Amylyx Pharmaceuticals Announces New England Journal of Medicine Publication of Pivotal AMX0035 Data Demonstrating Statistically Significant Benefit in People with ALS

- Patients Retained Function Longer on AMX0035 Versus Placebo; Study Achieved Its Primary Outcome of a Difference on the Revised ALS Functional Rating Scale

- AMX0035 is the First Investigational Therapy to Demonstrate Statistically Significant Benefit on this Prespecified Primary Outcome in People with ALS Since Approved Therapy Edaravone

- AMX0035 Showed Numerical Benefits on Secondary Outcomes Including Measures of Muscle Strength, Breathing, and Hospitalizations

- AMX0035 Was Generally Well Tolerated with Similar Rates of Adverse Events Recorded in the AMX0035 and Placebo Groups

Amylyx Pharmaceuticals, Inc., a pharmaceutical company focused on developing new treatments for amyotrophic lateral sclerosis (ALS), Alzheimer's disease and other neurodegenerative diseases, today announced the publication of results from the pivotal CENTAUR trial evaluating AMX0035 – an investigational neuroprotective therapy designed to reduce the death and dysfunction of motor neurons – in people with ALS in the New England Journal of Medicine (NEJM).

"CENTAUR met its prespecified primary outcome, showing a clinically meaningful and statistically significant treatment benefit on the Revised ALS Functional Rating Scale (ALSFRS-R), the most commonly used scale in clinics worldwide to measure function in ALS," said Sabrina Paganoni, M.D., Ph.D., principal investigator of the CENTAUR trial, investigator at the Sean M. Healey & AMG Center for ALS at Mass General and Assistant Professor of PM&R at Harvard Medical School and Spaulding Rehabilitation Hospital. "These results represent a major milestone for the ALS community, and I am thrilled about the promise of this therapy for people with ALS."

The CENTAUR trial of 137 individuals with ALS was conducted across 25 top medical centers in the U.S. through the Northeast ALS (NEALS) consortium. It demonstrated that treatment with AMX0035 was well tolerated and decreased the rate of decline in the ALSFRS-R compared to placebo in people with ALS.

"The data published today in the New England Journal of Medicine show that AMX0035 demonstrated a clinically meaningful benefit and a favorable safety profile for people living with ALS. This development is a breakthrough for the ALS community and we are working collaboratively and expeditiously with agencies worldwide to bring this potential new treatment option forward," said Josh Cohen, Co-CEO, Chairman and Co-Founder at Amylyx.

"The data published today makes a clear and compelling case that AMX0035 should be made available to people with ALS as soon as possible," said Calaneet Balas, President and CEO of The ALS Association. "We look forward to working with Amylyx, the FDA, and the entire community to help make that happen. We are grateful to all the Ice Bucket Challenge donors whose contributions helped make this trial possible."

CENTAUR-Results:

Primary Outcomes:

- After 24 weeks, patients treated with AMX0035 scored on average 2.32 points higher on the ALSFRS-R than the placebo group (p=0.03) using the study's primary prespecified analysis. A change from baseline analysis was also conducted and indicated that the AMX0035 group scored 2.92 points higher at the end of 24 week follow up (p=0.01).
    - The ALSFRS-R is a 48-point questionnaire measuring daily functions such as the ability to walk, dress independently, self-feed, speak and breathe.
    - Just a 1-2 point change in the ALSFRS-R score can indicate a significant reduction in a patient's ability to function independently. The ALSFRS-R measures many different daily functions so point differences can manifest differently in different patients. Some examples of a two point change on this scale include the difference between an individual eating successfully with some difficulty vs needing a feeding tube, or walking with assistance versus not walking at all.

Secondary Outcomes:

- In line with the primary outcome, patients on AMX0035 also showed numerical benefits on secondary outcomes including measures of muscle strength, breathing and hospitalization frequency, although the study was not powered for secondary outcomes.
    - Progression in lung function (percent predicted slow vital capacity) was numerically slower in patients taking AMX0035 (Least Squares Difference=5.11 points, p=0.08).
    - Participants in the AMX0035 group were hospitalized numerically less often (Hazard Ratio = 0.54, p=0.09).
    - Rate of decline in overall muscle strength (percent predicted ATLIS) was numerically slower in patients taking AMX0035 (Least Squares Difference=2.82 points, p=0.12). The effect of AMX0035 on progression was nominally statistically significant for the upper limbs measurements (Least Squares Difference=4.27 points, p=0.04).

Overall Safety:

- Nearly all participants (46 out of 48 patients in placebo (96%) vs 86 out of 89 patients in the AMX0035 group (97%)) reported one or more treatment-emergent adverse events (TEAEs) during the trial. Most were nonserious, did not lead to modification or interruption of study drug dosing, and were not considered related to the study.
- Overall, safety was comparable between the groups, with fewer serious adverse events in the active group as compared to the placebo group (9 out of 48 patients (19%) in placebo vs 11 out of 89 patients (12%) in the AMX0035 group).
- GI adverse events, which were generally characterized as mild by investigators, occurred more frequently in the active group in the first 3 weeks of the trial (28.1% vs 12.5% placebo) and returned to levels comparable to placebo thereafter.

Most CENTAUR participants (77%) were receiving an approved ALS therapy (riluzole, edaravone, or both) during and/or before trial entry. Sensitivity analyses accounting for the duration of treatment under riluzole, edaravone, or both confirmed that the treatment effect of AMX0035 was independent of background approved ALS therapies.

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

“I am so proud of the ALS community efforts that made this milestone possible,” said Dr. Merit Cudkowicz, M.D., Chief Medical Officer from ALS Finding a Cure®, Director of the Sean M. Healey & AMG Center for ALS, Chief of Neurology at Mass General, and the Julianne Dorn Professor of Neurology at Harvard Medical School. “The CENTAUR study was designed and run through NEALS, was supported by a partnership between The ALS Association and ALS Finding a Cure, and is a phenomenal example of what can happen when a community works closely together to accelerate ALS progress.”

AMX0035 Long-Term Survival and Extension Data, Future Plans

Participants who completed CENTAUR were given the option after the trial to enroll in an open-label extension study and receive AMX0035 long-term. 92% of eligible CENTAUR participants elected to enroll in the extension study. Interim data from the ongoing open-label extension study are being submitted to a peer-reviewed journal shortly and will be published in the coming months.

Long-term survival analysis for the patients in the AMX0035 and placebo groups has been conducted as well. These data will be submitted to a peer-reviewed journal in the near future.

“We are deeply grateful to all of the CENTAUR participants and our partners who have helped and continue to help develop this important therapy for those living with ALS,” said Justin Klee, Co-CEO and Co-Founder of Amylyx. “We also look forward in the coming months to sharing results from the CENTAUR open-label extension study and the long-term survival analysis, and we will continue to keep the community closely informed on next steps.”

About CENTAUR

CENTAUR was a 24-week, randomized, double-blind, placebo-controlled Phase 2/3 clinical trial that evaluated the safety and tolerability of AMX0035 and assessed the drug’s impact on disease progression as measured by the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) when compared to placebo. The trial also assessed the effects of AMX0035 on other measures that are critical to people with ALS, including muscle strength, lung vital capacity, and biomarkers of neuronal degeneration.

CENTAUR enrolled patients 18-80 years old with definite ALS and within 18 months of symptom onset. The trial did not restrict patients from receiving edaravone or riluzole.

About Amyotrophic Lateral Sclerosis (ALS)

ALS 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. The vast majority of patients with ALS (>90%) have sporadic disease, showing no clear family history. Approximately 6000 people are diagnosed with ALS in the United States every year with an approximately similar number of deaths every year.

About AMX0035

AMX0035 is an investigational neuroprotective therapy designed to reduce neuronal death and dysfunction. AMX0035 targets endoplasmic reticulum and mitochondrial dependent neuronal degeneration pathways in ALS and other neurodegenerative diseases.

About Amylyx Pharmaceuticals

Amylyx Pharmaceuticals, Inc. is a pharmaceutical company working on developing a novel therapeutic for amyotrophic lateral sclerosis (ALS), Alzheimer's disease and other neurodegenerative diseases.

(Source: https://www.businesswire.com/news/home/20200902005945/en/Amylyx-Pharmaceuticals-Announces-New-England-Journal-of-Medicine-Publication-of-Pivotal-AMX0035-Data-Demonstrating-Statistically-Significant-Benefit-in-People-with-ALS)