Thank you for joining the webinar!

We are admitting audience members from the waiting room.

Please allow a few moments for the webinar to begin.

HEALEY ALS Platform Trial Community Webinar

Expanded Access Q&A – Sept 12, 2024

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

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

NCRI 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 2015

SEELOS THERAPEUTICS

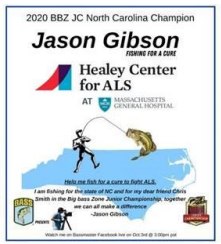
Calico

DENALI THERAPEUTICS

AMG The AMG Foundation

EAP Companion Program Supporters

- Healey & AMG Center for ALS
- Clearing Corporation Charitable Foundation
- Eddie and Jo Allison Smith Family Foundation
- Richard Stravitz Foundation
- I AM ALS
- Elliott & Frantz, Inc.
- **Community Fundraisers**
  - Tackle ALS – Team Change ALS
  - Ellen Corindia's Fundraiser
  - 2019 Olson Cornhole Tournament
  - 2019 Worthington Fore ALS
  - 2020 and 2021 Fishing for ALS Warriors
  - 2020 and 2021 sALSa For a Cure Pick Your Own Path Walk
  - 2020 and 2021 Lori's Shoes "Hope Is In the Bag"
  - 2021, 2022, and 2023 MLB Lou Gehrig Day 4-ALS
  - 2021 Russ Pallesen Fundraiser for EAP
  - 2021 Voices for ALS Golf Tournament
  - 2021 The Martha Olson-Fernandez Foundation Golf Tournament
  - 2021 Gwendolyn Strong Walk
  - TechVs.ALS
  - Ride to Endure
  - AxeALS
  - Race to Cure ALS
- **Big thanks to countless individual contributors**



Expanded Access Program Update

Suma Babu, MBBS., MPH
Assistant Professor of Neurology
Co-Director, Neurological Clinical Research Institute
Massachusetts General Hospital
Harvard Medical School, Boston, MA

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

agenda

EAP overview

Pridopidine EAP

RAPA-501 EAP

The EAP Engine: Central Operations Team at Neurological Clinical Research Institute at MGH

Admin & Communications

Juliana Araujo, Jesse Rosenthal
Allison Bulat, Judith Carey, Catherine Small

Contracts & Finance

Kristin Drake, Meredith Hasenoehrl
Carol Ann Hannan (not pictured), Jen Hagar, Silpa Mohapatra

Investigators

Suma Babu, James Berry, Sabrina Paganoni

Project Management

Lindsay Pothier, Jen Kulesa-Kelley
Molly Benson, Mackenzie Keegan, Victoria Wang
Amanda Castelluccio, Hang Phan

Data Management

Alex Leite, Joe Ostrow, Hong Yu

Systems Management

Derek Dagostino, Michelle Li, Issac Whitworth

Quality Assurance

Mayada Guzman, Preeti Paul

Expanded Access

FDA Definition:

- Sometimes called “compassionate use”
- Potential pathway for a patient with an immediately life-threatening or serious disease or condition
- Allows access to an investigational medical product outside of clinical trials
- Used when no comparable or satisfactory alternative therapy available

https://www.fda.gov/news-events/public-health-focus/expanded-access

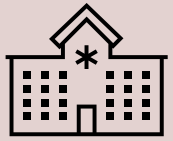
EAP paradigm is an extension of ALS clinical care

Clinical Care Realm

Research Realm

Aligning EAP study visits with clinical visits and and clinical labs

Aligning goals between IRB, FDA, industry sponsor, and Provider-Patient



Including clinical and research staffing resources

Utilizing clinic space for EAP study visits

Some institutions may use EMR for source documentation

Making sure protocol is followed for study conduct

Safety reporting (SAEs) is done in a timely and FDA/IRB compliant manner

Why EAP?
Or
Why not EAP?

- **Market gap:** Trial population is often not representative of the post-FDA approval consumers, creates insurance barriers.
- **Patient population:** 90% of ALS population in the US do not have access to experimental therapeutics nor do they have the opportunity to contribute to research
- **Financials:** Drug development is time consuming and expensive for drug manufacturers and research sites. Unfunded EAPs may be out of reach for patients to cover drug costs.
- **Industry apprehension:** Long term safety of some experimental drugs are unknown in early stages of development.
- **Usability:** Patients want less burdensome access to experimental therapeutics; clinics want to use their limited research staff and space resources carefully for trials, and observational research over EAPs

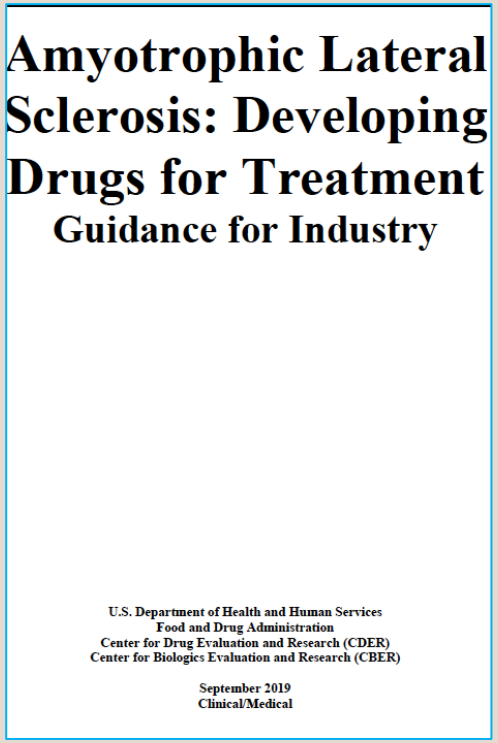
FDA's encouraging perspective on EAPs in ALS

- **Long term safety data:**

"*During development, sponsors should collect safety data, including data from open-label studies or expanded access programs, from patients across the spectrum of disease stages and severities, and whenever possible, data from patients who may not have been included in effectiveness studies but in whom, based on other data, the use of the drug following approval is likely.* " [Page 4]

- **Generalizability of safety and efficacy data:**

"There is a need to understand the safety and effectiveness of investigational drugs for ALS across disease stages….. An acceptable approach could include enrollment of a broad population with the conduct of the primary analysis in a study subset defined based on clinical characteristics and/or biomarkers, and analyses of the broader population being secondary and supportive" [Page 3]



Important FDA requirement for any EAP

Providing drug **will not interfere with clinical trials** that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use

Two NIH funded EAPs (2023)

Home - Neurology - ALS - News

PRESS RELEASE · OCT | 5 | 2023

Sean M. Healey & AMG Center for ALS awarded NIH U01 Grant to support Expanded Access to Pridopidine in Collaboration with Prilenia Therapeutics

Home - Neurology - ALS - News

PRESS RELEASE · OCT | 5 | 2023

Sean M. Healey & AMG Center for ALS awarded NIH U01 Grant to support Rapa Therapeutics' Expanded Access Protocol of Epigenetically Reprogrammed RAPA-501

Pridopidine EAP

More info: clinicaltrials.gov
NCT06069934

- 45 sites
- Target enrollment: 200 ALS individuals who:
  - do not qualify for clinical trials at the enrolling site and
  - have established care at a specialized ALS center
- Same dose as platform trial: 45 mg twice daily, oral

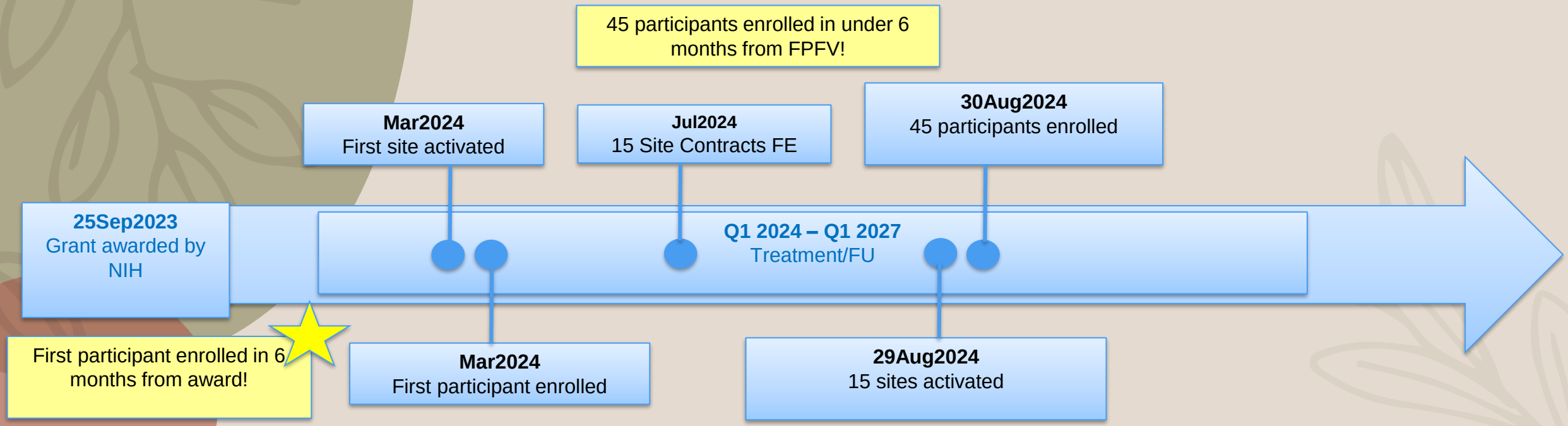
NIH National Institute of Neurological Disorders and Stroke

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

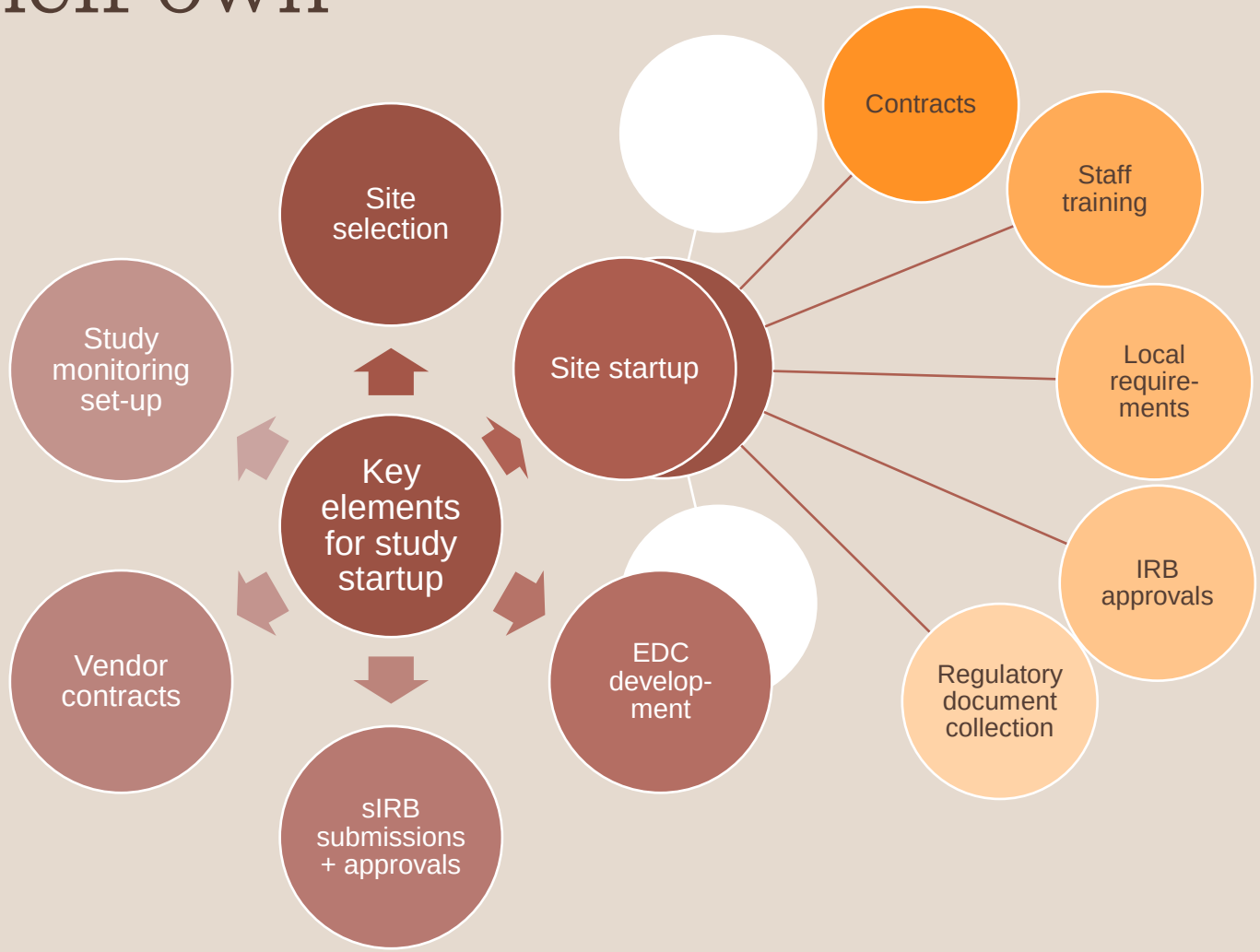
Massachusetts General Hospital
Founding Member, Mass General Brigham
Neurological Clinical Research Institute

Pridopidine EAP: Site Map

Pridopidine EAP 2		
	Planned	Actual as of 9/10/24
Sites	45	15 *Nearing activation: 9*
Participants	200	54 *Screening: 5*

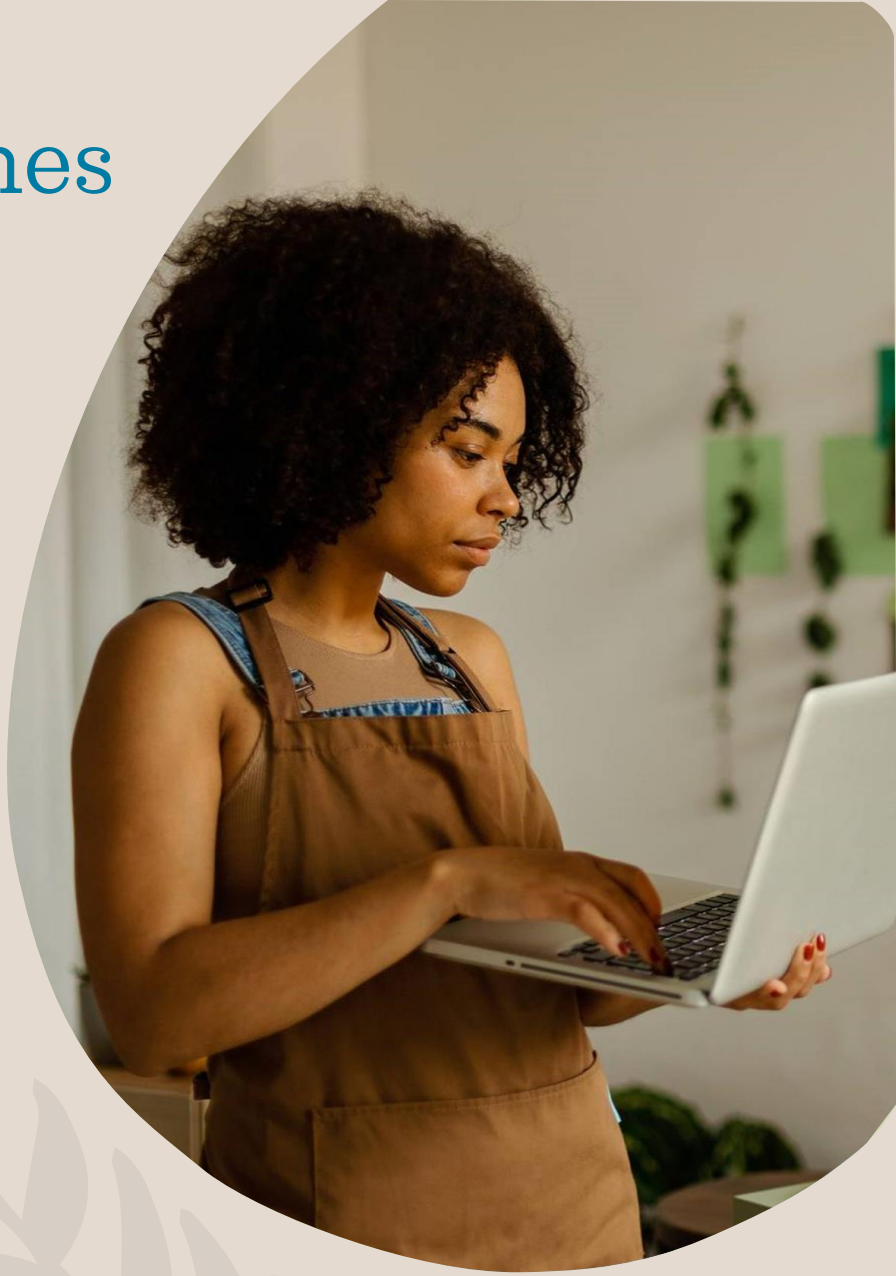

45 participants enrolled in under 6 months from FPFV!
Mar2024
First site activated
Jul2024
15 Site Contracts FE
30Aug2024
45 participants enrolled
25Sep2023
Grant awarded by NIH
Q1 2024 – Q1 2027
Treatment/FU
First participant enrolled in 6 months from award!
Mar2024
First participant enrolled
29Aug2024
15 sites activated

Multi-site EAPs: Complex and expensive central operations; Clinicians can join ongoing multi-site EAPs or create their own



Comparison of trial activation timelines

Study Startup Metrics		
Study Startup Stages	**Pridopidine EAP 2**	**Multi-Site Trials' Average ***
Total Study Start Up Time (Funding to First Participant First Visit)	186 days (6 months)	214 days (7 months)
Funding – IRB Submission	25 days (1 month)	103 days (3 months)
IRB Submission – Approval	40 days (1 month)	60 days (2 months)



Key Factors impacting Startup Timeline:

- Contract negotiations
  - Sponsor, vendors, sites
- Site start up
  - Study staff size and workload of multiple active projects
  - Institutional paperwork and site staff training on the protocol and outcomes
  - Local IRB cede approvals, in addition to central IRB
  - Newer sites are unfamiliar with differences between EAP and trials

*Cernik, Colin, et al. "Non-cancer clinical trials start-up metrics at an academic medical center: Implications for advancing research." *Contemporary Clinical Trials Communications*, vol. 22, June 2021, p. 100774.

RAPA-501 EAP

More info: clinicaltrials.gov
NCT06169176

- Up to 10 sites
- Target enrollment: 40 ALS individuals who:
  - do not qualify for clinical trials at the enrolling site and
  - have established care at a specialized ALS center and
  - have a vital capacity ≤ 50% predicted
- Treatment with RAPA-501 (4 infusions every 6 weeks, followed by 2 year safety monitoring)

NIH National Institute of Neurological Disorders and Stroke
Healey Center Sean M. Healey & AMG Center for ALS at Mass General
MGH Massachusetts General Hospital Neurological Clinical Research Institute

RAPA-501-ALS-EAP Study Progress

* out of 10 clinical study sites

^ out of 40 participants

thank you

SUMA BABU, MBBS., MPH
SBABU@MGH.HARVARD.EDU