



Amylyx Pharmaceuticals Announces Formal Intention to Remove RELYVRIO®/ALBRIOZA™ from the Market; Provides Updates on Access to Therapy, Pipeline, Corporate Restructuring, and Strategy

April 4, 2024

- Based on topline results from the Phase 3 PHOENIX trial of AMX0035 in ALS, Amylyx has started a process with the FDA and Health Canada of voluntarily discontinuing the marketing authorizations for RELYVRIO/ALBRIOZA
- RELYVRIO/ALBRIOZA will no longer be available for new patients as of today; Patients currently on therapy in the U.S. and Canada who, in consultation with their physician, wish to continue can be transitioned to a free drug program; PHOENIX Open Label Extension is ongoing
- Amylyx continues to advance AMX0035 in Wolfram syndrome and in progressive supranuclear palsy (PSP), and AMX0114 in ALS
- Interim data from the Phase 2 HELIOS trial of AMX0035 for the treatment of Wolfram syndrome are expected this month and will be presented during a webcast on April 10, 2024
- Restructuring plan reduces workforce by approximately 70% to focus resources on key clinical and preclinical programs and extends expected cash runway into 2026, through anticipated data readouts for AMX0035 in Wolfram syndrome and PSP, and AMX0114 in ALS

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 4, 2024-- [Amylyx Pharmaceuticals, Inc.](#) (NASDAQ: AMLX) (“Amylyx” or the “Company”) today announced the Company has started a process with the U.S. Food and Drug Administration (FDA) and Health Canada to voluntarily discontinue the marketing authorizations for RELYVRIO®/ALBRIOZA™ (sodium phenylbutyrate and taurursodiol [also known as ursodoxicoltaurine]; also known as AMX0035) and remove the product from the market in the U.S. and Canada based on topline results from the Phase 3 PHOENIX trial. RELYVRIO/ALBRIOZA will no longer be available for new patients as of today. Patients currently on therapy in the U.S. and Canada who, in consultation with their physician, wish to stay on treatment can be transitioned to a free drug program.

“While this is a difficult moment for the ALS community, we reached this path forward in partnership with the stakeholders who will be impacted and in line with our steadfast commitment to people living with ALS and other neurodegenerative diseases. The decision to remove RELYVRIO/ALBRIOZA from the market and provide therapy free of charge for those who wish to continue was informed by the PHOENIX trial results, engagement with regulatory authorities, and discussions with the ALS community. Thank you to each and every person who shared feedback with us and continues to support our commitment to the ALS community,” said Joshua Cohen and Justin Klee, Co-CEOs of Amylyx.

Amylyx will continue to evaluate and share learnings from PHOENIX to help inform future ALS research. At this time, Amylyx intends to continue to collect available data on survival at the encouragement of ALS specialists. The PHOENIX Open Label Extension (OLE) is ongoing. Topline data from PHOENIX will be presented at the American Academy of Neurology (AAN) Annual Meeting in Denver and online, taking place April 13-18, 2024. The presentation is scheduled to occur on April 16, 2024, during the Clinical Trials Plenary Session (9:15 a.m. – 11:30 a.m. MT) and will be made available on the [“Publications and Presentations”](#) section of the Company’s website following the conclusion of the presentation.

As part of the Company’s purpose to discover and develop innovative new treatment options for neurodegenerative diseases, Amylyx continues to advance two key programs investigating its lead asset AMX0035 in Wolfram syndrome and progressive supranuclear palsy (PSP), and AMX0114, an antisense oligonucleotide targeting calpain-2, in ALS.

“Our pipeline is supported by compelling clinical and preclinical science demonstrating the potential of AMX0035 and AMX0114 in neurodegenerative diseases. AMX0035 was designed to slow or mitigate neurodegeneration by targeting endoplasmic reticulum stress and mitochondrial dysfunction, two connected central pathways that lead to cell death and neurodegeneration. We are investigating AMX0035 in diseases where these two pathways are implicated, which includes Wolfram syndrome and progressive supranuclear palsy,” said Camille L. Bedrosian, MD, Chief Medical Officer of Amylyx. “We look forward to presenting interim data from our Phase 2 HELIOS study of AMX0035 in Wolfram syndrome, a rare, genetic, fatal neurodegenerative disease with no FDA-approved treatment options, later this month. In addition, our Phase 3 ORION study remains ongoing to evaluate AMX0035 for the treatment of progressive supranuclear palsy, a rare neurodegenerative disorder characterized as a tauopathy. We continue to plan for an interim analysis to evaluate the data from ORION that is now expected in mid-2025.”

Dr. Bedrosian continued, “We also remain focused on ALS and believe AMX0114 has strong potential for the treatment of ALS

and other diseases. Calpain-2 is considered an essential protein in the process of axonal degeneration and has been repeatedly linked to neurofilament biology in published studies. In our preclinical studies of AMX0114 and in multiple independent published studies, inhibition of calpain-2 has reduced cell death and degeneration and decreased neurofilament levels. We expect to initiate a clinical trial studying AMX0114 in ALS in the second half of this year.”

Amylyx also announced a restructuring to focus the Company’s financial resources on upcoming clinical milestones. The Company will reduce its workforce by approximately 70% and decrease external financial commitments outside of its priority areas. With these changes, Amylyx expects to have cash runway into 2026, which will allow the organization to deliver on key upcoming milestones, including data readouts from HELIOS (AMX0035 in Wolfram syndrome), ORION (AMX0035 in PSP), and its planned trial of AMX0114 in ALS.

“We are so thankful and grateful to our Amylyx team for their contributions and steadfast dedication,” said Cohen and Klee. “Together, the work we have accomplished across the world has helped build a vital foundation to achieve our mission of one day ending the suffering caused by neurodegenerative diseases, which continue to have critical, unaddressed needs.”

HELIOS Interim Data in Wolfram Syndrome Investor Webcast Details

Amylyx will host a virtual webcast with Dr. Fumihiko Urano, Principal Investigator of the Phase 2 HELIOS clinical trial in Wolfram syndrome and Professor Medicine in the Division of Endocrinology, Metabolism & Lipid Research at Washington University School of Medicine, to discuss interim HELIOS data on April 10, 2024, at 1:30 p.m. ET. A live webcast of the presentation can be accessed under “Events and Presentations” in the Investor section of the Company’s website, <https://investors.amylyx.com/news-events/events>, and will be available for replay for 90 days following the event.

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. We believe that our 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 AMX0114

AMX0114 is an antisense oligonucleotide designed to target the gene encoding calpain-2, a key contributor to the axonal (Wallerian) degeneration pathway. Axonal degeneration has been recognized as an important early contributor to the clinical presentation and pathogenesis of ALS and other neurodegenerative diseases. Calpain-2 has been implicated in the pathogenesis of ALS based on findings of elevated levels of calpain-2 and its cleavage products in postmortem ALS tissue, therapeutic benefit of calpain-2 modulation in animal models of ALS, and the role of calpain-2 in cleaving neurofilament, a broadly researched biomarker in ALS. Preclinical studies completed to date have shown that AMX0114 achieves potent, dose-dependent, and durable knockdown of CAPN2 mRNA expression and calpain-2 protein levels in human motor neurons. Moreover, in preclinical efficacy studies, treatment with AMX0114 reduced extracellular neurofilament light chain levels following neurotoxic insult in induced pluripotent stem cell (iPSC)-derived human motor neurons, and improved survival of iPSC-derived human motor neurons harboring ALS-linked, pathogenic TDP-43 mutations.

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. ALS affects around 30,000 people in the U.S., and more than 30,000 people are estimated to be living with ALS in Europe (European Union and the United Kingdom). People living with ALS have a median survival of approximately two years from diagnosis.

About the HELIOS Trial

The HELIOS trial ([NCT05676034](https://clinicaltrials.gov/ct2/show/study/NCT05676034)) is a 12-participant, open-label, proof of biology, 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 Wolfram Syndrome

Wolfram syndrome is an autosomal recessive neurodegenerative 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. Genetic and experimental evidence suggests that endoplasmic reticulum (ER) dysfunction is a critical pathogenic component of Wolfram syndrome. The prognosis of Wolfram syndrome is poor, and many people with the disease die prematurely with severe neurological disabilities.

About the ORION Trial

The ORION trial ([NCT06122662](https://clinicaltrials.gov/ct2/show/study/NCT06122662)) is a global, randomized, double-blind, placebo-controlled Phase 3 clinical trial designed to assess the efficacy, safety, and tolerability of AMX0035 compared to placebo in people living with progressive supranuclear palsy (PSP). The ORION Phase 3 trial was designed and planned in collaboration with key global academic leaders, people living with PSP and their caregivers, and industry advocacy organizations.

About PSP

Progressive supranuclear palsy (PSP) is a sporadic, rare, and adult-onset neurodegenerative disorder that affects walking and balance, eye movement, swallowing, and speech. People living with PSP have a life expectancy of six to eight years after initial diagnosis, and its epidemiology is similar to that of amyotrophic lateral sclerosis (ALS). PSP typically begins in late-middle age and rapidly progresses over time. The disease affects approximately seven in 100,000 people worldwide, and there are currently no disease-modifying therapies approved for the treatment of PSP.

PSP is characterized by abnormal tau inclusions and is consequently also known as a tauopathy. Similar to other neurodegenerative diseases, pathophysiologic changes underlying PSP are multifactorial, with several genetic and environmental factors likely contributing to tau dysfunction and aggregation.

Multiple pathways, including genetic mutations, endoplasmic reticulum (ER) stress, and the activation of unfolded protein response, mitochondrial dysfunction, and neuroinflammation have been implicated as contributors to tau dysfunction and aggregation.

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. For more information, visit [amylyx.com](https://www.amylyx.com) and follow us on [LinkedIn](#) and [X](#), (formerly 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, Amylyx' expectations regarding: interactions with regulatory authorities; the availability of RELYVRIO/ALBRIOZA for patients currently taking RELYVRIO/ALBRIOZA; the timing and significance of learnings from the PHOENIX trial, the PHOENIX survival analysis and the Open Label Extension; the continued evaluation of AMX0035 in other neurodegenerative diseases, including the timing for expected data readouts in the ORION and HELIOS studies; the potential for AMX0114 as a treatment for ALS and the planned initiation of a trial evaluating AMX0114 in ALS; and the impact of resource-conserving measures on extending the Company's cash runway, including the restructuring plan. 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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