Design of a Global Phase 3, Randomized, Placebo-Controlled Trial of a Fixed-Dose Sodium Phenylbutyrate and Taurursodiol Coformulation in Amyotrophic Lateral Sclerosis

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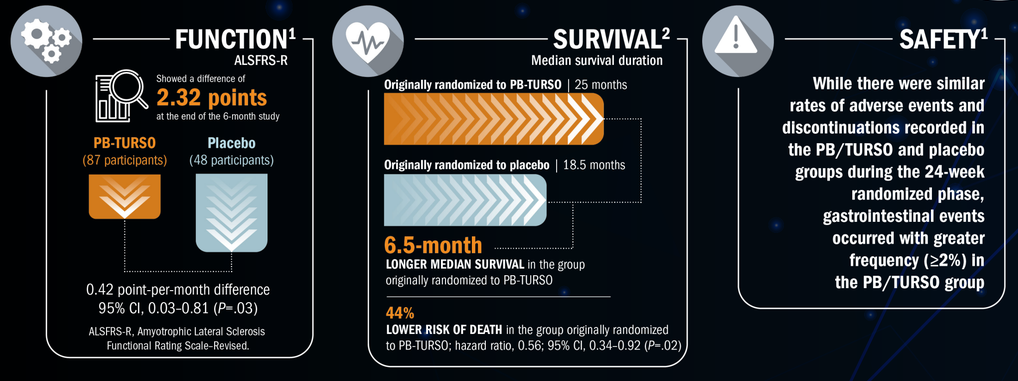
BACKGROUND AND OBJECTIVES

Phase 3 study A35-004 (PHOENIX) will build on the findings of phase 2 study AMX-3500 (CENTAUR)

AMX0035, or PB/TURSO, is an oral, fixed-dose coformulation of sodium phenylbutyrate (PB) and taurursodiol (TURSO; also known as ursodoxicoltaurine)[1]

CENTAUR

CENTAUR was a phase 2, multicenter study in adults with ALS encompassing a 6-month randomized, placebo-controlled phase and an open-label, long-term follow-up phase[1]



[a]PAV (>22 hours daily for >7 days)

References

1. Paganoni S, et al. *N Engl J Med*. 2020;383(10):919-930. 2. Paganoni S, et al. *Muscle Nerve*. 2021;63(1):31-39. 3. van Eijk RPA, et al. *Clin Epidemiol*. 2018;10:333-341.

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Disclosures

SP, LvdB, RvE, AA-C, JA, AC, PC, MC, AL, and CM are members of the steering committee for this study. MM, JT, EW, and PY are employees of Amylyx Pharmaceuticals.

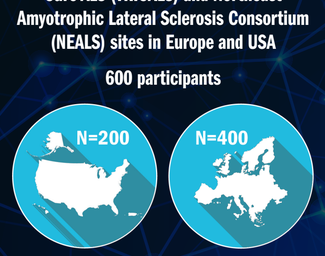
Study A35-004 (PHOENIX)

PHase 3 Trial to Evaluate the Safety and Efficacy of S**O**dium Ph**EN**ylbutyrate - Taurursod**I**ol (ursodo**X**icoltaurine) in ALS

Broader, larger, international population of people with amyotrophic lateral sclerosis (ALS)

~ 65 Treatment Research Initiative to Cure ALS (TRICALS) and Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS) sites in Europe and USA

600 participants



Key Entry Criteria

CENTAUR	PHOENIX
Definite ALS, El Escorial criteria	Definite ALS or Clinically probable ALS, El Escorial criteria
<18 months from symptom onset	<24 months from symptom onset
Slow vital capacity (SVC) >60%	SVC ≥55%
Riluzole/edaravone use permitted	Riluzole/edaravone use permitted

PHOENIX

Primary Study Objectives

- To determine the **safety** and **tolerability** of PB/TURSO
- To assess the impact of PB/TURSO treatment compared to placebo on **disease progression over 48 weeks** based on change from baseline of ALSFRS-R and survival[3]

Telemedicine-friendly study design

Safety

- Incidence and severity of adverse events and serious adverse events
- Incidence of abnormalities in clinical laboratory assessments
- Withdrawal from the trial

Primary Efficacy Outcome

- Joint assessment of ALSFRS-R total score progression over 48 weeks and survival[3]

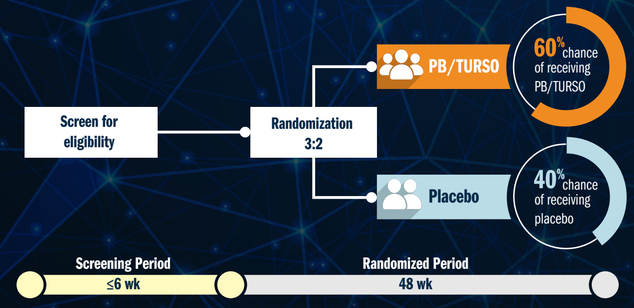
Secondary Efficacy Outcomes

- SVC
- Patient-reported outcomes (40-Item ALS Assessment Questionnaire, EuroQol 5-Dimension, and EuroQol Visual Analogue Scale)
- Time to transition through King's and MiToS stages
- Time to death, tracheostomy, or permanent assisted ventilation (PAV)[a]
- All-cause mortality will be assessed beyond the planned 48-week follow-up

Exploratory Outcomes

- Caregiver burden
- Plasma biomarkers of neuron damage and neuroinflammation

Trial to begin recruiting in Q3 2021



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