Amylyx Pharmaceuticals Receives U.S. FDA Fast Track Designation for AMX0114 for the Treatment of Amyotrophic Lateral Sclerosis

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- AMX0114 is an Amylyx-developed antisense oligonucleotide designed to target calpain-2, a key contributor to the axonal degeneration pathway in ALS

- Phase 1 LUMINA trial of AMX0114 underway; early cohort data expected in 2025

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 3, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to AMX0114, an investigational antisense oligonucleotide (ASO) targeting calpain-2 for the treatment of people living with amyotrophic lateral sclerosis (ALS).

"Obtaining FDA Fast Track designation for AMX0114 is an important step forward in our mission to develop potential treatments for people living with ALS, a relentlessly progressive and fatal disease with limited therapeutic options," said Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx. "This designation from the FDA recognizes both the seriousness of this devastating disorder and the encouraging preclinical evidence supporting AMX0114's potential to target calpain-2, which has been found to be an important contributor to axonal degeneration, a critical driver in ALS progression. We are committed to advancing AMX0114 as quickly and efficiently as possible, and we continue to anticipate early cohort data from the Phase 1 LUMINA clinical trial later this year. We look forward to continued interaction with the FDA as we work to expeditiously advance the development of AMX0114, with the ultimate goal of addressing the urgent, unmet needs of the ALS community."

The FDA's Fast Track designation is designed to facilitate the development and expedited review of therapies that are intended to treat serious and life-threatening conditions and demonstrate the potential to address an unmet medical need. A therapy that receives Fast Track designation may be eligible for more frequent meetings and communications with the FDA, as well as Priority Review if relevant criteria continue to be met.

Amylyx designed AMX0114 to target calpain-2, a calcium-activated protease. Peer-reviewed research has demonstrated that overactive calpain-2 activity may be an important driver of disease progression in ALS and other neurodegenerative diseases by executing the degeneration of axons, the long tubular neuronal segments which carry signals from neurons to the muscle or other neurons. In preclinical studies, AMX0114 showed improved neuronal survival and reductions in extracellular neurofilament light (NfL) levels across multiple disease models.

In April 2025, the Company announced the first participant was dosed in LUMINA, a multinational, randomized, double-blind, placebo-controlled, multiple ascending dose Phase 1 clinical trial designed to evaluate the safety and biological activity of AMX0114 in people living with ALS. LUMINA will also assess broadly researched ALS biomarkers, including changes from baseline in NfL levels. Approximately 48 participants will be randomized 3:1 to receive AMX0114 or placebo by intrathecal administration once every four weeks, for up to four doses. Amylyx expects 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. The U.S. Food and Drug Administration (FDA) has granted AMX0114 Fast Track designation for the 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 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 LUMINA

The Phase 1 LUMINA clinical trial (NCT06665165) is a multinational, randomized, double-blind, placebo-controlled, multiple ascending dose trial evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of AMX0114 in people living with

ALS. LUMINA is anticipated to enroll approximately 48 adult participants. LUMINA will also assess broadly researched ALS biomarkers, including change from baseline in neurofilament light (NfL) levels.

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 for AMX0114 as a treatment for ALS, the expected timeline for data readout, and the expectation for regulatory action. 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, 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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