Amylyx Pharmaceuticals to Discontinue ORION Program of AMX0035 for Progressive Supranuclear Palsy (PSP)

August 27, 2025

- AMX0035 did not show differences compared to placebo on primary or secondary outcomes at Week 24

- AMX0035 continued to be generally well-tolerated

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 27, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced the decision to discontinue the ORION program of AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO, also known as ursodoxicoltaurine]) in adults living with progressive supranuclear palsy (PSP).

AMX0035 did not show differences compared to placebo on primary or secondary outcomes at Week 24. Based on these results, the Company will discontinue the Phase 2b trial and open-label extension and will not initiate the Phase 3 portion of the program. Safety data were consistent with safety data from prior studies, and AMX0035 continued to be generally well-tolerated.

"We set a high bar for AMX0035 in PSP and made a commitment to base our decision-making on the totality of the data and the potential for clinically meaningful outcomes for those living with PSP. While we are disappointed in these results, we believe these data will inform the PSP trial literature as well as deepen scientific understanding of this devastating disease. We extend our gratitude to the participants, their families and care partners, the ORION sites, and the entire PSP community for their collaboration on this study," said Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx.

"Amylyx remains committed to advancing potential new treatments for communities with high unmet needs. Our highest priority and focus remain on the pivotal Phase 3 LUCIDITY trial of avexitide, with enrollment expected to complete in 2025 and topline data anticipated in the first half of 2026. We are also continuing development of AMX0035 in Wolfram syndrome and progressing AMX0114 in ALS, with early cohort data from the Phase 1 LUMINA trial expected in 2025," said Joshua Cohen and Justin Klee, Co-CEOs of Amylyx.

Amylyx continues to expect its cash runway to extend through the end of 2026.

About PSP

Progressive supranuclear palsy (PSP) is a sporadic, rare, and fatal neurodegenerative disorder that affects movement, gait, balance, eye movements, swallowing, and speech. People living with PSP have a life expectancy of six to eight years after initial diagnosis. 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.

About AMX0035

AMX0035 is an oral, fixed-dose combination of sodium phenylbutyrate (PB) and taurursodiol (TURSO; also known as ursodoxicoltaurine outside of the U.S.). AMX0035 was 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. Amylyx believes that our proprietary combination of PB and TURSO and their complementary mechanisms of action will allow us to synergistically target abnormal cell death to better prevent neurodegeneration than treatment targeted at either mechanism of action alone. AMX0035 is being studied as a potential treatment for Wolfram syndrome.

About Avexitide

Avexitide is an investigational, first-in-class glucagon-like peptide-1 (GLP-1) receptor antagonist that has been evaluated in five Phase 1 and Phase 2 clinical trials for post-bariatric hypoglycemia (PBH) and has also been studied in congenital hyperinsulinism (HI). The U.S. Food and Drug Administration (FDA) has granted avexitide Breakthrough Therapy Designation for both indications, Rare Pediatric Disease Designation in congenital HI, and Orphan Drug Designation for the treatment of hyperinsulinemic hypoglycemia (which includes PBH and congenital HI). Avexitide is designed to bind to the GLP-1 receptor on pancreatic islet beta cells and inhibit the effect of GLP-1 to mitigate hypoglycemia by decreasing insulin secretion and stabilizing blood glucose levels. In PBH, excessive GLP-1 can lead to the hypersecretion of insulin and subsequent debilitating hypoglycemic events. In two Phase 2 PBH clinical trials, avexitide demonstrated highly statistically significant reductions in hypoglycemic events. These events can lead to autonomic and neuroglycopenic symptoms that can have a devastating impact on daily living.

About Post-Bariatric Hypoglycemia (PBH)

Post-bariatric hypoglycemia (PBH) is a condition that is estimated to affect approximately 8% of people in the U.S. who have undergone the two most common types of bariatric surgery, sleeve gastrectomy and Roux-en-Y gastric bypass (approximately 160,000 people in the U.S.). PBH is thought to be caused by an excessive glucagon-like peptide-1 (GLP-1) response leading to hypoglycemia and impaired quality of life. PBH can cause debilitating hypoglycemic events associated with inadequate supply of glucose to the brain, known as neuroglycopenia. Clinical manifestations can include impaired cognition, loss of consciousness, and seizures. PBH is also associated with a high degree of disability that can result in major disruptions to independent living. There are no approved therapies for PBH.

About the LUCIDITY Trial

LUCIDITY (NCT06747468) is an approximately 75-participant, multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial evaluating the efficacy and safety of avexitide in participants with PBH following Roux-en-Y gastric bypass (RYGB) surgery. The Phase 3 trial is being conducted at approximately 20 sites in the U.S. Participants will be randomized 3:2 to receive either 90 mg of avexitide subcutaneously once daily or placebo. The trial includes an up to six-week screening period, including a three-week run-in period, and a 16-week double-blind treatment period. Participants who complete the double-blind period will be eligible to enter an open-label extension (OLE) period with a duration of 32 weeks. The primary efficacy objective of LUCIDITY will evaluate the FDA-agreed upon primary outcome of reduction in the composite of Level 2 and Level 3 hypoglycemic events through Week 16. Safety and tolerability will also be evaluated.

About Amylyx Pharmaceuticals

At Amylyx, our mission is to usher in a new era of treating diseases with high unmet needs. Where others see challenges, we see opportunities that we pursue with urgency, rigorous science, and unwavering commitment to the communities we serve. We are currently focused on three investigational therapies across several neurodegenerative and endocrine diseases in which we believe they can make the greatest impact. 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 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, Amylyx’ expectations regarding: the discontinuation of the Phase 2b/3 clinical trial of AMX0035 in PSP; the timing for enrollment completion and topline data readout of the Phase 3 LUCIDITY trial of avexitide; the development of AMX0035 as a treatment for Wolfram syndrome; the timing of early cohort data from the Phase 1 LUMINA trial of AMX0114; and its cash runway. 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: the success, cost, and timing of Amylyx’ program development activities; Amylyx’ ability to execute on its regulatory development plans and expectations regarding the timing of results from its planned data announcements and initiation of clinical studies; Amylyx’ ability to fund operations, and the impact that global macroeconomic uncertainty, geopolitical instability, and public health events 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’ Annual Report on Form 10-K for the year ended December 31, 2024, 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, except as required by law.

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