Amylyx Pharmaceuticals Announces Oral Presentation of Safety and Tolerability Data on AMX0035 from Clinical Trials at 2022 American Academy of Neurology Annual Meeting

April 2, 2022

- Summary of data from CENTAUR and PEGASUS showed AMX0035 was safe and well tolerated in clinical trials in amyotrophic lateral sclerosis (ALS) and Alzheimer's disease (AD)

- Majority of treatment-emergent adverse events (TEAEs) associated with AMX0035 were gastrointestinal in both trials with no new safety signals identified

- Findings help further clarify the safety profile of AMX0035

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 2, 2022-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) ("Amylyx" or the "Company") today announced the presentation of safety and tolerability data on AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO; also known as ursodoxicoltaurine]) as assessed in the CENTAUR and PEGASUS clinical trials in participants with amyotrophic lateral sclerosis (ALS) and Alzheimer's disease (AD), respectively. The data support the overall safety profile of AMX0035 as findings from this analysis show adverse event incidence was generally similar between AMX0035 and placebo groups in both sets of trial participants.

"The results of this analysis provide additional insights and clarifications on the overall safety and tolerability of AMX0035 in people with two different conditions, ALS and AD, and how these diseases might impact the results," said Sabrina Paganoni, M.D., Ph.D., principal investigator of the CENTAUR trial, investigator at the Healey & AMG Center for ALS at Massachusetts General Hospital and Associate Professor of PM&R at Harvard Medical School and Spaulding Rehabilitation Hospital. "The comparison of TEAEs across both the CENTAUR and PEGASUS clinical trials suggests the higher overall incidence of TEAEs in CENTAUR trial participants, including muscular weakness and falls, could be attributed to the natural progression of ALS, as they were not observed in people with AD."

In the CENTAUR trial participants (AMX0035, n=89; placebo, n=48) completing the 24-week randomized phase were eligible to enroll in an open-label extension phase and receive AMX0035 (≤132 weeks, week 24 reported). PEGASUS was a 24-week randomized trial in adults with AD or mild cognitive impairment (AMX0035, n=51; placebo, n=44). Evaluation of AMX0035's safety and tolerability was the primary objective of both trials. Results of the summary of the clinical trials showed that:

- The majority of TEAEs associated with AMX0035 were gastrointestinal, consistent with the observed individual safety profiles of the components of AMX0035.
    - In both trials, diarrhea and, to a lesser extent, abdominal discomfort/pain, abdominal distension, and dyspepsia were more frequent with AMX0035 versus placebo.
- No new safety signals were identified.
    - While the majority of participants in the phase 2 studies experienced TEAEs, they were largely non-serious, mild or moderate in intensity, and assessed as unrelated to treatment with study medication.
- Findings in AD further elucidated the safety profile of AMX0035, as TEAEs in the CENTAUR trial appear to have been largely disease driven.
    - Further comparison of the TEAEs across both trials suggests that the higher overall incidence of TEAEs in the CENTAUR trial was attributable to symptoms of natural ALS progression, namely muscular weakness and falls, which were among the most common TEAEs in CENTAUR.

"We are committed to the discovery and development of new treatment options with the potential to offer hope and extend function in those living with neurodegenerative diseases affected by the progressive loss of certain abilities," said Machelle Manuel, Ph.D., Head of Global Medical Affairs of Amylyx. "We are pleased to share the findings from this analysis further characterizing the safety profile of AMX0035 with the medical and scientific community at AAN this year."

The abstract, "Safety of a Fixed-Dose Coformulation of Sodium Phenylbutyrate and Taurursodiol in Amyotrophic Lateral Sclerosis and Alzheimer's Disease: Integrated Clinical Trials Experience," was selected for an oral presentation in the ALS and Motor Neuron Disorders scientific session, and will be presented on Monday, April 4, 2022 (1:00-3:00 p.m. PT / 4:00-6:00 p.m. ET).

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 (≥2%) in the AMX0035 group. Detailed data from CENTAUR is published in the *New England Journal of Medicine* (NEJM) and *Muscle and 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 the PEGASUS Trial

PEGASUS (NCT03533257) was a randomized, double-blind, multi-center, placebo-controlled trial evaluating the safety, tolerability and activity of AMX0035 in 95 adults with dementia or late mild cognitive impairment (MCI) due to AD over 24 weeks of treatment. The trial was designed to evaluate tolerability in this patient population while also assessing efficacy measures and diverse, disease-relevant markers to allow for evaluation and correlation of imaging-based markers, neurobiological changes, functional measures, and cognitive outcomes in a broad group of people with AD.

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 www.amylyx.com and follow us on LinkedIn and Twitter. For investors please visit www.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 the of 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: Amylyx' strategy, business plans and objectives for 2022 and beyond; the potential of AMX0035 as a treatment for ALS and AD and the efficacy and safety profile of AMX0035; the timing, progress and results of our Phase 3 PHOENIX clinical trial of AMX0035; the potential of AMX0035 or other future therapeutic candidates as a treatment for neurodegenerative diseases; and expectations regarding our longer-term strategy. 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 commercial and regulatory 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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