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.
HEALEY ALS Platform Trial

Monthly EAP Update – November 9, 2023
Multi-PIs – Healey Center for ALS at MGH

- Suma Babu, MBBS, MPH
  - Assistant Professor of Neurology, Harvard Medical School

- James Berry, MD, MPH
  - Winthrop Family Scholar in ALS Sciences
  - Averill Healey Endowed Chair in ALS
  - Director, MGH Neurological Clinical Research Institute (NCRI)

- Sabrina Paganoni, MD, PhD
  - Co-Director, MGH Neurological Clinical Research Institute (NCRI)
ACT for ALS - A new opportunity to expand access and collect real world data in parallel to clinical trials via EAP

- Signed into law on Dec 23, 2021
- Grants for Research on Therapies via Intermediate-Size EAPs for ALS
- NIH U01 grant mechanism
Expanded Access Protocol (EAP): What is it & for who is it?

• “a pathway for patients with a serious and life-threatening disease to access an investigational product (IP) treatment outside of clinical trials when there are no comparable or satisfactory therapies available.”

• For patients who do not qualify to participate in a clinical trial. The criteria for participation in an EAP are generally broad and inclusive
FDA encourages EAPs while developing drugs for 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]
Trehalose EAP

More info: clinicaltrials.gov NCT05597436
Study Design

- Planned enrollment: 70 pALS at up to 25 sites
- Weekly IV infusions of trehalose, 90.5 mg/mL, at a dose of 0.75 g/kg
- Infusions may take place at the study center or at home

Cohort 1 (Trehalose Naïve)
- Patients who do not qualify for any reasonably accessible ongoing clinical trial.

Cohort 2 (RGE Rollover)
- Patients who have completed Regimen E of the HEALEY ALS Platform Trial and are not eligible for enrollment in another treatment regimen of the platform study.
Site Startup Overview

**Study Startup**

- **Key elements for site activation:**
  - Clinical Site Agreement (CSA)
  - sIRB approval
  - Regulatory Document Collection
  - Local Requirements (IRB, infusion center, pharmacy, etc.)

**Site activation and enrollment**

- 46 enrolled (Cohort 1 = 35, Cohort 2 = 15)
- 18 sites activated
- 18 sites in startup
- 7 participants in screening or scheduled
- 7 sites in startup

- **Startup**
  - Q4 2022 > Q1 2023

- **Enrollment**
  - Q1 2023 > Q1 2024

- **Treatment Follow-up**
  - Q1 2023 > Q3 2024

- **Closeout and Reporting**
  - Q4 2024 > Q1 2025

Data cut 11/7/23
Study Sites & Enrollment updates: ~70% enrolled in 7 months since site activation!

<table>
<thead>
<tr>
<th>Trehalose EAP</th>
<th>Planned</th>
<th>Actual as of 11/7/23</th>
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<tbody>
<tr>
<td>Sites</td>
<td>25</td>
<td>18</td>
</tr>
<tr>
<td>Participants</td>
<td>70</td>
<td>46</td>
</tr>
</tbody>
</table>
Two additional NIH funded EAPs to be enrollment ready by Spring 2024
We are currently in the startup phase for these two new EAPs.

Key elements for study startup:
- Site selection
- Site startup
- Data Capture System development
- sIRB submissions + approvals
- Vendor contracts
- Study monitoring set-up
- Contracts
- Staff training
- Local requirements
- IRB approvals
- Regulatory document collection
Pridopidine EAP2

More info: clinicaltrials.gov NCT06069934
Pridopidine EAP

- 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
Pridopidine is a Sigma-1 receptor (S1R) agonist

➢ Prior clinical data from Healey ALS Platform Trial:
  • demonstrates a favorable safety and tolerability profile
  • did not meet primary and secondary endpoints in the Platform Trial, but showed benefit in slowing bulbar and speech decline
RAPA-501 EAP

More info will be available on clinicaltrials.gov soon
Rapa-501 EAP

➢ Up to 10 sites

➢ Target enrollment: 40 ALS individuals who
  ➢ do not qualify for clinical trials at the enrolling site
  ➢ have established care at a specialized ALS center and
  ➢ have a vital capacity ≤ 50% predicted

➢ Treatment with RAPA-501 infusions
RAPA-501 Mechanism of Action
Induced (i)T_{REG} Cell With Hybrid Th2 Anti-Inflammatory Function

- In ALS pathogenic T cells facilitate axonal degradation and injury.
- Activated RAPA-501 can inhibit pathogenic Th1 cells, which will reduce T cell killing of motor neurons to slow ALS pathogenesis.
For the most up to date information on EAPs, visit the Sean M. Healey & AMG Center for ALS website:

Additional information on EAPs:

➢ FDA
  • fda.gov/news-events/expanded-access/expanded-access-information-patients

➢ Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS)
  • neals.org/als-trials/expanded-access