Amylyx Pharmaceuticals Announces FDA Has Lifted the Clinical Hold on AMX0114 Phase 1 Clinical Trial for the Treatment of Amyotrophic Lateral Sclerosis

January 21, 2025

• Company will move forward with trial sites across North America

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 21, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced that the U.S. Food and Drug Administration (FDA) has lifted the clinical hold placed on the Phase 1 clinical trial of AMX0114, an investigational antisense oligonucleotide (ASO) targeting calpain-2 for people living with amyotrophic lateral sclerosis (ALS). With the clinical hold lifted, Amylyx is now working to open U.S. sites for screening, enrollment, and dosing.

The announcement comes as Amylyx expects to initiate the Phase 1 LUMINA clinical trial in Canada in the beginning of 2025. LUMINA is a multicenter, randomized, placebo-controlled, multiple ascending dose trial evaluating the safety and biological activity of AMX0114.

LUMINA will also assess ALS biomarkers, including change from baseline in neurofilament light (NfL) levels. Approximately 48 people living with ALS will be randomized 3:1 to receive AMX0114 or placebo by intrathecal administration once every four weeks for a total of up to 4 doses.

"Based on several preclinical efficacy studies and what is known about the central role of calpain-2 in the process of axonal degeneration, we believe AMX0114 has the potential to be a treatment for ALS and other diseases," said Camille L. Bedrosian, MD, Chief Medical Officer of Amylyx. "Calpain-2 is a well-established target in a number of neurological diseases and a protease known to cleave many substrates including neurofilament, tau, and TDP43 proteins. In addition to being considered an essential protein in the process of axonal degeneration, calpain-2 has been repeatedly linked to neurofilament biology in published studies. We are dedicated to investigating therapies to potentially treat people living with ALS, and we are excited to work with study investigators and clinical trial sites across North America to enroll participants in LUMINA."

Amylyx continues to anticipate early cohort data from LUMINA in 2025.

About AMX0114

AMX0114 is an investigational antisense oligonucleotide (ASO) targeting calpain-2 (*CAPN2*) for the potential treatment of ALS. In preclinical studies, treatment with AMX0114 resulted in potent, dose-dependent, and durable reduction in CAPN2 mRNA and calpain-2 protein levels in disease-relevant cell models of axonal degeneration. This translated to improved neuronal survival, including in a model of TDP-43 ALS, and reductions in extracellular neurofilament light (NfL) levels across multiple disease models and paradigms of neuronal injury. AMX0114 was well-tolerated in in vivo preclinical safety studies.

About LUMINA

The Phase 1 LUMINA study (NCT06665165) is a multicenter, randomized, placebo-controlled, multiple ascending dose trial evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of AMX0114 in 48 adults living with ALS. LUMINA will also assess change from baseline in calpain-2 levels, neurofilament light (NfL) levels, and other pharmacodynamic biomarkers of ALS.

About ALS

Amyotrophic lateral sclerosis (ALS, also known as motor neuron disease) is a relentlessly progressive and fatal neurodegenerative disorder caused by motor neuron death in the brain and spinal cord. Motor neuron loss in ALS leads to deteriorating muscle function, the inability to move and speak, respiratory paralysis, and eventually, death. More than 90% of people with ALS have sporadic disease, showing no clear family history.

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 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 for AMX0114 as a treatment for ALS and the planned initiation of a trial evaluating AMX0114 in ALS. 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; 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, 2023, 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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