# Amylyx Pharmaceuticals Announces First Participant Dosed in Pivotal Phase 3 LUCIDITY Trial of Avexitide in Post-Bariatric Hypoglycemia

April 30, 2025

- *Amylyx expects completion of recruitment for the LUCIDITY trial in 2025, with topline data in first half of 2026*
- *Pivotal Phase 3 LUCIDITY trial evaluating avexitide, a GLP-1 receptor antagonist with FDA Breakthrough Therapy Designation and Orphan Drug Designation; FDA-agreed-upon primary outcome of reduction in hypoglycemic events*
- *Avexitide has been previously evaluated in five post-bariatric hypoglycemia (PBH) clinical trials of avexitide showing consistent, dose-dependent effects, including statistically significant reductions in hypoglycemic events*
- *The Company continues to expect cash runway through the end of 2026*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 30, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced that the first participant has been dosed in the pivotal Phase 3 LUCIDITY clinical trial of avexitide, an investigational, first-in-class glucagon-like peptide-1 (GLP-1) receptor antagonist, for the treatment of post-bariatric hypoglycemia (PBH).

"The first participant dosed in our Phase 3 LUCIDITY trial marks a milestone in the clinical development of avexitide, moving us one step closer toward potentially bringing this investigational therapy to people living with post-bariatric hypoglycemia," said Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx. "With robust data generated to date from five previous clinical trials in PBH, we are excited about the potential for avexitide to address the persistent, recurrent, and debilitating hypoglycemic events associated with PBH. As we work toward bringing a much-needed treatment to the PBH community, we want to thank those who are living with PBH who provided invaluable feedback on the LUCIDITY study design. Additionally, we are grateful for the collaboration of the avexitide clinical trial investigators."

"Post-bariatric hypoglycemia places a tremendous burden on individuals, with frequent and unpredictable hypoglycemic events that can cause severe symptoms such as impaired cognition, loss of consciousness, and seizures," said Dr. Marilyn Tan, MD, FACE, Principal Investigator of the LUCIDITY clinical trial and Clinical Associate Professor of Medicine at Stanford University School of Medicine. "These events disrupt independent living, often making it difficult to drive, work, live alone, or engage in social activities. Avexitide has the potential to significantly reduce hypoglycemic events, offering a much-needed therapeutic option for those living with PBH."

LUCIDITY (NCT06747468) 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 (RYGB) surgery, across approximately 20 U.S. sites. The U.S. Food and Drug Administration (FDA)-agreed-upon primary endpoint of LUCIDITY is reduction in the composite of Level 2 and Level 3 hypoglycemic events through Week 16. The trial includes similar inclusion and exclusion criteria to previous Phase 2 trials of avexitide in PBH. Safety and tolerability will also be evaluated.

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 of the study will be eligible to enter an open-label extension (OLE) period with a duration of 32 weeks. Amylyx presented the design of LUCIDITY in December 2024, and the poster is available on the "Publications" page of the Amylyx website.

LUCIDITY was informed by data from five PBH clinical trials of avexitide showing consistent, dose-dependent effects, including statistically significant reductions in hypoglycemic events. Avexitide was generally well tolerated, with a favorable safety profile replicated across clinical trials.

The Company continues to expect cash runway through the end of 2026, which will support the completion of recruitment for the pivotal Phase 3 LUCIDITY clinical trial of avexitide in PBH expected in 2025, with a data readout anticipated in the first half of 2026.

**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 affects approximately 8% of people in the U.S., or approximately 160,000 people, who have undergone the two most common types of bariatric surgery, which include sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB). 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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