Amylyx Pharmaceuticals Announces Publication of Survival Analysis Comparing CENTAUR to Historical Clinical Trial Control

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Results demonstrated a 10.4 month difference in overall survival and a 52% lower risk of death over the duration of the follow-up period

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 10, 2023-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) (“Amylyx” or the “Company”) today announced the publication of a post hoc analysis in the peer-reviewed medical journal, *Annals of Clinical and Translational Neurology* comparing the long term survival of participants in the CENTAUR study versus a historical clinical trial control group. The results of this post hoc analysis, which demonstrated that the median overall survival was 10.4 months longer in the CENTAUR AMX0035 group than in the historical clinical trial control group, are consistent with the data previously presented at the 2023 American Academy of Neurology Annual Meeting.

A previously reported intent-to-treat (ITT) overall survival analysis comparing participants originally randomized to AMX0035 versus participants originally randomized to placebo demonstrated a 4.8 month longer survival for the AMX0035 group. However, this ITT analysis did not account for the fact that 71% of participants originally randomized to placebo received AMX0035 during the OLE phase of the trial, which may lead to an underestimation of the effect of AMX0035 on survival. The post hoc survival analysis published today compared CENTAUR clinical trial participants who received AMX0035 against a propensity score-matched, AMX0035-naïve external control cohort from the Pooled Resource Open-Access ALS Clinical Trials (PRO-ACT) database. The results demonstrated a longer survival and a 52% lower risk of death over the duration of follow-up in the CENTAUR AMX0035 group versus the PRO-ACT external control group. These results using an external control aligned with prior analysis using statistical models adjusting for placebo-to-active crossover in CENTAUR (RPSFTM).

“The PRO-ACT database is comprised of thousands of harmonized longitudinal records from ALS clinical trials and helps advance scientific research by providing access to robust longitudinal participant data,” said Sabrina Paganoni, MD, PhD, and Melanie Quintana, PhD, leading authors of the study from Sean M. Healey and AMG Center for ALS & the Neurological Clinical Research Institute, Massachusetts General Hospital and Berry Consultants, respectively. “Incorporation of placebo-to-active crossover in ALS trials can cause an underestimation of the effect of these therapies on overall survival in ITT analyses. Analyses using optimally matched external controls like this one may provide additional context for survival outcomes in ALS trials incorporating placebo-to-active crossover.”

“This analysis is important because the survival difference seen helps support the robustness and clinical meaningfulness of the ITT overall survival analysis on CENTAUR,” said Machelle Manuel, PhD, Head of Global Medical Affairs at Amylyx. “Given the rapid progression of the disease, every day matters to families impacted by ALS, and we appreciate the opportunity to share these findings.”

The PRO-ACT database is the largest source of open-access data relating to outcomes from ALS clinical trials including longitudinal data from 29 Phase 2 and 3 ALS clinical trials. The PRO-ACT project is led by Alex Sherman at the Neurological Clinical Research Institute (NCRI) at Mass General Hospital and is currently sponsored by The ALS Association. The external control group was constructed from PRO-ACT by selecting control participants with available ALSFRS-R data and known mortality information that met key eligibility criteria from CENTAUR. Propensity score matching was utilized to account for potential imbalances in baseline characteristics and other variables across trials. The comparison groups were well-matched for baseline demographic and clinical characteristics. The PRO-ACT external control group also demonstrated an identical mean change in ALSFRS-R total score from baseline through 24 weeks compared to the CENTAUR placebo group (-1.66 points/month), further supporting that the PRO-ACT external control group was a well-matched treatment-naïve comparator for the survival analysis.

“The PRO-ACT initiative merges data from existing publicly and privately conducted ALS clinical trials to generate an invaluable resource for accelerating discovery in the field of ALS. This database allows anyone interested in moving ALS research forward an aid to do so quickly,” said Alex Sherman, Director of the Center for Innovation and Biomedical Informatics (CIB) at NCRI and Healey & AMG Center at Mass General, Principal Associate in Neurology at Harvard Medical School, leader of the team that created the PRO-ACT database, and the current Principal Investigator of the PRO-ACT platform. “Analyses like the one published here further our shared mission of accelerating the discovery of treatments and a cure for ALS.”

PRO-ACT is a critical database that gives the ALS research community new information that could open up new pathways and approaches to developing new treatments. Amylyx donated data from the CENTAUR clinical trial to the PRO-ACT database.

About RELYVRIO®/ALBRIOZA ™/AMX0035

RELYVRIO® (also known as AMX0035), an oral, fixed-dose combination of sodium phenylbutyrate and taurursodiol (known as ursodoxicoltaurine outside of the U.S.), is approved 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. The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) is re-examining its initial opinion on the current application for conditional marketing authorisation of AMX0035, under the trade name ALBRIOZA®, for the treatment of ALS in the European Union. AMX0035 is being explored for the potential treatment of other neurodegenerative diseases. The formulation of RELYVRIO, ALBRIOZA, and AMX0035 are identical.

RELYVRIO® (sodium phenylbutyrate and taurursodiol) Safety Information for United States

WARNINGS AND PRECAUTIONS

Risk in Patients with Enterohepatic Circulation Disorders, Pancreatic Disorders, or Intestinal Disorders

RELYVRIO contains taurursodiol, which is a bile acid. In patients with disorders that interfere with bile acid circulation, there may be an increased risk for worsening diarrhea, and patients should be monitored appropriately for this adverse reaction. Pancreatic insufficiency, intestinal malabsorption, or intestinal diseases that may alter the concentration of bile acids may also lead to decreased absorption of either of the components of RELYVRIO. Because different enterohepatic circulation, pancreatic, and intestinal disorders have varying degrees of severity, consider consulting with a specialist. Patients with disorders of enterohepatic circulation (e.g., biliary infection, active cholecystitis), severe pancreatic disorders (e.g., pancreatitis), and intestinal disorders that may alter concentrations of bile acids (e.g., ileal resection, regional ileitis) were excluded from the study; therefore, there is no clinical experience in these conditions.

Use in Patients Sensitive to High Sodium Intake

RELYVRIO has a high salt content. Each initial daily dosage of 1 packet contains 464 mg of sodium; each maintenance dosage of 2 packets daily contains 928 mg of sodium. In patients sensitive to salt intake (e.g., those with heart failure, hypertension, or renal impairment), consider the amount of daily sodium intake in each dose of RELYVRIO and monitor appropriately.

ADVERSE REACTIONS

The most common adverse reactions (at least 15% and at least 5% greater than placebo) with RELYVRIO were diarrhea, abdominal pain, nausea, and upper respiratory tract infection. Gastrointestinal-related adverse reactions occurred throughout the study but were more frequent during the first 3 weeks of treatment.

Please click here for RELYVRIO Full U.S. Prescribing Information.

About the CENTAUR Trial

CENTAUR was a multicenter Phase 2 clinical trial in 137 participants with ALS encompassing a 6-month randomized placebo-controlled phase and an open-label long-term follow-up phase. The trial met its primary efficacy endpoint of reducing functional decline as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R).

Overall, reported rates of adverse events and discontinuations were similar between AMX0035 and placebo groups during the 24-week randomized phase; however, gastrointestinal events occurred with greater frequency (≥2%) in the AMX0035 group. Detailed data from CENTAUR is published in the New England Journal of Medicine (NEJM) and Muscle & Nerve.

The CENTAUR trial was funded, in part, by the ALS ACT grant and the ALS Ice Bucket Challenge, and was supported by The ALS Association, ALS Finding a Cure (a program of The Leandro P. Rizzuto Foundation), the Northeast ALS Consortium, and the Sean M. Healey & AMG Center for ALS at Mass General.

About Amylyx Pharmaceuticals

Amylyx Pharmaceuticals, Inc. is committed to supporting and creating more moments for the neurodegenerative 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 and related comments in our earnings conference call 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 timing of review of its initial opinion and an anticipated final recommendation from the CHMP regarding whether to approve AMX0035 for the treatment of ALS in Europe; the potential of AMX0035 (sodium phenylbutyrate and taurursodiol) as a treatment for ALS and other neurodegenerative diseases including Wolfram syndrome and PSP; the Company’s beliefs regarding the benefits of AMX0035 in ALS and other neurodegenerative diseases, the potential of AMX0035 to be a foundational therapy for ALS and a potential, future cure; the ongoing commercialization of RELYVRIO and ALBRIOZA; expectations regarding the timing of initiation of the Company’s Phase 3 ORION trial of AMX0035 for the treatment of PSP and of the results of the Company’s Phase 2 HELIOS trial of AMX0035 for the treatment of Wolfram syndrome; statements regarding coverage by insurance plans for ALBRIOZA and the timing of, and the Company’s ability to, finalize and sign product listing agreements with the remaining public drug plans for ALBRIOZA in Canada; the potential continued market acceptance and market opportunity for RELYVRIO and ALBRIOZA and opportunities for growth; expectations regarding the speed of access to RELYVRIO; the potential for new pipeline programs and clinical indications for AMX0035; statements regarding regulatory developments; the Company’s expectations with respect to its progress through IND enabling studies of AMX0114 and other advancements in its pipeline; the Company’s expectations regarding its financial performance; and expectations regarding the Company’s longer-term strategy. 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 successfully commercialize RELYVRIO in the United States and ALBRIOZA in Canada, Amylyx’ ability to execute on its commercial and regulatory strategy, regulatory developments, expectations regarding the timing of a decision from the EMA regarding AMX0035 for the treatment of ALS, Amylyx’ ability to fund operations, and the impact that global macroeconomic uncertainty, geopolitical instability and public health events, such as COVID-19, 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’ 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 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.

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