Amylyx Pharmaceuticals Announces First Participant Dosed in Phase 1, Multiple Ascending Dose LUMINA Trial of AMX0114 in People Living with Amyotrophic Lateral Sclerosis

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- Amylyx expects early cohort data from LUMINA this year

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 9, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced that the first participant has been dosed in LUMINA, the Company's Phase 1, multinational, randomized, double-blind, placebo-controlled, multiple ascending dose clinical trial of AMX0114, an investigational, potent antisense oligonucleotide (ASO) targeting calpain-2, in people living with amyotrophic lateral sclerosis (ALS). The Company continues to expect early cohort data from LUMINA in 2025.

The LUMINA trial (NCT06665165) will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of AMX0114 in people living with ALS. LUMINA will also assess broadly researched ALS biomarkers, including change from baseline in neurofilament light chain (NfL) levels. LUMINA is anticipated to enroll approximately 48 people living with ALS across North America. Participants 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.

"AMX0114 targets calpain-2, which has been found to be an important contributor to axonal degeneration and studied over decades of research as a potential target for the treatment of ALS and other neurodegenerative diseases. In preclinical studies, AMX0114 showed improved neuronal survival and reductions in extracellular NfL levels across multiple disease models. We are excited to progress AMX0114 into the clinic for people with ALS as we work to advance a potential therapy for this relentlessly progressive, fatal disease," said Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx.

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. Preclinical studies in ALS models suggest that the inhibition of calpain-2 may improve neuron survival and mitigate axonal degeneration.

"ALS is a devastating and fatal neurodegenerative disease with limited treatment options, underscoring the urgent need for new therapeutic approaches that target the underlying mechanisms driving ALS progression. AMX0114 represents a potential therapeutic approach to inhibiting one of the fundamental drivers of axonal degeneration," said Sabrina Paganoni, MD, PhD, principal investigator of the LUMINA trial, investigator at the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital, and member of the Scientific Advisory Board of the Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS). "Dosing the first participant in LUMINA is a step toward a potential treatment option for people living with ALS and their loved ones."

More information about the LUMINA clinical trial can be found at www.clinicaltrials.gov, NCT06665165.

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 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 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

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 and the expected timeline for data readout. 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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Media
Amylyx Media Team
(857) 799-7274
amylyxmediateam@amylyx.com

Investors
Lindsey Allen
(857) 320-6244
Investors@amylyx.com

Source: Amylyx Pharmaceuticals, Inc.