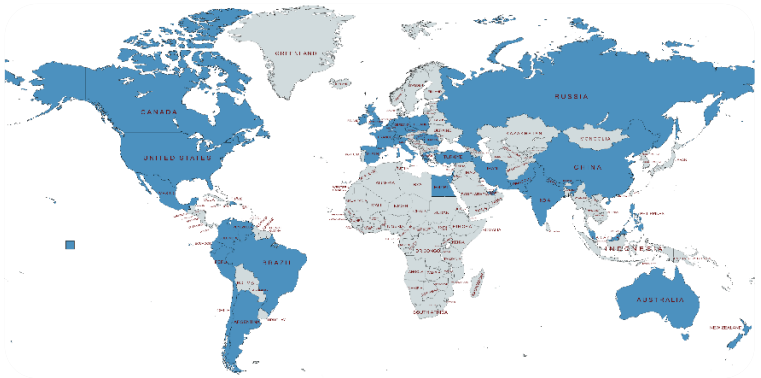
Press Release

"DNL343 is a novel investigational ALS therapy that targets eIF2B, a central regulator of the integrated stress response (ISR). The ISR appears to be overactive in ALS, leading to the formation of stress granules containing TDP-43. Buildup of TDP-43 is harmful and leads to neuronal degeneration. In the lab, inhibition of the ISR by DNL343 dissolves TDP-43 containing stress granules and decreases ISR biomarkers.

The safety, pharmacokinetics, and pharmacodynamics of DNL343 have been characterized in both healthy participants and people with ALS, in a Phase 1 (N=47) and a Phase 1b (N=29) study, respectively, with dosing for up to 28 days. Results from both studies demonstrated that once-daily oral dosing with DNL343 was generally well tolerated and exhibited extensive Cerebrospinal Fluid (CSF) penetration. In addition, robust inhibition of biomarkers associated with the ISR pathway was observed in blood samples from study participants."

The Patient Navigator Team is a central resource for information

Patient Navigator Team
Building Community & Partnership in ALS Research



Catherine Small

Allison Bulat

Patient Navigator: Central Resource

Weekly Webinars: News & Updates

ALS Link

Phone: 833-425-8257 (HALT ALS)

E-mail:healeyalsplatform@mgh.harvard.edu

We are immensely grateful to the trial participants and to everyone in the ALS community who is supporting research in many different ways

Progress in ALS would not be possible without your partnership

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