Amylyx Pharmaceuticals Announces Positive Long-Term Results from Phase 2 HELIOS Clinical Trial of AMX0035 in People with Wolfram Syndrome

May 12, 2025

- *Data at Week 48 demonstrated that treatment with AMX0035 led to sustained stabilization or improvement in multiple outcomes related to disease progression, including pancreatic function, glycemic control, vision, and overall symptom burden*
- *AMX0035 continued to be generally well-tolerated in all participants*
- *Week 48 data and discussions with FDA will inform the design of a Phase 3 trial of AMX0035 in Wolfram syndrome*
- *Amylyx continues to expect cash runway through the end of 2026*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 12, 2025-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced positive Week 48 data from the Phase 2 open-label HELIOS clinical trial of AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO, also known as ursodoxicoltaurine]) in adults living with Wolfram syndrome. These results were presented at the Joint Congress of the European Society for Pediatric Endocrinology (ESPE) and the European Society of Endocrinology (ESE) in Copenhagen, Denmark and are available on the "Presentations" page of the Amylyx website.

Consistent with the HELIOS trial's previously presented primary efficacy outcome of improvement in pancreatic function, as measured by C-peptide response to a mixed-meal tolerance test at Week 24, treatment with AMX0035 through Week 48 demonstrated continued and sustained improvement in pancreatic beta cell function.

Treatment with AMX0035 from Week 24 to Week 48 also showed sustained improvements or stabilization in glycemic control, as measured by hemoglobin A1c (HbA1c) and time in target glucose range assessed by continuous glucose monitoring, as well as visual acuity. All participants with available measurements met the responder criteria, defined as either improvement or no change, on both the Patient Global Impression of Change (PGI-C) and Clinician Global Impression of Change (CGI-C) at Weeks 24 and 48, indicating stability or improvement in their Wolfram syndrome-related symptoms. Results from qualitative on-study interviews further supported the potential positive impact of AMX0035 on symptom burden.

Safety data were consistent with safety data from prior studies of AMX0035. All adverse events (AEs) were mild or moderate, and there were no serious AEs related to AMX0035 treatment.

"The results of the Phase 2, open-label HELIOS trial continue to demonstrate that AMX0035 has the potential to favorably alter the trajectory of Wolfram syndrome, a progressive disorder with no approved treatment options. The consistency of the Week 48 results across multiple measures of disease progression that meaningfully impact the daily lives of those living with Wolfram syndrome, including pancreatic function, glycemic control, and vision, reinforce the previously reported Week 24 findings. Additionally, the majority of participants reported meaningful improvement in at least one Wolfram syndrome-related symptom during interviews, underscoring the real-world importance of these results," said Fumihiko Urano, MD, PhD, Principal Investigator of the Phase 2 HELIOS clinical trial in Wolfram syndrome and the Samuel E. Schechter Professor of Medicine in the Division of Endocrinology, Metabolism & Lipid Research at Washington University School of Medicine in St. Louis.

"These long-term results reinforce both our positive data at Week 24 and our belief in the potential of AMX0035 to stabilize and even improve key manifestations of Wolfram syndrome, a relentlessly progressive disorder," said Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx. "With these findings, we are focused on working closely with the FDA to inform the design of a Phase 3 trial. Our ultimate aim is to address the unmet needs that are still a reality for people living with this devastating disorder. We want to thank the Wolfram syndrome community for their continued collaboration and support."

HELIOS (NCT05676034) is a single-site, single-arm, open-label, Phase 2 trial designed to evaluate the safety and tolerability of AMX0035, as well as its effects on various measures of endocrinological, neurological, and ophthalmological function in adult participants living with Wolfram syndrome. The U.S. Food and Drug Administration (FDA) and the European Commission granted Orphan Drug Designation to AMX0035 for the treatment of Wolfram syndrome in November 2020 and August 2024, respectively.

As outlined in the table below, results through Week 48 of the HELIOS trial showed treatment with AMX0035 resulted in improvement or stabilization across measures of glycemic control, visual acuity, and overall symptom burden with AMX0035. Notably, HELIOS showed improvements in the primary endpoint of C-peptide response, as measured by area under the curve from 0-120 minutes during a Mixed Meal Tolerance Test (MMTT). In the Per Protocol group, the mean change from baseline to Week 24 was 20.2 min*ng/mL [standard error (SE) 11.2], and, at Week 48, the mean change from baseline was +34.5 minutes ng/mL(min*ng/mL) [13.0]; descriptive p-value=0.0263). Long-term data at Week 48 included 10 participants in the Per Protocol

population with genetically confirmed Wolfram syndrome (one participant was excluded from the Per Protocol population due to not meeting the study inclusion criteria of genetically confirmed Wolfram syndrome) and 11 participants in the Intent-to-Treat (ITT) population. One participant discontinued between Week 24 and Week 48 for reasons unrelated to safety.

	Week 24 Per Protocol (N=11)	Week 48 Per Protocol (N=10)	Week 24 ITT (N=12)	Week 48 ITT (N=11)
C-Peptide Response (min*ng/mL) *mean change from baseline in Area Under the Curve (0 to 120 minute interval)*	+20.2 (SE:11.2)	+34.5 (SE:13.0)	+3.8 (SE: 19.3)	+14.2 (SE: 23.4)
Hemoglobin A1c (%) *mean change from baseline*	-0.16 (SE: 0.13%)	-0.40 (SE: 0.22%)	-0.09 (SE: 0.14)	-0.25 (SE: 0.25)
Time in Target Glucose Range (%) *mean change from baseline*	+5.7% (SE: 3.9%)	+9.6% (SE: 5.8%)	+5.2 (SE: 3.6)	+7.9 (SE: 5.6)
Best Corrected Visual Acuity (LogMAR) *mean change from baseline*	-0.04 (SE: 0.06)	-0.08 (SE: 0.08)	-0.04 (SE: 0.06)	-0.09 (SE: 0.07)
Clinician Report Global Impression of Change (CGI-C) *% meeting responder criteria of no change or improvement given the progressive nature of disease*	100%	100%	100%	100%
Patient Reported Global Impression of Change (PGI-C) *% meeting responder criteria of no change or improvement given the progressive nature of disease*	100%	100%	100%	100%

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. Amylyx believes that its proprietary combination of PB and TURSO and their complementary mechanisms of action will allow us to synergistically target abnormal cell death to better prevent neurodegeneration than treatment targeted at either mechanism of action alone. AMX0035 is being studied as a potential treatment for Wolfram syndrome and progressive supranuclear palsy, two neurodegenerative diseases.

About Wolfram Syndrome

Wolfram syndrome is a rare, monogenic, progressive neurodegenerative disorder that progressively impacts multiple organs and systems. Wolfram syndrome is characterized by childhood-onset diabetes mellitus, optic nerve atrophy, and neurodegeneration. Common manifestations of Wolfram syndrome include diabetes mellitus and diabetes insipidus, gradual vision loss leading to blindness, hearing loss, neurogenic bladder, difficulties with balance and coordination, and difficulty breathing that can lead to respiratory failure. Wolfram syndrome is caused by pathogenic variants in Wolfram syndrome type 1 gene (*WFS1*) that leads to premature mortality. Because of the clear link between *WFS1* mutations and endoplasmic reticulum (ER) stress, Wolfram syndrome is considered a prototypical ER stress disorder. Wolfram syndrome affects approximately 3,000 people living in the U.S., and there are currently no approved treatment options.

About the HELIOS Trial

HELIOS (NCT05676034) is a 12-participant, single-site, single-arm, open-label, Phase 2 trial designed to evaluate the safety and

tolerability of AMX0035, as well as its effects on various measures of endocrinological, neurological, and ophthalmologic function in adult participants living with Wolfram syndrome. Participants in HELIOS receive AMX0035 for up to 144 weeks followed by a four-week safety follow-up. Primary and secondary outcomes are assessed at Week 24 and at longer-term time points. The FDA and the European Commission granted Orphan Drug Designation to AMX0035 for the treatment of Wolfram syndrome in November 2020 and August 2024, respectively.

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 of AMX0035 (sodium phenylbutyrate and taurursodiol) as a treatment for Wolfram syndrome; planned discussions with the FDA related to AMX0035 for the treatment of Wolfram syndrome; and expected cash runway. 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20250512643540/en/

Media
Amylyx Media Team
(857) 320-6191
amylyxmediateam@amylyx.com

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

Source: Amylyx Pharmaceuticals, Inc.