# Amylyx Pharmaceuticals Receives Orphan Drug Designation From the European Commission for AMX0035 for the Treatment of Wolfram Syndrome

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*- New designation follows the U.S. Food and Drug Administration (FDA) Orphan Drug Designation for AMX0035 in Wolfram syndrome granted in 2020*

*- Topline data for all 12 participants from Phase 2 HELIOS trial studying impact of AMX0035 on endocrine, metabolic, and neurodegenerative aspects of Wolfram syndrome anticipated fall 2024*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 2, 2024-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced the European Commission (EC), based on a positive opinion issued by the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA), has granted Orphan Drug Designation for AMX0035, Amylyx' proprietary, fixed-dose combination of sodium phenylbutyrate (PB) and taurursodiol (TURSO; also known as ursodoxicoltaurine outside of the U.S.) for the treatment of Wolfram syndrome.

Wolfram syndrome is a prototypical disease of endoplasmic reticulum (ER) stress that is rare, progressive, and monogenic and is characterized by childhood-onset diabetes mellitus, optic nerve atrophy, deafness, diabetes insipidus, and neurodegeneration. There are currently no drugs approved for Wolfram syndrome, and many people with the disease die prematurely with severe neurological disabilities.

The FDA previously granted AMX0035 Orphan Drug Designation for the treatment of Wolfram syndrome in 2020. The EMA grants Orphan Drug Designation status for products intended for the treatment, prevention, or diagnosis of rare, life-threatening, or chronically debilitating conditions where the product may represent a significant benefit over existing treatments.

Amylyx recently presented positive data from an interim analysis of its Phase 2 HELIOS study, including eight participants with Wolfram syndrome assessed at Week 24, which demonstrated that AMX0035 improved pancreatic function and glycemic control, as measured by C-peptide, HbA1c, and other markers of glucose metabolism. All eight participants met prespecified responder criteria showing either improvement or stabilization of disease according to both the Patient Reported Global Impression of Change (PGIC) and the Clinical Reported Global Impression of Change (CGIC) scales. The majority of participants reported some improvement in vision. In Wolfram syndrome, progressive decline and worsening of outcomes would have been expected on all measures, so disease improvement or stabilization alone is clinically meaningful. AMX0035 was generally well tolerated in all participants. The Company anticipates reporting topline data from all 12 participants at Week 24 this fall.

"Wolfram syndrome is a disease where there are well-defined measurable biomarkers, rigorous supporting preclinical data, and clear rationale for our potential therapy based on its mechanism of action. Specifically, Wolfram syndrome is considered a prototypical endoplasmic reticulum (ER) stress disorder because of the clear link between *WFS1* mutations and ER stress. AMX0035 is believed to target ER stress and mitochondrial dysfunction," said Camille L. Bedrosian, MD, Chief Medical Officer at Amylyx. "The interim data from HELIOS showed stabilization or even improvement across key outcomes at Week 24. HELIOS follows strong preclinical research with data showing clear effects in cellular and animal models. We look forward to reporting topline data from all participants at Week 24 this fall. We aim to address an urgent unmet medical need, given there are no approved treatment options for Wolfram syndrome."

**About Wolfram Syndrome**

Wolfram syndrome is rare, progressive, monogenic disease characterized by childhood-onset diabetes, optic nerve atrophy, and neurodegeneration. Common manifestations of Wolfram syndrome include diabetes mellitus, optic nerve atrophy, central diabetes insipidus, sensorineural deafness, neurogenic bladder, and progressive neurologic difficulties. The prognosis of Wolfram syndrome is poor, and many people with the disease die prematurely with severe neurological disabilities. Literature suggests approximately 3,000 people are living with Wolfram syndrome in the United States.

Wolfram syndrome is often characterized as a prototypical disease of endoplasmic reticulum (ER) stress. ER stress and mitochondrial dysfunction are believed to drive the underlying disease pathophysiology in Wolfram syndrome. Individuals with Wolfram syndrome generally have mutations in the *WFS1* gene, which encodes wolframin, a protein spanning the membrane of the ER. Wolframin is thought to play a role in protein folding and aid in the maintenance of ER function by regulating calcium levels. Loss of wolframin function leads to ER stress and impaired mitochondrial dynamics.

**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 simultaneously targeting endoplasmic reticulum (ER) stress and mitochondrial dysfunction, two connected central pathways that lead to cell death and neurodegeneration. Preclinical studies have provided evidence that the proprietary combination of PB and TURSO and their complementary mechanisms of action targets cell death and better prevents neurodegeneration than targeting either mechanism of action alone. AMX0035 is being studied as a potential treatment in neurodegenerative diseases, including Wolfram syndrome and progressive supranuclear palsy (PSP).

**About the HELIOS Trial**

The HELIOS trial (NCT05676034) is a 12-participant, open-label Phase 2 trial designed to study the effect of AMX0035 on safety and tolerability, and various measures of endocrinological, neurological, and ophthalmologic function in adult participants living with Wolfram syndrome.

**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: interactions with regulatory authorities; the ongoing evaluation of AMX0035 in Wolfram syndrome, including that early-stage results may not reflect later-stage results and the timing for expected topline data in the HELIOS study; and the potential for AMX0035 to help people living with Wolfram syndrome. Any forward-looking statements in this press release 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 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 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.

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