Amylyx Pharmaceuticals Announces New Safety and Tolerability Cohort 1 Data of AMX0114 in ALS from First-in-Human LUMINA Trial

December 5, 2025

- AMX0114 was generally well-tolerated, with no treatment-related serious adverse events

- Amylyx will proceed with opening enrollment of second cohort

- Data are being presented at the 36th International Symposium on ALS/MND

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 5, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced the presentation of early safety and tolerability data from its Phase 1 LUMINA trial of AMX0114 and results from ongoing work characterizing biomarkers of AMX0114 target engagement at the 36th International Symposium on ALS/MND (MNDA) held from December 5-7 in San Diego, California. AMX0114 was generally well-tolerated in LUMINA trial participants enrolled in cohort 1 (n=12), with no treatment-related serious adverse events (SAEs). Based on these data, Amylyx expects to begin enrolling the second cohort of participants in Canada later this month and in the U.S. in January.

"LUMINA is a first-in-human study, and we are encouraged by these data as we continue to advance AMX0114 as a potential treatment for this rapidly progressive disease with high unmet need. The safety and tolerability analysis allows LUMINA to proceed with its next cohort of participants, which is critical given that this community has no time to wait," said Sabrina Paganoni, MD, PhD, principal investigator of the LUMINA trial, investigator at the Sean M. Healey & AMG Center for ALS at Mass General Brigham, and member of the Scientific Advisory Board of the Network of Excellence for ALS (NEALS).

The LUMINA trial (NCT06665165) is a 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). LUMINA is evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of AMX0114 in people living with ALS and assessing both novel and broadly researched ALS biomarkers, including change from baseline in neurofilament light chain (NfL) levels. Amylyx expects biomarker data from the first cohort of LUMINA participants (n=12) in the first half of 2026.

"We appreciate the partnership with LUMINA sites and participants to achieve complete enrollment of the first cohort. In addition, we are pleased that to date no drug-related SAEs or dose-limiting toxicities were observed, which represent important early steps in this study," said Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx. "AMX0114 is designed to inhibit calpain-2, a calcium-activated protease that is one of the fundamental drivers of axonal degeneration and consequent disease progression in ALS. Preclinical studies have demonstrated that treatment with AMX0114 resulted in potent, dose-dependent, and durable reduction in calpain-2 protein levels, translating to improved neuronal survival and reductions in extracellular NfL levels. We look forward to presenting cohort 1 biomarker data at a medical meeting in the first half of next year."

The MNDA presentation details are as follows:

Friday, December 5, 2025, Session A, 5:30-7pm Pacific Time:

Title: A Phase 1, Multicenter, Randomized, Placebo-Controlled Multiple Ascending Dose Study to Evaluate the Safety and Tolerability of AMX0114 in Amyotrophic Lateral Sclerosis (LUMINA)
Presenting Author: Sabrina Paganoni, MD, PhD, Sean M. Healey and AMG Center for ALS & the Neurological Clinical Research Institute, Massachusetts General Hospital, Harvard Medical School, Spaulding Rehabilitation Hospital, Harvard Medical School
Poster Number: CLT-14

Saturday, December 6, 2025, Session 6B: Biomarkers, 10:50-11:10am Pacific Time:

Title: Characterizing the CSF Biomarker Signature of Calpain-2 Activity in ALS and the Biomarker Impact of Calpain-2 Inhibition in a Preclinical Model of ALS
Presenting Author: Robert Bowser, PhD, Barrow Neurological Institute and nVector, Inc.

For MNDA conference information, visit https://symposium.mndassociation.org/. Abstracts have been published as an online open access supplement of Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration. The presentations will be available on the "Events & Presentations" tab of the Amylyx website.

About AMX0114

AMX0114 is an investigational antisense oligonucleotide (ASO) with U.S. Food and Drug Administration (FDA) Fast Track designation for the potential treatment of ALS. AMX0114 targets calpain-2 (*CAPN2*), a calcium-activated protease that is one of the fundamental drivers of axonal degeneration and consequent disease progression in 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 generally well-tolerated in LUMINA trial participants enrolled in cohort 1 (n=12), with no treatment-related serious adverse events (SAEs).

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 will also assess change from baseline in calpain-2 levels, neurofilament light (NfL) levels, and other pharmacodynamic biomarkers of ALS. LUMINA is anticipated to enroll approximately 48 adult participants. 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. Study sites are active in Canada and the United States, and the first cohort has been fully enrolled. Amylyx expects to begin enrolling the second cohort of participants in Canada in December and in the U.S. in January.

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. One of the ways ALS progresses is through axonal degeneration, which disrupts neural connectivity and contributes significantly to disease pathology. 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, the expected timeline for enrollment of future cohorts, 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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