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AMYLYX PHARMACEUTICALS ANNOUNCES TOPLINE RESULTS FROM GLOBAL PHASE 3 PHOENIX TRIAL OF AMX0035 IN ALS

- PHOENIX Study Did Not Meet Prespecified Primary or Secondary Endpoints

- Data From 664-Participant Study Reinforce That AMX0035 is Generally Safe and Well-Tolerated

- Within the Next Eight Weeks, Amylyx Will Continue to Engage With Regulatory Authorities and the ALS Community to Share Topline Data; Amylyx Will Share Plans for RELYVRIO/ALBRIOZA in ALS Which May Include Voluntarily Withdrawing RELYVRIO/ALBRIOZA From the Market

- At This Time, RELYVRIO/ALBRIOZA Will Continue to be Available for People Living With ALS; Amylyx Has Voluntarily Decided to Pause Promotion; Related Patient Support Services Will Remain in Place

Amylyx Pharmaceuticals announced topline results from PHOENIX, a global, 48-week, randomized, placebo-controlled Phase 3 clinical trial of AMX0035 (sodium phenylbutyrate and taurursodiol [also known as ursodoxicoltaurine]; RELYVRIO® in the U.S., ALBRIOZA™ in Canada) in people living with amyotrophic lateral sclerosis (ALS). PHOENIX did not meet its primary endpoint of reaching statistical significance (p=0.667) as measured by change from baseline in the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) total score at Week 48, nor was there statistical significance seen in secondary endpoints. Amylyx plans to present the data from PHOENIX at an upcoming medical meeting and will publish the results in a medical journal later this year.

Amylyx will continue to engage with regulatory authorities and the broader ALS community, including ALS specialists and other multidisciplinary experts, people living with ALS, and advocates, to discuss the results from PHOENIX within the next eight weeks and make informed decisions. Amylyx intends to share plans for RELYVRIO/ALBRIOZA in ALS, which may include voluntarily withdrawing RELYVRIO/ALBRIOZA from the market. At this time, RELYVRIO/ALBRIOZA and its related patient support program will continue to be available for people living with ALS. Amylyx has voluntarily decided to pause promotion of the medication during this time.

“We are surprised and deeply disappointed by the PHOENIX results following the positive data from the CENTAUR trial. Our main priority at the moment is sharing the information

with people living with ALS and their treating physicians; this is part of our continued commitment to them and our mission. Over the next eight weeks, our team will continue to engage with regulatory authorities and the ALS community to discuss the results from PHOENIX. We will be led in our decisions by two key principles: doing what is right for people living with ALS, informed by regulatory authorities and the ALS community, and by what the science tells us. On behalf of the entire Amylyx team, we are grateful to the ALS community and for the dedication of trial participants, investigators, and study site teams. With data collected from 664 participants in PHOENIX, we are certain there will be important learnings that will help inform future ALS research. We are steadfast in our commitment to the ALS community and our mission, including with AMX0035 where it has shown potential in neurodegenerative diseases such as Wolfram syndrome and progressive supranuclear palsy, and with AMX0114, our investigational antisense oligonucleotide targeting calpain-2, in ALS," said Justin Klee and Joshua Cohen, Co-CEOs of Amylyx.

PHOENIX Study Results:

The Phase 3 PHOENIX study enrolled 664 adults living with ALS. Participants were randomized three-to-two to receive either AMX0035 or placebo, with both treatment groups receiving standard-of-care. Continuation of a stable dosing regimen of riluzole and/or edaravone was permitted.

- **PHOENIX did not meet the primary endpoint:** There was no significant difference observed between participants treated with AMX0035 and placebo in ALSFRS-R total score change from baseline at Week 48 (p=0.667). No significant difference was observed in the subset of participants who met the CENTAUR trial criteria. There were also no significant differences observed across secondary endpoints.
- **Consistent safety and tolerability profile:** AMX0035 was well-tolerated in PHOENIX. There were no new safety signals, reinforcing the favorable and manageable safety profile observed with AMX0035 to date.
- European participants who completed the 48-week randomized phase had the option to enroll in an open label extension of the trial of up to two years in duration, which remains ongoing.

Science of AMX0035:

AMX0035, a specially formulated oral fixed-dose combination of PB and TURSO, has been shown in numerous preclinical studies to have a robust, synergistic effect in targeting two different destructive neurodegenerative disease pathways by mitigating endoplasmic reticulum stress and the associated unfolded protein response and mitochondrial dysfunction thereby reducing neuronal cell death. Additionally, AMX0035 has been shown to also reduce markers associated with neurodegenerative diseases in clinical trials, including a reduction of tau, a key protein aggregate shared across several neurodegenerative diseases, and YKL-40, a marker of neuroinflammation.

About the PHOENIX Trial

PHOENIX was a 48-week, randomized, placebo-controlled, global Phase 3 clinical trial further evaluating the safety and efficacy of AMX0035 (sodium phenylbutyrate and taurursodiol) for the treatment of ALS. The primary efficacy outcome of the trial was change from baseline in ALS Functional Rating Scale-Revised (ALSFRS-R) total score at 48 weeks. Secondary endpoints include quality of life patient-reported outcome assessments, overall survival, and respiratory function as measured by slow vital capacity (SVC). Safety and tolerability were also assessed.

European participants who completed the 48-week trial had the option to enroll in an open-label extension (OLE) phase. During this phase, all participants receive AMX0035, and continued safety and efficacy measures will be assessed.

About AMX0035 / RELYVRIO® / ALBRIOZA™

AMX0035 is an oral, fixed-dose combination of sodium phenylbutyrate and taurursodiol (known as ursodoxicoltaurine outside of the U.S.). It is approved 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 studied for the potential treatment of other neurodegenerative diseases, and Amylyx is exploring its treatment in other populations and regions. The formulation of RELYVRIO, ALBRIOZA, and AMX0035 is identical.

Source: **Amylyx.com**