Amylyx Pharmaceuticals Announces First Participant Dosed in Phase 2 Study of AMX0035 for the Treatment of Wolfram Syndrome

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- Recently published preclinical data demonstrate initial proof-of-concept for the therapeutic development of AMX0035 (sodium phenylbutyrate and taurursodiol) in Wolfram syndrome

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 13, 2023-- Amylyx Pharmaceuticals, Inc. (NASDAQ: AMLX) ("Amylyx" or the "Company") today announced that the first participant has been dosed in the HELIOS study, a Phase 2 clinical trial of AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO]) for the treatment of Wolfram syndrome (WS).

HELIOS is an exploratory open-label proof of biology study assessing the effect of AMX0035 safety and tolerability, and various measures of endocrinological, neurological and ophthalmologic function. Amylyx anticipates topline results from HELIOS in 2024.

More information on the HELIOS clinical study can be found at www.clinicaltrials.gov, NCT05676034.

Researchers from the Washington University School of Medicine in St. Louis, in collaboration with Amylyx, recently published preclinical data exploring the potential of AMX0035 as a novel therapeutic approach for WS. These data were published in the peer-reviewed *Journal of Clinical Investigation Insight*, characterizing a pathogenic variant in the *WFS1* gene (*WFS1* c.1672C>T, p.R558C), identifying a platform for further genotype-phenotype analysis, and providing initial proof-of-concept for the therapeutic development of AMX0035 in WS. The study demonstrated that iPSC-derived WS models can provide a model of genotype-phenotype relationships that correlate with clinical observations. Study highlights related to AMX0035 included:

- Administration of AMX0035 improved WFS1 protein expression, increased insulin secretion, and inhibited cell death in β cells with the WFS1 c.1672C>T, p.R558C variant. AMX0035 also prevented cellular death in patient-derived neuronal progenitor cells. Gene enrichment analysis revealed that treatment with AMX0035 ameliorated organelle dysfunction, mitophagy, endoplasmic reticulum (ER) stress, and apoptosis.
- Furthermore, AMX0035 delayed the onset of the diabetic phenotype *in vivo* in the *Wfs1*-knockout mouse model of Wolfram syndrome.

"WS is a rare, progressive, and often fatal neurodegenerative disease. Preclinical data showed that a combination treatment of two chemicals, namely AMX0035, may restore cellular functioning in a cellular model of WS," said Fumihiko Urano, MD, PhD, Principal Investigator of the HELIOS clinical trial, and Professor of Medicine and of Pathology and Immunology in the Division of Endocrinology, Metabolism & Lipid Research at Washington University School of Medicine. "There continues to be a significant unmet need for people living with WS and we look forward to building upon our preclinical findings as part of HELIOS to explore the safety, tolerability, and preliminary clinical activity in people living with WS."

"The WS community is in critical need of treatments to potentially improve their outcomes and standard of day-to-day living," said Joshua Cohen and Justin Klee, Co-CEOs of Amylyx. "We believe AMX0035 has scientific potential in several neurodegenerative diseases. We look forward to continuing to work to study AMX0035 in additional populations, including WS, and advancing progress in collaboration with the WS community including clinicians, researchers, and those living with the disease and their caregivers."

Amylyx announced that the FDA granted orphan drug designation to AMX0035 for the treatment of WS in November 2020. The FDA may grant this designation to drugs and biologics intended to treat a rare disease or condition affecting fewer than 200,000 persons in the U.S. Orphan designation qualifies a company for certain benefits, including financial incentives to support clinical development and the potential for seven years of market exclusivity in the U.S. upon regulatory approval.

About Wolfram Syndrome

Wolfram syndrome (WS) is an autosomal recessive neurodegenerative disease characterized by childhood-onset diabetes, optic nerve atrophy, and neurodegeneration. Common manifestations of WS include diabetes mellitus, optic nerve atrophy, central diabetes insipidus, sensorineural deafness, neurogenic bladder, and progressive neurologic difficulties. Genetic and experimental evidence suggest that endoplasmic reticulum (ER) dysfunction is a critical pathogenic component of WS. The prognosis of WS is poor, and many people with the disease die prematurely with severe neurological disabilities.

About Amylyx Pharmaceuticals

Amylyx Pharmaceuticals, Inc. is committed to supporting and creating more moments for the neurodegenerative disease community through the discovery and development of innovative new treatments. Amylyx is headquartered in Cambridge, Massachusetts and has operations in Canada and EMEA. For more information, visit amylyx.com and follow us on LinkedIn and Twitter. 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, statements

regarding the Phase 2 clinical trial of AMX0035 for the treatment of WS, including expectations regarding the timing of trial results, and the potential of AMX0035 as a treatment option for WS and its potential to address unmet needs and improve outcomes for the WS community. Any forward-looking statements in this statement 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, the likelihood of preclinical results to be predictive of clinical trial results, Amylyx' ability to execute on its strategy, regulatory developments, expectations regarding the timing of regulatory review of AMX0035, Amylyx' ability to fund operations, and the impact that the COVID-19 pandemic, global macroeconomic uncertainty and geopolitical instability will have on Amylyx' operations, as well as those risks and uncertainties set forth in Amylyx' United States Securities and Exchange Commission (SEC) filings, including Amylyx' Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, 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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