



Amylyx Pharmaceuticals Announces Publication of New CENTAUR Trial Analyses Further Demonstrating Significant Survival Benefit with AMX0035 in People with ALS

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- An analysis using the rank-preserving structural failure time model (RPSFTM), a method frequently employed in oncology to account for placebo crossover, estimated a 10.6-month longer median survival duration for AMX0035 participants
- Participants randomized to receive AMX0035 and who continued into the open-label extension (OLE) phase showed an 18.8-month longer median survival duration than participants who never received AMX0035 in a subgroup analysis

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 5, 2022-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) ("Amylyx" or the "Company") today announced the publication of long-term survival analyses of the Phase 2 CENTAUR trial adjusting for treatment crossover of the placebo group. The post hoc analyses suggested a larger survival benefit for AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO; also known as ursodoxicoltaurine]) when adjusting for placebo crossover ranging from 10.6 to 18.8 months compared with 6.9 months seen in the original prespecified intent-to-treat (ITT) analysis in participants with amyotrophic lateral sclerosis (ALS). These results are published in the peer-reviewed medical journal, [Muscle & Nerve](#).

"Trials that incorporate placebo-to-active treatment crossover are critically important in rapidly fatal diseases like ALS, however, this design may underestimate the clinical effect of investigational therapies," said Machele Manuel, Ph.D., Head of Global Medical Affairs of Amylyx. "Fortunately, statistical models, like the RPSFTM, allow us to adjust results for treatment crossover. Here, similar to the prespecified ITT analysis, we observed a significant survival benefit for AMX0035 in the survival analyses adjusting for treatment crossover, potentially offering those living with ALS and their families hope of sharing more memories and milestones together."

Survival analyses incorporated updated participant vital status information from the prior interim ITT analysis. The final dataset compared time to death (all-cause mortality) from the point of randomization in the Phase 2 CENTAUR trial through a cutoff date of July 20, 2020 (longest follow-up, 35 months after randomization) and the date of the final open-label extension (OLE) phase participant visit (March 1, 2021, up to 42 months after randomization). Vital status could be determined for all but one participant who was censored at the date of last follow-up. Post hoc analyses performed included a RPSFTM and subgroup analysis.

- As of the July 2020 cutoff date, results of the final overall survival ITT analysis showed a significantly longer median survival duration of 6.9 months in those originally randomized to AMX0035 compared to those originally randomized to placebo (hazard ratio [HR], 0.57; 95% CI, 0.35–0.92; $P=$.023).
 - At the March 2021 cutoff date, results showed a significantly lower hazard of death and longer median survival duration of 4.8 months in those originally randomized to AMX0035 compared to those originally randomized to placebo (HR 0.64; 95% CI, 0.42-1.00; $P=$.048).
- Results of the statistical methods that account for treatment crossover (RPSFTM and subgroup analyses) showed a greater survival benefit compared to ITT analysis.
 - As of the July 2020 cutoff date, the observed median survival of 25.8 months in those originally randomized to AMX0035 compared to RPSFTM-adjusted median survival of 15.2 months in those originally randomized to placebo, a 10.6-month difference, with an HR of 0.39 (95% CI, 0.17–0.88; $P=$.023).
 - The RPSFTM analysis models what the survival outcome from the placebo group would have been had participants not switched to AMX0035 in the OLE phase.
 - At the March 2021 cutoff date, the same RPSFTM analyses were performed and yielded consistent results.
- As of the July 2020 cutoff date, post hoc assessment of subgroups based on randomization group as well as enrollment in the OLE phase demonstrated that participants who were originally randomized to AMX0035 and then enrolled in the OLE phase survived 18.8 months ($P<$.0001) longer than participants who never received AMX0035.

"The results of these long-term analyses of the CENTAUR trial provide further evidence that AMX0035 may offer a survival benefit in people with ALS and provide insights into potential new approaches to analyze survival data in ALS trials," said Sabrina Paganoni, M.D., Ph.D., principal investigator of the CENTAUR trial, investigator at the Sean M. Healey & AMG Center for ALS at Mass General and Associate Professor of PM&R at Harvard Medical School and Spaulding Rehabilitation Hospital. "As a serious and fatal disease, time is invaluable for those living with ALS and their families, and any potential treatment that may offer more time is important."

About AMX0035

AMX0035 is a proprietary oral fixed-dose combination of two small molecules: sodium phenylbutyrate (PB), which is a small molecular chaperone designed to reduce the unfolded protein response (UPR), preventing cell death resulting from the UPR, and taurursodiol (TURSO; also known as ursodoxicoltaurine), which is a Bax inhibitor designed to reduce cell death through apoptosis. PB and TURSO were combined in a fixed-dose formulation in an effort to reduce neuronal death and dysfunction. AMX0035 is designed to target the endoplasmic reticulum and mitochondrial-dependent neuronal degeneration pathways in ALS and other neurodegenerative diseases.

About the CENTAUR Trial

CENTAUR was a multicenter Phase 2 clinical trial in 137 participants with ALS encompassing a 6-month randomized placebo-controlled phase and an open-label long-term follow-up phase. The trial met its primary efficacy endpoint of reducing functional decline as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R).

Overall, reported rates of adverse events and discontinuations were similar between AMX0035 and placebo groups during the 24-week randomized phase; however, gastrointestinal events occurred with greater frequency ($\geq 2\%$) in the AMX0035 group. Detailed data from CENTAUR is published in the *New England Journal of Medicine* (NEJM) and *Muscle & Nerve*.

The CENTAUR trial was funded, in part, by the ALS ACT grant and the ALS Ice Bucket Challenge, and was supported by The ALS Association, ALS Finding a Cure (a program of The Leandro P. Rizzuto Foundation), the Northeast ALS Consortium, and the Sean M. Healey & AMG Center for ALS at Mass General.

About Amylyx Pharmaceuticals

Amylyx Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company working on developing a novel therapeutic for amyotrophic lateral sclerosis (ALS) and other neurodegenerative diseases. For more information, visit [amylyx.com](https://www.amylyx.com) and follow us on [LinkedIn](#) and [Twitter](#). For investors, please visit investors.amylyx.com.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding the potential approval of AMX0035 for the treatment of ALS; the potential of AMX0035 as a treatment for ALS and the potential benefits of administration of AMX0035; and expectations regarding our longer-term strategy, including the potential for AMX0035 to address other neurodegenerative diseases. Any forward-looking statements in this statement are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of Amylyx' program development activities, Amylyx' ability to execute on its strategy, regulatory developments, expectations regarding the timing of FDA review of AMX0035 for the treatment of ALS, Amylyx' ability to fund operations, and the impact that the ongoing COVID-19 pandemic will have on Amylyx' operations, as well as those risks and uncertainties set forth in Amylyx' United States Securities and Exchange Commission (SEC) filings, including Amylyx' Annual Report on Form 10-K for the year ended December 31, 2021, and subsequent filings with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Amylyx undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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