# Amylyx Pharmaceuticals Announces First Participant Dosed in the Global Phase 3 ORION Study of AMX0035 in Progressive Supranuclear Palsy (PSP)

December 22, 2023

*- Largest ever PSP clinical trial will evaluate the efficacy and safety of AMX0035 in adults with PSP compared to placebo*

*- Trial to enroll approximately 600 participants across the U.S., Canada, Europe, and Japan*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 22, 2023-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced that the first participant has been dosed in ORION, a randomized, double-blind, placebo-controlled Phase 3 clinical trial of AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO]) for the treatment of progressive supranuclear palsy (PSP). The Phase 3 trial will enroll approximately 600 participants in approximately 100 sites across the United States, Canada, the European Union, the United Kingdom, and Japan, making this the largest PSP clinical trial to date.

More information on the ORION clinical trial can be found at www.clinicaltrials.gov, NCT06122662.

"There is a pressing unmet need within the PSP community for new and effective treatment options, as no disease-modifying therapies have been approved for the treatment of the disease," said Dr. Kristophe Diaz, Executive Director and Chief Science Officer at CurePSP. "We're looking forward to continuing our collaboration on ORION, recognizing that a united global effort is essential to usher in promising advancements and raise awareness for people living with PSP and their families."

The primary efficacy endpoint will evaluate change in disease progression from baseline to Week 52 as measured by total score on the 28-item Progressive Supranuclear Palsy Rating Scale (PSPRS), an established and validated endpoint in PSP clinical trials.

Secondary efficacy endpoints are disease progression as measured by a modified 10-item PSPRS score and motor aspects of activities of daily life as measured by the Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part 2 (MDS-UPDRS Part II). Exploratory outcomes include changes in activities of daily living, cognitive function, quality of life, overall survival, brain regional volumes, fluid biomarkers of neuronal injury/inflammation, and caregiver burden.

Safety and tolerability will be evaluated by assessing the frequency of treatment emergent adverse events (TEAEs) and serious adverse events (SAEs). Participants completing the 52-week randomized, placebo-controlled phase of the trial will have the option to enroll in an Open Label Extension where all participants will receive AMX0035 for up to an additional year. Topline results are anticipated in 2-3 years.

"AMX0035 has a strong scientific rationale in PSP, targeting key upstream pathways in disease pathophysiology including the unfolded protein response and mitochondrial dysfunction. Furthermore, PSP is a tauopathy associated with tau dysfunction, tau aggregation, and widespread neurodegeneration, and AMX0035 has been shown to reduce p-tau in a previous Alzheimer's disease trial. These components are essential to the pathophysiology of PSP, and we are excited about the strong scientific rationale supporting AMX0035 in PSP," said Prof. Dr. Günter Höglinger, Director of the Department of Neurology at Ludwig-Maximilians-University (LMU) Hospital, Munich, Germany, and Primary Investigator of the Phase 3 ORION clinical trial.

"Given PSP is a relentlessly progressive disease, it is imperative that we respond to the unmet needs of the community with a sense of urgency. Our current focus is on activating clinical trial sites in all participating regions in order to complete the trial as quickly and efficiently as possible, gearing toward what could potentially be the first therapy for the PSP community," said Lahar Mehta, MD, Head of Global Clinical Development at Amylyx.

**About AMX0035 / RELYVRIO®/ ALBRIOZA™ / ALBRIOZA®**

AMX0035 is an oral, fixed-dose combination of sodium phenylbutyrate and taurursodiol (known as ursodoxicoltaurine outside of the U.S.). It is approved as RELYVRIO® to treat amyotrophic lateral sclerosis (ALS) in adults in the U.S. and approved with conditions as ALBRIOZA™ for the treatment of ALS in Canada. AMX0035 is being studied for the potential treatment of other neurodegenerative diseases, and Amylyx is exploring its treatment in other populations and regions. The formulation of RELYVRIO, ALBRIOZA, and AMX0035 is identical.

**About the ORION Trial**

The Phase 3 ORION trial (NCT06122662) is a global, randomized, double-blind, placebo-controlled Phase 3 clinical trial designed to assess the efficacy, safety, and tolerability of AMX0035 compared to placebo in people living with progressive supranuclear palsy (PSP). Approximately 600 participants will be enrolled across the United States, Canada, the European Union, the United

Kingdom, and Japan. The ORION Phase 3 trial was designed and planned in collaboration with key global academic leaders, people living with PSP and their caregivers, and industry advocacy organizations.

**About PSP**

Progressive supranuclear palsy (PSP) is a sporadic, rare and adult-onset neurodegenerative disorder that affects walking and balance, eye movement, swallowing, and speech.

People living with PSP have a life expectancy of six to eight years after initial diagnosis, and its epidemiology is similar to that of amyotrophic lateral sclerosis (ALS). PSP typically begins in late-middle age and rapidly progresses over time. The disease affects approximately seven in 100,000 people worldwide, and there are currently no disease-modifying therapies approved for the treatment of PSP.

PSP is characterized by abnormal tau inclusions and is consequently also known as a tauopathy. Similar to other neurodegenerative diseases, pathophysiologic changes underlying PSP are multifactorial with several genetic and environmental factors likely contributing to tau dysfunction and aggregation.

Multiple pathways, including genetic mutations, endoplasmic reticulum (ER) stress and the activation of unfolded protein response, mitochondrial dysfunction, and neuroinflammation have been implicated as contributors to tau dysfunction and aggregation.

**About Amylyx Pharmaceuticals**

Amylyx Pharmaceuticals, Inc. is committed to supporting and creating more moments for the neurodegenerative community through the discovery and development of innovative new treatments. Amylyx is headquartered in Cambridge, Massachusetts and has operations in Canada, EMEA, and Japan. For more information, visit amylyx.com and follow us on LinkedIn and X, formerly known as 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, the potential of AMX0035 as a treatment for ALS and the Company’s plans to explore the use of AMX0035 for other neurodegenerative diseases including PSP, the timelines for the ORION study in PSP, and expectations regarding our longer-term strategy. Any forward-looking statements in this press release 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: Amylyx’ ability to fund operations, 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 and outcome of EMA’s review of AMX0035 for the treatment of ALS, Amylyx’ reliance on third parties, including to conduct clinical trials and manufacture products, and the effect of global economic uncertainty and financial market volatility caused by economic effects of rising inflation and interest rates, the COVID-19 pandemic, geopolitical instability, changes in international trade relationships and military conflicts, as well as the risks and uncertainties set forth in Amylyx’ United States Securities and Exchange Commission (SEC) filings, including Amylyx’ Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, 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. Subject to any obligations under applicable law, 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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