Functional and Long-Term Survival Data of AMX0035 in Amyotrophic Lateral Sclerosis: Results of the CENTAUR Trial

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AMYLYX

- AMX0035 is an oral, fixed-dose coformulation of the compounds sodium phenylbutyrate (PB) and taurursodiol (TURSO) designed to reduce neuronal death in people with ALS by simultaneously mitigating endoplasmic reticulum stress and mitochondrial dysfunction. CENTAUR was a randomized, double-blind, placebo-controlled trial conducted at 25 centers of the Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS) in the United States from June 2017 through September 2019

- Packaged in sachets (3g PB, 1g TURSO per sachet)
- Dissolved in water and administered BID by mouth or via feeding tube
- Taste, appearance, and solubility matched to placebo

CENTAUR Phase 2 Study Design

Screening Period (≤42 days)	Randomized Period (24 weeks)	Open Label Extension (OLE) (up to 132 weeks; ongoing)

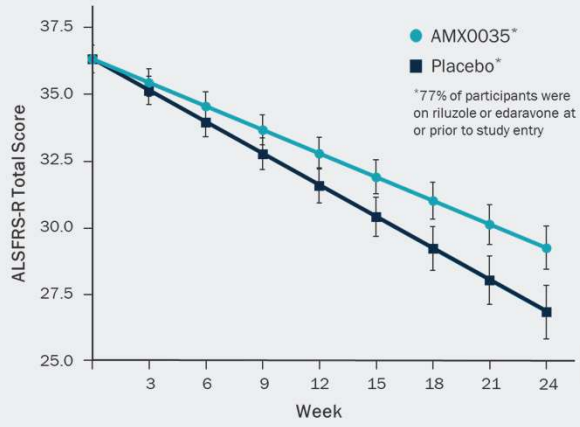
Screened for eligibility (n=177) → Randomized 2:1 (n=137) → AMX0035 (n=89) / Placebo (n=48) → AMX0035 (n=90)

- Definite ALS, El Escorial criteria
- <18 months from symptom onset
- Slow vital capacity (SVC) >60%
- 92% (90/98) of eligible participants enrolled in OLE

Approved therapies for ALS (riluzole and edaravone) allowed

Change of slope in ALSFRS-R (Primary Efficacy Endpoint)
Randomized Period

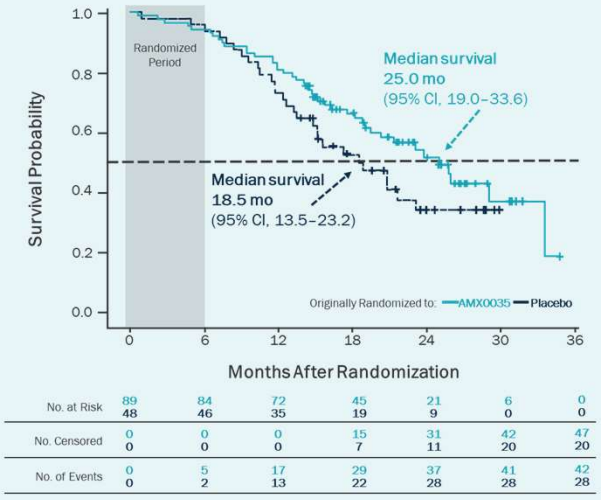
ALSFRS-R Total at Week 24



- Significant slowing of functional decline among participants randomized to AMX0035 relative to placebo
- Difference: 0.42 points/mo, (95% CI 0.03–0.81), P=0.03
  - 2.32 points at the end of the six-month study

Prespecified Overall Survival Analysis
Spans Randomized Period and OLE

Overall Survival for All Participants Randomized in CENTAUR



No. at Risk	89 48	84 46	72 35	45 19	21 9	6 0	0 0
No. Censored	0 0	0 0	0 0	15 7	31 11	42 20	47 20
No. of Events	0 0	5 2	17 13	29 22	37 28	41 28	42 28

- Risk of death was 44% lower in the originally randomized to AMX0035 group; HR 0.56 (95% CI 0.34-0.92), P=0.02
- 6.5 month longer median survival in the group originally randomized to AMX0035

Safety
Randomized Period

- Nearly all participants (AMX0035, 97%; placebo, 96%) reported one or more AEs during the trial. Most did not lead to modification or interruption of study drug dosing and were not considered related to treatment
  - Events that occurred with greater (≥2%) frequency in the AMX0035 group were primarily gastrointestinal

CENTAUR

- Administration of AMX0035 is associated with both a statistically significant functional and survival benefit in people with ALS
- Similar rates of adverse events were recorded in the AMX0035 and placebo groups during the 24-week randomized period

For more information, join the Pipeline Session Oral Presentation
Tuesday, February 23 11:30 AM EST

References
1. Paganoni S, et al. N Engl J Med. 2020;383:919-930.
2. Paganoni S, et al. Muscle Nerve. 2020. https://doi.org/10.1002/mus.27091.

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