Amylyx Pharmaceuticals Announces Publication of Data Showing the Encouraging Effects of AMX0035 on Cerebrospinal Fluid Biomarkers of Core Alzheimer's Disease Pathology and Neurodegeneration

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- Findings from exploratory analysis of the PEGASUS trial provide preliminary evidence that AMX0035 engages multiple pathological pathways related to neurodegeneration, including tau

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 12, 2024-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) ("Amylyx" or the "Company") today announced the publication of exploratory analyses on cerebrospinal fluid (CSF) biomarkers from participants with Alzheimer's disease (AD) from the Phase 2 PEGASUS trial. Data analyses suggest that treatment with AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO]) resulted in consistent changes in AD and neurodegeneration CSF biomarkers in participants with a broad range of disease severity. The results were published in the peer-reviewed medical journal *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, a journal of the Alzheimer's Association.

"Alzheimer's disease is defined by amyloid plaques and tau tangles, but it's now understood that these pathologies are accompanied by alterations in multiple cell and molecular pathways, including neuronal dysfunction, neurodegeneration, and oxidative stress, driving the progression of this relentless disease," said Steven E. Arnold, MD, Professor of Neurology at Harvard Medical School and Translational Neurology Head and Managing Director of the Interdisciplinary Brain Center and the inaugural E. Gerald Corrigan, PhD Endowed Chair at Massachusetts General Hospital. "The results from this exploratory analysis suggest that AMX0035 engages important pathways implicated in the pathogenesis of Alzheimer's disease and other neurodegenerative diseases."

Of the 95 participants in the intent-to-treat (ITT) cohort of the PEGASUS trial, 67 had CSF samples at baseline and Week 24. Within this CSF subcohort, treatment effects were analyzed for biomarkers spanning multiple pathophysiological processes in AD. These biomarkers included core AD biomarkers, such as amyloid beta 42/40 (Aβ42/40) ratio, phosphorylated tau181 (p-tau181) and total tau; biomarkers reflecting synaptic and neuronal degeneration, including neurogranin and fatty acid binding protein-3 (FABP3); biomarkers associated with gliosis, including YKL-40 (also known as chitinase 3-like protein 1); the oxidative stress marker 8-hydroxy-2-deoxyguanosine (8-OHdG); and additional biomarkers associated with neurodegeneration, inflammation, and metabolism.

The exploratory analyses showed that compared to placebo, AMX0035 reduced levels of p-tau181 and total tau. AMX0035 treatment also reduced levels of synaptic and neuronal degeneration biomarkers in the CSF, specifically neurogranin and FABP3, as well as YKL-40, a biomarker that has been shown to correlate with cortical volume loss and rate of cognitive decline. A 2023 publication showed AMX0035 reduced YKL-40 in ALS.

"These data lend further support to the preclinical and clinical evidence that AMX0035 has the potential to treat neurodegenerative diseases associated with tau dysfunction and tau aggregation. One such disease is progressive supranuclear palsy, also known as PSP. Our ORION trial studying AMX0035 in PSP remains ongoing," commented Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx. "There is a pressing unmet need for new and effective treatments in PSP, and we are encouraged by our findings that further support the potential of AMX0035."

About AMX0035

AMX0035 is an investigational, oral, fixed-dose combination of sodium phenylbutyrate (PB) and taurursodiol (TURSO; also known as ursodoxicoltaurine outside of the U.S.). AMX0035 is designed to slow or mitigate neurodegeneration by targeting endoplasmic reticulum (ER) stress and mitochondrial dysfunction, two connected central pathways that lead to cell death and neurodegeneration. Preclinical studies have provided evidence that AMX0035 may reduce cell death and improve cellular function, also supporting the synergistic effect of AMX0035 compared to individual compounds. AMX0035 is being studied as a potential treatment in neurodegenerative diseases, including Wolfram syndrome and progressive supranuclear palsy (PSP).

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 mild cognitive impairment or mild to moderate dementia due to Alzheimer's disease (AD) over 24 weeks of treatment. The trial was designed to evaluate safety and tolerability in this patient population while also assessing the effects of PB and TURSO on mechanistic targets of engagement and disease biology in a broad group of people with AD.

About the ORION Trial

The ORION trial (NCT06122662) is a global, randomized, double-blind, placebo-controlled Phase 2b/3 clinical trial designed to assess the efficacy, safety, and tolerability of AMX0035 compared to placebo in people living with progressive supranuclear palsy (PSP). ORION 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 is committed to the discovery and development of new treatment options for communities with high unmet needs, including people living with serious and fatal diseases. The Company has preclinical or clinical development programs underway in neurodegenerative, neuroendocrine, and endocrine diseases. Since its founding, Amylyx has been guided by science to address unanswered questions, keeping communities at the heart and center of all decisions. Amylyx is headquartered in Cambridge, Massachusetts. For more information, visit amylyx.com and follow us on LinkedIn and X. For investors, please visit investors.amylyx.com.

Forward-Looking Statements

Statements contained in this press release and related comments in our earnings conference call 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 (sodium phenylbutyrate and taurursodiol) as a treatment for neurodegenerative diseases including PSP and AD; the Company's beliefs regarding the benefits of AMX0035 in neurodegenerative diseases; and the potential for new pipeline programs and clinical indications for AMX0035. Any forward-looking statements in this press release and related comments in the Company's earnings conference call 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 successfully execute on its clinical development strategy, regulatory strategy, regulatory developments, Amylyx' ability to fund operations, and the impact that global macroeconomic uncertainty, geopolitical instability and public health events, such as COVID-19, will have on Amylyx' operations, 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 March 31, 2024, and subsequent filings with the SEC. All forward-looking statements contained in this press release and related comments in our earnings conference call 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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