Alzheon Announces Efficacy Outcomes from Two Prior Tramiprosate Phase 3 Studies

Patients with Mild to Moderate Alzheimer's Disease and APOE4/4 Genotype Showed Robust and Sustained Efficacy on Cognitive and Functional Co-Primary Outcomes over 78 weeks with Favorable Safety Profile

Data Presented at the 8th Clinical Trials on Alzheimer's Disease Congress Supports Phase 3 Clinical Development of ALZ-801 in APOE4/4 Homozygous Patients with Mild to Moderate AD

FRAMINGHAM, Mass., November 6, 2015 – Alzheon, Inc., today announced results of a new analysis from two independent Phase 3 studies of tramiprosate in the subgroup of Alzheimer's disease (AD) patients with APOE4/4 genotype.

These analyses showed that apolipoprotein E4/4 (APOE4/4) subjects who received tramiprosate, the biologically-active agent of ALZ-801, had significant, clinically meaningful and sustained cognitive improvement on the Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-cog) on top of standard of care through 78 weeks. The ADAS-cog benefit of twice daily tramiprosate 150 mg compared to placebo was sustained and increased over time to maximal benefit of up to 4 points at 65-78 weeks. These pro-cognitive effects in APOE4/4 carriers are further supported by significant efficacy trends on the functional Clinical Dementia Rating-Sum of Boxes (CDR-SB) outcome of approximately 1 point at 65 and 78 weeks.

These new analyses are presented in a late breaking podium session[1] and in a poster[2] at the 8th Clinical Trials on Alzheimer's Disease Congress in Barcelona, Spain, held November 5-7, 2015. This efficacy outcomes data supports Alzheon's plan for accelerated development of ALZ-801, an optimized prodrug of tramiprosate, in the genetically well-defined population of symptomatic AD patients with APOE4/4 genotype.

Anton P. Porsteinsson, MD, Professor of Psychiatry at the University of Rochester School of Medicine and Dentistry and Director of the Alzheimer's Disease Care, Research and Education Program at the University of Rochester in Rochester, NY, and an investigator in the North American (NA) Phase 3 clinical trial, commented: "Apolipoprotein E4 carriers comprise up to 60 percent of AD patients, with APOE4/4 homozygotes representing approximately 10-15 percent of all AD patients. This genetically well-defined population has an 8-12 fold increased risk of developing AD as well as

more rapidly progressive disease, usually becoming symptomatic a decade earlier than non-carriers of apolipoprotein E4 genotype. We also know from recent imaging studies that APOE4/4 homozygotes have the highest rate of positive amyloid scans, at approximately 90-95 percent positivity. Unfortunately, these patients are also at the highest risk of developing vasogenic edema, known as ARIA-E, with some amyloid targeted candidate drugs. This makes it imperative to develop drugs for this population that provide meaningful efficacy without a safety trade-off. "

Dr. Porsteinsson also added: "These analyses with tramiprosate in the APOE4/4 subgroups, which are consistent across two Phase 3 studies, are very promising, and suggest a substantial and sustained efficacy benefit on cognition throughout the 18 months of treatment, on top of the maximal symptomatic AD treatments they are receiving, and seems higher than the ADAS-cog benefit seen with current drugs in development."

The combined North America (NA) and EU data described in the late breaking presentation by Dr. Porsteinsson summarized the cognitive and functional efficacy for two twice-daily doses of tramiprosate (100 mg and 150 mg) on the co-primary outcomes ADAS-cog and CDR-SB in APOE4/4 homozygous AD subjects. The merged data sets include approximately 250 APOE4/4 patients. The two doses were well tolerated and showed a favorable safety profile in both studies.

In the NA trial, approximately 15 percent of patients were APOE4/4, out of a total study population of approximately 1,000 patients with Mini Mental State Examination (MMSE) of 16-26 (mean 20.5), between 50-85 years of age (mean 71 years), and on a stable dose of acetylcholinesterase inhibitors (about 100 percent), alone or with memantine (about 50 percent). For the ADAS-cog cognitive outcome, the analysis showed a significant treatment effect at the 150 mg twice-daily dose, and a trend at the lower dose. For the composite functional outcome CDR-SB at the 150 mg twice-daily dose, there was a significant and clinically meaningful benefit at 65 weeks and a trend at 78 weeks. The dropout rate in the study was approximately 20 percent and similar across the 3 arms.

The EU trial also included APOE4/4 patients whose data was used in the subgroup analyses, and were part of the overall study of more than 900 AD subjects, which had identical design and inclusion criteria as the NA trial, except for excluding the use of memantine. Similar results were obtained in the EU study, and results from the merged datasets further support the ADAS-cog and CDR-SB findings from the NA trial.

"These promising results from two independent datasets continue to support our accelerated development plan for ALZ-801," stated Martin Tolar, MD, PhD, Founder, President and Chief Executive Officer of Alzheon. "Once we have data from the ALZ-801 multiple ascending dose study, which is underway, we will advance ALZ-801 into Phase 3 in this very targeted, genetically defined population with high medical need."

About Alzheon

Alzheon, Inc. is committed to developing innovative medicines for patients suffering from Alzheimer's disease and other neurological and psychiatric disorders. Our lead clinical candidate, ALZ-801, is a first in-class, oral inhibitor of amyloid aggregation and neurotoxicity – hallmarks of Alzheimer's disease. ALZ-801 is an optimized, novel prodrug that builds on the established safety and efficacy profile of the active compound in clinical trials of more than 2,000 patients. Our mission is to apply our discovery platform and development experience to unlock new classes of therapeutics that make a difference in patients' lives by directly addressing the underlying pathology of devastating neurodegenerative disorders. For more information, please visit www.alzheon.com.

The details for the presentations are as follows:

1. Late Breaking Presentation (LB #5)
   - Title: *"Robust and Sustained Efficacy of Tramiprosate in APOE4/4 Homozygous Patients with Mild and Moderate AD: Combined Data Sets from Two 78-week Phase 3 Trials"*
   - Presenter: Anton P. Porsteinsson, MD, Professor of Psychiatry at the University of Rochester School of Medicine and Dentistry and Director of the Alzheimer's Disease Care, Research and Education Program at the University of Rochester, Rochester, N.Y.
   - Authors: Anton P. Porsteinsson, MD; Jeffrey Cummings, MD, Cleveland Clinic; Miia Kipivelto, MD, PhD, Karolinska University Hospital, Stockholm, Sweden; John Hey, PhD, Alzheon, Inc.; Jeremy Y. Yu, MD, PhD, Alzheon, Inc.; Aidan Power, MD, Alzheon, Inc.; Menghis Bairu, MD, Serenus Biotherapeutics, Inc.; Martin Tolar, MD, PhD, Alzheon, Inc.; Susan Abushakra, MD, Alzheon, Inc.
2. Poster Presentation (P1-24)
   - Title: *"Cognitive and Functional Efficacy of Tramiprosate in APOE4+ Patients with Mild to Moderate Alzheimer's Disease: Sub-group Analyses of the Phase 3 North American and European Trials"*
   - Authors: John Hey, PhD, Alzheon, Inc.; Jeremy Y. Yu, MD, PhD Alzheon, Inc.; Martin Tolar, MD, PhD, Alzheon, Inc.; Menghis Bairu, MD, Serenus Biotherapeutics, Inc.; John Sampalis, PhD, McGill University

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