



Amylyx Pharmaceuticals Announces Acquisition of Phase 3-ready GLP-1 Receptor Antagonist (Avexitide) with FDA Breakthrough Therapy Designation

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- Avexitide is a novel, first-in-class GLP-1 receptor antagonist with the potential to treat hyperinsulinemic hypoglycemia
- FDA Breakthrough Therapy Designation granted for avexitide for post-bariatric hypoglycemia (PBH) and congenital hyperinsulinism
- Acquisition builds on Amylyx' endocrine and neuroscience expertise and aligns with pipeline focus of delivering important potential treatment options to communities with high unmet needs
- Phase 3 program for avexitide in PBH expected to begin in Q1 2025, with data readout anticipated in 2026; FDA has agreed to the primary endpoint expected to be utilized in Phase 3
- Data from two Phase 2 studies of avexitide in people with PBH demonstrated highly statistically significant reductions in severe hypoglycemic events, an endpoint supported by the FDA
- Avexitide was generally well tolerated, with a favorable safety profile replicated across five clinical trials in people with PBH
- Management to host conference call and webcast today at 8:00 a.m. Eastern Time

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 10, 2024-- [Amylyx Pharmaceuticals, Inc.](#) (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced the acquisition of avexitide from Eiger BioPharmaceuticals, Inc. ("Eiger"). Avexitide has been studied for the potential treatment of hyperinsulinemic hypoglycemia to date.

"Since Amylyx was founded, we have been guided by a rigorous approach to our science to bring potential treatments to communities with high unmet needs. When we reviewed all the compelling data supporting avexitide, it clearly aligned with our strategic scientific criteria, expertise, and community values, and we are excited to build upon the important work done to date to study this asset," said Joshua Cohen and Justin Klee, Co-CEOs of Amylyx.

Avexitide is an investigational, first-in-class glucagon-like peptide-1 (GLP-1) receptor antagonist that has been evaluated in five clinical trials for post-bariatric hypoglycemia (PBH) and has also been studied in congenital hyperinsulinism (HI), two indications characterized by hyperinsulinemic hypoglycemia. 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 block the effect of GLP-1 to mitigate hypoglycemia by decreasing insulin secretion and stabilizing glucose levels. In PBH, excessive GLP-1 can lead to the hypersecretion of insulin and subsequent severe hypoglycemic events, including autonomic and neuroglycopenic symptoms if left unaddressed.

In previous Phase 2 and Phase 2b studies in PBH, avexitide showed statistically significant reductions in hypoglycemic events characterized by low blood glucose, including severe hypoglycemic events with altered mental and/or physical function requiring assistance. FDA guidance for industry combined with initial FDA feedback specific to the pivotal Phase 3 program of avexitide for PBH suggest that reduction in hypoglycemia events could be an endpoint to support approval following positive results from a pivotal Phase 3 clinical trial.

Amylyx expects to begin the Phase 3 program for avexitide in PBH in Q1 2025. Furthermore, Amylyx is actively engaging in discussions with the broader congenital HI community, including experts in the field, to develop a path forward based on promising Phase 2 study results conducted at Children's Hospital of Philadelphia. Avexitide will be added to Amylyx' current pipeline programs that have been in research and development for several years: AMX0035 for the treatment of Wolfram syndrome, AMX0035 for the treatment of progressive supranuclear palsy, and AMX0114, the Company's antisense oligonucleotide targeting calpain-2 for the treatment of amyotrophic lateral sclerosis, or ALS.

Avexitide in PBH: Key Clinical Trial Results to Date

The following table shows key results from the Phase 2, randomized, placebo-controlled crossover study (PREVENT) that evaluated efficacy and safety of avexitide for treatment of PBH following Roux-en-Y gastric bypass surgery. The results showed that, compared with placebo, avexitide 30 mg twice daily (BID) and 60 mg once daily (QD) significantly increased mean plasma glucose nadir (prespecified primary endpoint) and lowered insulin peak, corresponding to 50% and 75% fewer participants requiring rescue during mixed meal tolerance testing, respectively. Significant reductions in rates of Levels 1, 2, and 3 hypoglycemia were observed. Continuous glucose monitoring (CGM) demonstrated reductions in time in hypoglycemia without induction of clinically relevant hyperglycemia.

Outcome ^a	Avexitide 30 mg BID		Avexitide 60 mg QD	
	Improvement vs. Placebo	p-value	Improvement vs. Placebo	p-value
N=17				

Post Prandial Glucose Nadir (Primary Endpoint)	21% higher	0.001	26% higher	0.0002
Peak Insulin Level (Secondary Endpoint)	23% lower	0.029	21% lower	0.042
Rate of Level 1 Hypoglycemia	30% lower	0.072	61% lower	0.001
Rate of Level 2 Hypoglycemia	40% lower	0.040	60% lower	0.004
Rate of Level 3 (Severe) Hypoglycemia	23% lower	0.22	56% lower	0.014

^aLevel 1 hypoglycemia: self-monitoring of blood glucose (SMBG) <70 mg/dL; Level 2 hypoglycemia: SMBG <54 mg/dL; Level 3 hypoglycemia: a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.

Avexitide was generally well tolerated. The most common adverse events were injection site bruising, headache, and nausea; these occurred more often with placebo than either avexitide dose. No participants withdrew due to adverse events.

A Phase 2b open-label, investigator-initiated, cross-over study of higher dose avexitide (45 mg BID and 90 mg QD) was completed in a broader eligible population of 16 participants with PBH following Roux-en-Y gastric bypass surgery, vertical sleeve gastrectomy, esophagectomy, Nissen fundoplication, or gastrectomy. This trial met both its primary endpoint of number of diurnal Level 2 hypoglycemia events (glucose <54mg/dL) as measured by CGM as well as its secondary endpoints, which includes the rate of Level 2 hypoglycemia, rate of Level 3 hypoglycemia, percent diurnal time <70 mg/dL as measured by CGM, and percent diurnal time <54 mg/dL as measured by CGM.

Avexitide was successful in reducing the frequency of hypoglycemia up to 65% and the amount of time in hypoglycemia up to 64%. The below table shows results of avexitide at both doses of 45 mg BID and 90 mg QD compared to medical nutrition therapy alone.

Outcome	Avexitide 45 mg BID		Avexitide 90 mg QD	
	Decrease from Baseline	p-value	Decrease from Baseline	p-value
Rate of Level 1 Hypoglycemia	54% lower	0.003	68% lower	0.0005
Rate of Level 2 Hypoglycemia (Secondary Endpoint) ^a	57% lower	0.003	53% lower	0.004
Rate of Level 3 (Severe) Hypoglycemia (Secondary Endpoint) ^b	68% lower	0.0003	66% lower	0.0003

^aRate of Level 2 hypoglycemia: self-monitoring of blood glucose (SMBG) <54 mg/dL.

^bRate of Level 3 hypoglycemia: severe event characterized by altered mental and/or physical function requiring assistance.

There were no reported serious adverse events, and adverse events were mostly mild to moderate and resolved without medical treatment. The most common adverse events included diarrhea, headache, bloating, and injection site reaction/bruising. No participant withdrew due to adverse events.

"PBH is a debilitating condition with no approved treatment options, and we look forward to advancing this critical work with avexitide into Phase 3 for individuals with PBH based on the totality of data from five clinical trials, and informed by our ongoing work to address endocrine and metabolic aspects of Wolfram syndrome. We also are continuing our conversations with the congenital HI community regarding the clinical development of avexitide in congenital HI to develop a path forward," said Camille L. Bedrosian, MD, Chief Medical Officer of Amylyx. "While we are excited to study this new scientific pathway in hyperinsulinemic hypoglycemia, our research in ALS and other neurodegenerative diseases continues through our AMX0035 and AMX0114 programs, guided by the understanding that people living with these devastating diseases have no time to wait – we must continue to research and collaborate with urgency."

Transaction Details

On July 9, 2024, Amylyx completed the acquisition of substantially all of the rights, title and interests in, to and under those assets and interests used by the seller in the development, manufacture and commercialization of avexitide from Eiger for \$35.1 million plus the aggregate amount of determined cure costs and assumed liabilities. As part of the transaction, Amylyx assumed certain contractual obligations from Eiger, including a 3% royalty on future sales of avexitide in PBH, if approved, to certain academic institutions.

Investor Conference Call Information

Amylyx' management team will host a conference call and webcast today, July 10, 2024, at 8:00 a.m. ET to discuss the asset acquisition. To access the conference call, please dial +1 (800) 836-8184 (U.S. and Canada) or +1 (646) 357-8785 (international) at least 10 minutes prior to the start time

and ask to be joined into the Amylyx Pharmaceuticals call. A live audio webcast of the call will be available under “Events and Presentations” in the Investor section of the Company’s website, <https://investors.amylyx.com/news-events/events>, and will be 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 2 clinical studies for post-bariatric hypoglycemia (PBH) and has also been studied in congenital hyperinsulinism (HI), with U.S. Food and Drug Administration (FDA) Breakthrough Therapy Designation for both indications and FDA Rare Pediatric Disease Designation in congenital HI. Avexitide is designed to bind to the GLP-1 receptor on pancreatic islet beta cells and block the effect of excessive GLP-1 to mitigate hypoglycemia by decreasing insulin secretion and stabilizing glucose levels. In PBH, excessive GLP-1 can lead to the hypersecretion of insulin and subsequent severe hypoglycemic events. In two Phase 2 PBH 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)

Symptomatic post-bariatric hypoglycemia (PBH) is a condition that affects approximately 8% of people who have undergone bariatric surgery. It is characterized by exaggerated secretion of glucagon-like peptide-1 (GLP-1), dysregulated secretion of insulin, and a rapid drop in blood sugar. PBH can cause severe hypoglycemic events associated with brain glucose starvation, known as neuroglycopenia, including impaired cognition, cardiac arrhythmias, loss of consciousness, and seizures. PBH is associated with a high degree of disability and can result in major disruptions to life, including falls, motor vehicle accidents, and job and income loss. It is estimated that ~160,000 people are currently living with symptomatic PBH in the U.S., classifying it as an orphan condition.

About Congenital Hyperinsulinism (HI)

Congenital hyperinsulinism (HI) is a rare disease characterized by hypersecretion of insulin leading to severe, persistent hypoglycemia in infants and young children with limited therapeutic options. Common symptoms of congenital HI include lack of energy, irritability, lethargy, and excessive hunger. Repeated episodes of low blood glucose increase the risk for serious complications such as breathing difficulties, seizures, intellectual disability, vision loss, brain damage, and coma.

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. Preclinical studies have provided evidence that the proprietary combination of PB and TURSO and their complementary mechanisms of action targets cell death and better prevents neurodegeneration than targeting either mechanism of action alone. AMX0035 is being studied as a potential treatment in neurodegenerative diseases, including Wolfram syndrome and progressive supranuclear palsy (PSP).

About AMX0114

AMX0114 is an antisense oligonucleotide designed to target the gene encoding calpain-2, a key contributor to the axonal (Wallerian) degeneration pathway. Axonal degeneration has been recognized as an important early contributor to the clinical presentation and pathogenesis of ALS and other neurodegenerative diseases. Calpain-2 has been implicated in the pathogenesis of ALS based on findings of elevated levels of calpain-2 and its cleavage products in postmortem ALS tissue, therapeutic benefit of calpain-2 modulation in animal models of ALS, and the role of calpain-2 in cleaving neurofilament, a broadly researched biomarker in ALS. Preclinical studies completed to date have shown that AMX0114 achieves potent, dose-dependent, and durable knockdown of CAPN2 mRNA expression and calpain-2 protein levels in human motor neurons. Moreover, in preclinical efficacy studies, treatment with AMX0114 reduced extracellular neurofilament light chain levels following neurotoxic insult in induced pluripotent stem cell (iPSC)-derived human motor neurons, and improved survival of iPSC-derived human motor neurons harboring ALS-linked, pathogenic TDP-43 mutations.

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. 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](#) (formerly 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, Amylyx’ expectations regarding: plans for initiating a Phase 3 clinical program of avexitide, including interactions with regulatory authorities; the possibility that results from a Phase 3 program could support FDA approval of avexitide in PBH; and expectations regarding the benefits of the acquisition of avexitide. 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 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, 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. 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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