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

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BACKGROUND

- AMX0035 is an oral, fixed-dose combination of sodium phenylbutyrate (PB) and taurursodiol (TURSO, also known as ursodoxicoltaurine), hereafter referred to as PB and TURSO[1]
- The PHase 3 SOdium PhENylbutyrate and TaurursodIol (UrsodoXicoltaurine) (PHOENIX) trial (NCT05021536; EudraCT 2021-000250-26) is an ongoing international, phase 3 trial[1,2]
- PHOENIX will evaluate the safety and efficacy of PB and TURSO in a larger, more heterogeneous population of people living with ALS over a longer duration than the phase 2 CENTAUR trial[1]

OBJECTIVE

- Provide an update on the PHOENIX trial

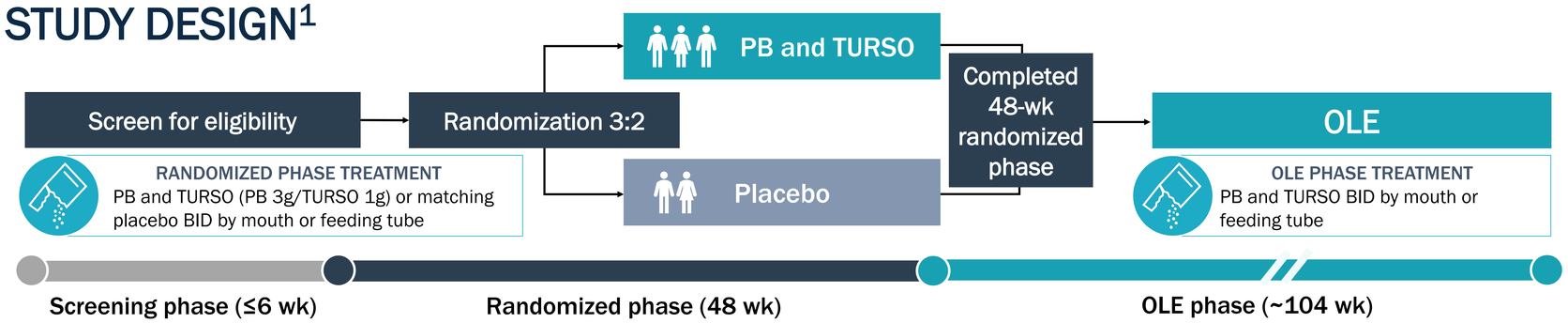
TARGET ENROLLMENT[1]

- ≈65 sites
- ≈600 adults

COUNTRIES WITH ENROLLING SITES[2]

Current as of date of presentation (December 6 – 9, 2022)

STUDY DESIGN[1]



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

Primary Efficacy Outcome

- Joint assessment of ALSFRS-R total score progression over 48 weeks adjusted for mortality

Secondary Efficacy Outcome

- 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

Key OLE Phase Outcomes

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

CURRENT STATUS

The trial is underway; recruitment is more than halfway complete

Recruitment is ongoing in Europe[2]

- The majority of PHOENIX participant recruitment has been in Europe and will continue to be
- The PHOENIX OLE phase will continue in Europe

Recruitment is closed in the United States[2]

- On September 29, 2022, the FDA approved PB and TURSO for the treatment of ALS in adults[3]
- If US participants and their clinicians decide to continue treatment with PB and TURSO, they will transition to commercial product. US trial investigators will be notified about specific processes
- The PHOENIX OLE phase will NOT open in the United States. However, US participants will be followed for long-term survival status

AMX0035 is an investigational drug in EMA and not approved for use.

DISCUSSION

- PHOENIX is underway and recruiting in Europe as planned[2]
- PHOENIX features a participant-centric design and incorporates a larger, more heterogeneous population of people living with ALS followed for a longer duration than CENTAUR[1]
- The PHOENIX study is designed to be telemedicine friendly, with a total of ≤6 in-person visits
- The additional OLE phase for European participants will further extend the assessment of safety and efficacy of PB and TURSO in ALS. US participants will be followed for long-term survival status despite no OLE phase in the US

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Reference

1. Van den Berg LH, et al. International Phase 3 Trial Evaluating Sodium Phenylbutyrate and Taurursodiol in Amyotrophic Lateral Sclerosis (PHOENIX). Poster presented at 17th International Congress on Neuromuscular Diseases. July 5-9, 2022; Brussels, Belgium. **2.** ClinicalTrials.gov identifier: NCT05021536. Clinicaltrials.gov. Updated August 3, 2022. Accessed September 26, 2022. https://clinicaltrials.gov/ct2/show/NCT05021536. **3.** Relyvrio. Prescribing Information. Amylyx Pharmaceuticals, Inc.

Disclosures

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

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; NEALS, Northeast ALS Consortium; NIV, noninvasive ventilation; OLE, open-label extension; PAV, permanent assisted ventilation; PEG, percutaneous endoscopic gastrostomy; RCP, randomized placebo-controlled phase; SVC, slow vital capacity; TRICALS, Treatment Research Initiative to Cure ALS.

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