Amylyx Pharmaceuticals to Present Clinical Trial Design of ORION, a Phase 3 Global Study of AMX0035 in Progressive Supranuclear Palsy (PSP), at the Neuro2023 PSP and CBD International Research Symposium

October 19, 2023 at 9:00 AM EDT

- ORION is a randomized, double-blind, placebo-controlled Phase 3 clinical trial evaluating the safety, efficacy, and tolerability of AMX0035 in adults with PSP

- Study anticipates enrolling approximately 600 participants globally, with trial initiation anticipated by the end of 2023

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 19, 2023-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) (“Amylyx” or the “Company”) today announced an upcoming presentation at Neuro2023 on the design of ORION, a planned global, Phase 3 clinical trial of AMX0035 (sodium phenylbutyrate and taurursodiol [PB&TURSO]) in progressive supranuclear palsy (PSP). Neuro2023: The PSP and CBD International Research Symposium will take place on October 19-20, 2023, at the Pan Pacific Hotel in London, UK.

“We designed ORION in collaboration with the broader PSP community, including people living with the disease, advocacy leaders, clinicians, researchers, and other experts in the field, and we are excited to launch what will potentially be the largest PSP trial to date,” said Lahar Mehta, MD, Head of Global Clinical Development at Amylyx. “There is robust scientific rationale supporting the evaluation of AMX0035 in PSP, and we look forward to the initiation of our Phase 3 trial which is anticipated by the end of this year.”

Details of the poster presentation at Neuro2023 are as follows:

Thursday, October 19, 2023, 5:00 pm – 7:00 pm BST

- **Title:** Design of a Global Phase 3, Randomized, Double-blind, Placebo-Controlled Trial of AMX0035 in Progressive Supranuclear Palsy (A35-009 ORION)

For conference information, visit: https://www.psp.org/event/neuro2023-the-psp-and-cbd-international-research-symposium/

The presentation is available on the “Publications” tab of the Amylyx website.

“There are currently no disease-modifying therapies approved for the treatment of PSP, a rapidly progressive and fatal tauopathy and movement disorder,” said Prof. Dr. Günter Höglinger, Director of the Department of Neurology at Ludwig-Maximilians-University (LMU) Hospital, Munich, Germany, and Primary Investigator of the Phase 3 ORION clinical trial. “Based on preclinical evidence, AMX0035 is proposed to directly target cell organelle function and mitigate both the unfolded protein response and mitochondrial dysfunction, two pathways that are associated with several neurodegenerative diseases, including PSP. We look forward to investigating AMX0035’s potential in targeting these two pathways that are implicated in tau dysfunction and aggregation in PSP, which then lead to neurodegeneration.”

ORION Trial Design

ORION 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. Approximately 600 participants will be enrolled across North America, Europe, and Japan, with study initiation anticipated by the end of 2023 starting in the United States.

The primary efficacy endpoint evaluates change in disease progression from baseline to Week 52 as measured by total score on the 28-item Progressive Supranuclear Palsy Rating Scale (PSPRS), an established and validated endpoint in PSP clinical trials.

Secondary efficacy endpoints are disease progression as measured by a modified 10-item PSPRS score and motor aspects of activities of daily life as measured by the Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part 2 (MDS-UPDRS Part II). Exploratory outcomes include changes in activities of daily living, cognitive function, quality of life, overall survival, brain regional volumes, fluid biomarkers of neuronal injury/inflammation, and caregiver burden.

Safety and tolerability will be evaluated by assessing the frequency of treatment emergent adverse events (TEAEs) and serious adverse events (SAEs).

The ORION Phase 3 trial was designed and planned in collaboration with key global academic leaders, people living with PSP, and industry advocacy groups.

Additional key elements of the study design:

- The study will enroll ambulant adults, 40-80 years of age, with probable or possible PSP (also known as Richardson’s syndrome) according to International Parkinson and Movement Disorder Society 2017 criteria and less than 5 years since developing PSP symptoms. Key eligibility criteria include:
  - A score of <40 on the 28-item PSPRS
  - A score of ≥24 on the Mini Mental State Examination

    - Study partner required
    - No feeding tube use
    - On stable dose of antiparkinsonian drugs for 60 days before enrollment
- After a screening period, participants will be randomized in a 3 to 2 manner to receive AMX0035 or matching placebo for 52 weeks (randomized phase).
- For all participants who complete the randomized phase, a 52-week open label extension phase will be available for continued access to AMX0035 to further characterize the long-term efficacy and safety of AMX0035 in this population.

Additional details regarding trial enrollment and eligibility criteria will be shared upon initiation of the trial, which is anticipated to start by the end of 2023.

About AMX0035

AMX0035 is an oral, fixed-dose combination of sodium phenylbutyrate and taurursodiol (known as ursodoxicoltaurine outside of the U.S.), which was granted full approval as RELYVRIO® to treat amyotrophic lateral sclerosis (ALS) in adults in the U.S. and approved with conditions as ALBRIOZA™ for the treatment of ALS in Canada. AMX0035 is being explored in other populations and regions, as well as for the potential treatment of other neurodegenerative diseases. The formulation of RELYVRIO, ALBRIOZA and AMX0035 are identical.

About PSP

Progressive supranuclear palsy (PSP) is a rare and adult-onset neurological disorder that affects body movements, 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 ALS. PSP typically begins in late-middle age and rapidly progresses over time.

Multiple pathways likely contribute to the pathophysiology of PSP, which is characterized by tau protein deposition in subcortical regions resulting in widespread neurodegeneration. The disease affects approximately seven in 100,000 people worldwide, and there are currently no disease-modifying therapies approved for the treatment of PSP.

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 X, formerly known as 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, our plans to make AMX0035 available in Europe; the ongoing commercialization of RELYVRIO and ALBRIOZA; the potential continued market acceptance and market opportunity for RELYVRIO and ALBRIOZA; the potential of AMX0035 as a treatment for ALS and the Company’s plans to explore the use of AMX0035 for other neurodegenerative diseases including PSP; the timelines for the ORION study in PSP, and expectations regarding our longer-term strategy. 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: Amylyx’ ability to fund operations, the success, cost, and timing of Amylyx’ program development activities, Amylyx’ ability to execute on its commercial and regulatory strategy, regulatory developments, expectations regarding the timing and outcome of EMA’s review of AMX0035 for the treatment of ALS, Amylyx’ reliance on third parties, including to conduct clinical trials and manufacture products, and the effect of global economic uncertainty and financial market volatility caused by economic effects of rising inflation and interest rates, the COVID-19 pandemic, geopolitical instability, changes in international trade relationships and military conflicts, as well as the 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 June 30, 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. Subject to any obligations under applicable law, 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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