Amylyx Pharmaceuticals Announces Publication of Data Showing Randomization to AMX0035 Prolonged Tracheostomy/Ventilation-free Survival and Reduced Occurrence of First Hospitalization

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- *Adding to previously reported overall functional and survival benefit data for AMX0035, these findings support effect of AMX0035 on disease progression in ALS*
- *Randomization to AMX0035 resulted in a lower occurrence of* death or *tracheostomy/permanent assisted ventilation by 49% and first hospitalization by 44% over the Phase 2 trial and duration of follow-up*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 16, 2022-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) (“Amylyx” or the “Company”) today announced the publication of long-term prespecified analyses assessing the occurrence of key events in addition to death from the Phase 2 CENTAUR trial including tracheostomy, permanent assisted ventilation (PAV), and first hospitalization. Data analyses demonstrated that early administration of AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO; also known as ursodoxicoltaurine]) resulted in a lower occurrence of tracheostomy/PAV and delayed first hospitalization during the trial and follow-up period in participants with amyotrophic lateral sclerosis (ALS). These results are published in the peer-reviewed medical journal, *Journal of Neurology, Neurosurgery and Psychiatry*.

“People living with ALS often require medical interventions like mechanical ventilation as the disease progresses and impacts the muscles of respiration,” 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. “These interventions come at a great cost, both personally and financially, for people living with the disease and developing therapies that can help delay these interventions can have a positive impact on their lives.”

The analyses encompassed the occurrence of the following key events from the point of randomization in the Phase 2 CENTAUR trial through a cutoff date of July 20, 2020 (longest post-randomization follow-up, 35 months): death (all-cause), tracheostomy (either for respiratory distress or airway clearance), PAV (defined as non-invasive ventilation >22 hours/day for >7 days), and hospitalizations specifically for ALS-related procedures (placement of a feeding tube, tracheostomy for management of secretions or respiratory support, or diaphragm pacing system) or due to a severe or serious adverse event, including those relating to progression or complications of ALS. The prespecified analysis population was the modified intent-to-treat population, comprising all randomized participants who received at least one dose of originally assigned trial medication and had at least one post-baseline ALS Functional Rating Scale-Revised (ALSFRS-R) total score. All randomized participants within this population were included in the analyses, including those who: discontinued from the trial; were lost to follow-up; or did not continue into the open-label extension phase. Results of this long-term analysis of CENTAUR showed:

- Risk of any key event was 47% lower in those originally randomized to the AMX0035 group (n=87) versus those randomized to placebo (n=48, 71% of whom received delayed-start AMX0035 in the OLE phase) (hazard ratio [HR], 0.53; 95% CI, 0.35–0.81; *P*=.003).
- Risk of death or tracheostomy/PAV was 49% lower in the group originally randomized to AMX0035 treatment (HR, 0.51; 95% CI, 0.32–0.84; *P*=.007).
- Risk of first hospitalization was 44% lower in those originally randomized to the AMX0035 group (HR, 0.56; 95% CI, 0.34–0.95; *P*=.03).
- As of the analysis cutoff with the longest follow up of 35 months, median key event-free survival duration was 4.8 months longer in participants originally randomized to AMX0035 versus placebo, and median tracheostomy/PAV-free survival duration was 7.3 months longer.
- As of the cutoff date, median time to first hospitalization was not yet reached in the group originally randomized to AMX0035, compared with 14.1 months in the group originally randomized to placebo.

“We’re encouraged by the positive data that we continue to collect from the CENTAUR study on the potential benefits of AMX0035 for people with ALS, including a lower occurrence of first hospitalization based on data collected up to 35 months following administration,” said Machelle Manuel, Ph.D., Head of Global Medical Affairs of Amylyx. “These results suggest that AMX0035, if approved, may help extend the time before greater care needs arise – a meaningful benefit for those living with ALS and their loved ones. We will continue to explore other potential benefits of AMX0035 during the follow-up period and plan to evaluate its potential in other neurodegenerative diseases.”

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.

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 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: Amylyx' strategy, business plans and objectives for 2022 and beyond; the potential of AMX0035 as a treatment for ALS, the efficacy and safety profile of AMX0035 and the potential for regulatory approval of AMX0035 as a treatment for ALS in the U.S., Canada and Europe; the potential commercial launch of AMX0035 as a treatment for ALS, if approved, and the ability to scale operations to prepare for commercial launch; 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 generally; 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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