International Phase 3 Trial Evaluating Sodium Phenylbutyrate and Taurursodiol in Amyotrophic Lateral Sclerosis (PHOENIX)

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BACKGROUND

- PB and TURSO (AMX0035) is an oral, fixed-dose coformulation of sodium phenylbutyrate (PB) and ursodoxicoltaurine (TURSO, also known as taurursodiol). The exact mechanism by which PB and TURSO exerts its effect is unknown; it is hypothesized to reduce neuronal death via pathways in the endoplasmic reticulum and mitochondria.
- In the CENTAUR trial, administration of PB and TURSO resulted in significant retention of function and longer overall survival in people with ALS, with a similar safety profile to placebo[1,2]
- Overall AE incidence was similar in both groups, but early gastrointestinal events occurred with greater frequency in the PB and TURSO group[1,2]

PHOENIX (NCT05021536; EudraCT 2021-000250-26)

is an ongoing international, phase 3 trial aimed at demonstrating the safety and efficacy of PB and TURSO featuring a people-centric design in a larger, more heterogeneous population over a longer duration

Primary Objectives

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

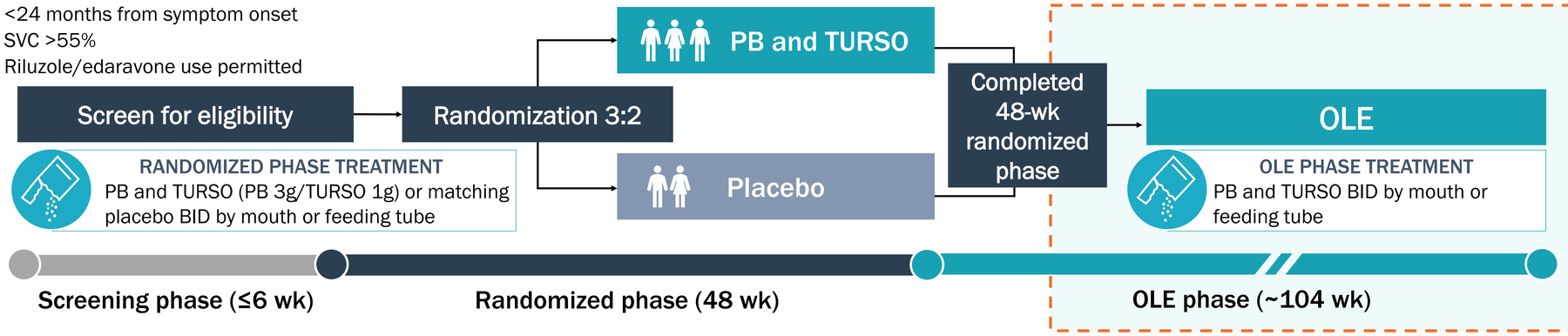
Target Enrollment

- ~65 sites
- ~600 adults
  - Approximately 400 EU, 200 US

METHODS

Key inclusion criteria

- Clinically definite ALS or clinically probable ALS, revised El Escorial criteria
- <24 months from symptom onset
- SVC >55%
- Riluzole/edaravone use permitted



Key OLE Phase Outcomes

- Function (ALSFRS-R)
- Overall survival
- Time to key events (tracheostomy, PAV, NIV, PEG tube placement, hospitalization >24 h)
- Safety

Primary Efficacy Outcome

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

Secondary Efficacy Outcomes

- SVC change from baseline to week 48
- Patient-reported outcomes (ALSAQ-40, EQ-5D, EQ-VAS)
- Time to transition through King's and MiToS stages
- Time to death, tracheostomy, or PAV (NIV >22 h/d for >7 d)
- All-cause mortality beyond the planned 48-week follow-up

Safety

- Incidence and severity of AEs and serious AEs
- Incidence of abnormalities in clinical laboratory assessments
- Withdrawal from trial

- The PHOENIX trial is underway; recruitment has stopped in the US and is ongoing in Europe
- An OLE will provide PB and TURSO for up to 2 years for all participants completing the 48-week randomized-controlled phase

For more information on PHOENIX and participating sites

www.amylyxalstrial.com

Abbreviations

AE, adverse event; ALS, amyotrophic lateral sclerosis; ALSAQ-40, Amyotrophic Lateral Sclerosis Assessment Questionnaire (40-item); ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised; BID, twice daily; EMA, European Medicines Agency; EQ-5D, EuroQol-5D; EQ-VAS, EQ Visual Analog Scale; FDA, US Food and Drug Administration; MiToS, Milano Torino Functional Staging; NIV, noninvasive ventilation; OLE, open-label extension; PAV, permanent assisted ventilation; PEG, percutaneous endoscopic gastrostomy; SVC, slow vital capacity.

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.

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Disclosures

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

PB and TURSO is an investigational product and has not been determined to be safe and effective by the FDA or EMA.

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