Design of the International, Randomized, Placebo-Controlled Phase 3 PHOENIX Trial (A35-004) of AMX0035 in ALS

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BACKGROUND AND OBJECTIVES

Phase 3 PHOENIX trial will build on the findings of phase 2 CENTAUR trial

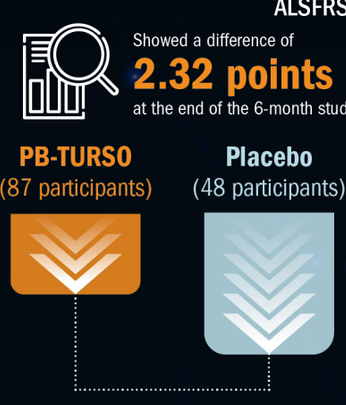
AMX0035, or PB-TURSO, is an oral, fixed-dose coformulation of sodium phenylbutyrate (PB) and taurursodiol (also known as ursodoxicoltaurine)[1]

CENTAUR

CENTAUR TRIAL | CENTAUR was a 24-week US multicenter, randomized, placebo-controlled trial[1]

FUNCTION[1]
ALSFRS-R

Showed a difference of **2.32 points** at the end of the 6-month study



0.42 point-per-month difference
95% CI, 0.03–0.81 (*P*=0.03)

ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised.

SURVIVAL[2]
Median survival duration

6.5-month **LONGER MEDIAN SURVIVAL** in the group originally randomized to PB-TURSO

44% **LOWER RISK OF DEATH** in the group originally randomized to PB-TURSO; HR, 0.56; 95% CI, 0.34–0.92 (*P*=0.02)

SAFETY[1]

Similar rates of adverse events were recorded in the PB-TURSO and placebo groups during the 24-week randomized period

Discontinuations related to adverse events occurred more frequently in the PB-TURSO group than in the placebo group

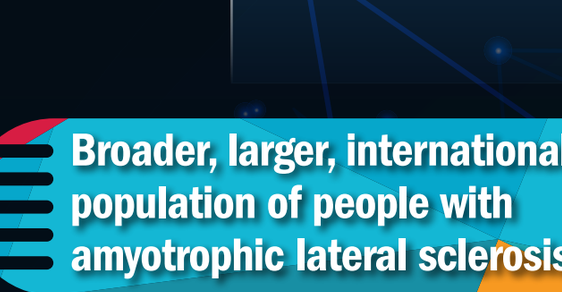
PHOENIX TRIAL

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

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

~ 55 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]

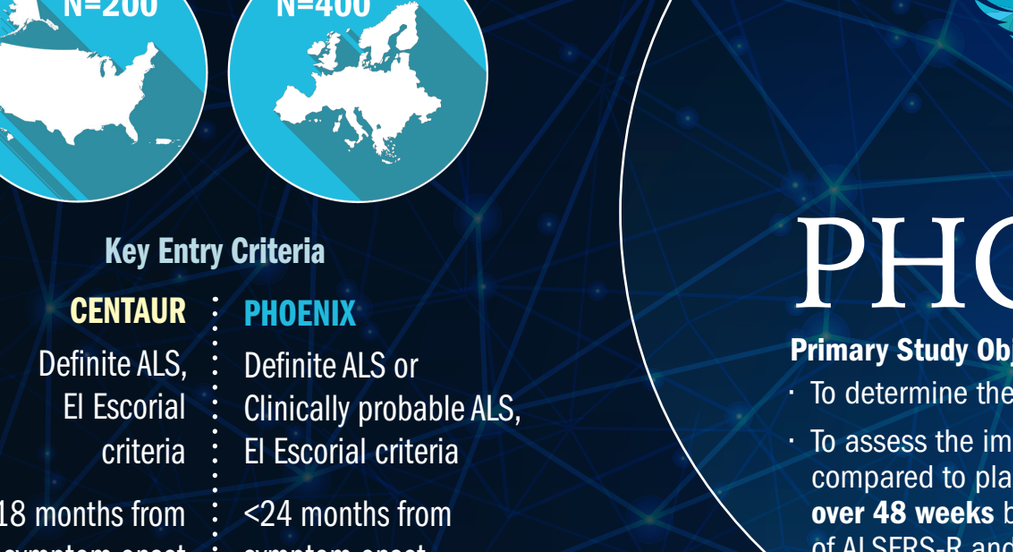
Secondary Efficacy Outcomes

- SVC using self-administered spirometer
- 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



Post-trial PB-TURSO will be made available to participants completing the 48-week study period in accordance with each region's regulatory guidance

[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;10:333-41.

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Disclosures

LvdB, SP, RvE, AA-C, 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.