Amylyx Pharmaceuticals Presents New Exploratory Analyses from Phase 2 and Phase 2b Clinical Trials of Avexitide in Post-Bariatric Hypoglycemia at ENDO 2025

July 13, 2025

- Pivotal Phase 3 LUCIDITY trial of avexitide, a potential first-in-class GLP-1 receptor antagonist with FDA Breakthrough Therapy designation, underway in post-bariatric hypoglycemia; completion of recruitment expected in 2025, with topline data anticipated in first half of 2026

- In the Phase 2b trial, avexitide 90 mg once daily led to a 64% least-squares mean reduction in the composite rate of Level 2 and Level 3 hypoglycemic events in post-bariatric hypoglycemia, the FDA-agreed upon primary outcome that LUCIDITY is evaluating

- Population pharmacokinetic and pharmacodynamic data demonstrated avexitide 90 mg once daily has sustained therapeutic exposure for 24 hours

- Amylyx to host an in-person and virtual investor event today, July 13, 2025, at 6:00 p.m. PT / 9:00 p.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 13, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced the presentation of new exploratory analyses from the Phase 2 PREVENT and Phase 2b clinical trials of avexitide, an investigational, first-in-class glucagon-like peptide-1 (GLP-1) receptor antagonist for the treatment of post-bariatric hypoglycemia (PBH) at the Endocrine Society's annual meeting (ENDO 2025).

In the Phase 2b trial, avexitide 90 mg once daily, the dose being evaluated in the pivotal Phase 3 LUCIDITY trial, led to a 64% least-squares (LS) mean reduction (p=0.0031) vs. baseline in the composite rate of Level 2 and Level 3 hypoglycemic events in PBH, with more than half of the participants experiencing no events during the treatment period. LUCIDITY is a multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial evaluating the efficacy and safety of avexitide in approximately 75 participants with PBH following Roux-en-Y gastric bypass surgery. The FDA-agreed-upon primary endpoint of LUCIDITY is reduction in the composite of Level 2 and Level 3 hypoglycemic events. Consistent reductions in composite rate of Level 2 and Level 3 hypoglycemic events also were seen with avexitide 45 mg twice daily studied in the Phase 2b trial and avexitide 30 mg twice daily and 60 mg once daily studied in the Phase 2 PREVENT trial. New pharmacokinetic (PK) and pharmacodynamic (PD) data were also presented demonstrating continuous pharmacologic activity of the 90 mg once daily dose regimen for a 24-hour period.

"Post-bariatric hypoglycemia can profoundly disrupt daily life, requiring individuals to carefully manage meals, social interactions, and routines, often while living in fear of their next hypoglycemic event. The new analysis presented at ENDO 2025 continues to support that avexitide may significantly reduce the frequency of these events," said Marilyn Tan, MD, FACE, Principal Investigator of the LUCIDITY trial and Clinical Associate Professor at Stanford University.

Camille L. Bedrosian, MD, Chief Medical Officer of Amylyx, added, "Post-bariatric hypoglycemia is a serious and underrecognized condition with no FDA-approved treatments. The data presented show that, in an exploratory analysis from the Phase 2 PREVENT and Phase 2b clinical trials, avexitide significantly reduced the composite rate of Level 2 and 3 hypoglycemic events, including at the 90 mg once daily dose that is being studied in our pivotal Phase 3 LUCIDITY trial. We are particularly encouraged that over half of participants did not experience Level 2 or Level 3 hypoglycemic events during the treatment period. In addition, the pharmacokinetic and pharmacodynamic data demonstrated continuous pharmacologic activity of avexitide 90 mg once daily dose over 24 hours. We continue to be encouraged by avexitide's potential to deliver consistent, meaningful benefit to people living with PBH."

The population PK and PD analyses presented at ENDO 2025 demonstrated that avexitide 90 mg once daily maintained consistent GLP-1 receptor inhibition from morning to midnight and between doses. *In vitro* potency studies showed an IC_{50} of approximately 20-30 nM (70-100 ng/mL), indicating robust target inhibition even in the presence of significant levels of GLP-1. PK modeling demonstrated that avexitide plasma levels exceeded IC_{50} for a full 24-hour period.

LUCIDITY was informed by data from five PBH clinical trials of avexitide showing consistent, dose-dependent effects, including statistically significant and clinically meaningful reductions in hypoglycemic events. Avexitide was generally well-tolerated, with a favorable safety profile replicated across clinical trials. Completion of recruitment for LUCIDITY is expected in 2025, with a data readout anticipated in the first half of 2026 and, if approved, commercial launch anticipated in 2027.

The presentation and posters are available on the "Presentations" tab of the Amylyx website.

Webcast Information

Amylyx will host an investor event today, July 13, 2025, at 6:00 p.m. PT / 9:00 p.m. ET in San Francisco to discuss post-bariatric hypoglycemia and avexitide. A live webcast of the presentation and Q&A portion of the event can be accessed under “Events and Presentations” in the Investor section of the Company’s website, https://investors.amylyx.com/events-presentations. The webcast will be archived and available for replay for 90 days following the event.

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 will be 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 potential of avexitide as a treatment for PBH; expectations regarding the timing for recruitment completion and topline data readout of the Phase 3 LUCIDITY trial of avexitide in PBH; and expectations regarding timing for potential commercialization of avexitide. 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 execute on its regulatory development plans and expectations regarding the timing of results from its planned data announcements and initiation of clinical studies; the risk that early-stage results may not reflect later-stage results; 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 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, except as required by

law.

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