Alzheon to Present Biomarker, Brain Preservation, and Clinical Results from Pivotal Program of Oral ALZ-801/Valiltramiprosate at 16th Annual Clinical Trials in Alzheimer's Disease Conference

Fully Enrolled Pivotal APOLLOE4 Phase 3 Trial Progressing Successfully, Enabling Topline Data Readout and NDA Filing in 2024

ALZ-801 Tablet Inhibits Formation of Soluble Toxic Amyloid Aggregates and Acts Upstream from All Late-Stage Amyloid Targeting Treatments

Robust and Statistically Significant P-tau$_{181}$ Reduction in Plasma, Combined with Preservation of Brain Volume and Positive Correlations with Cognitive Effects, Reinforces Potential of ALZ-801 to Slow Alzheimer's Disease Progression

ALZ-801 Safety Results Remained Favorable & Consistent with Prior Formulation's Data in Over 2,800 AD Patients, with no Increased Risk of Vasogenic Brain Edema

FRAMINGHAM, Mass., October 17, 2023 — Alzheon, Inc., a clinical-stage biopharmaceutical company developing a portfolio of product candidates and diagnostic assays for patients suffering from Alzheimer's disease (AD) and related neurodegenerative disorders, today announced its participation in the upcoming Clinical Trials in Alzheimer's Disease (CTAD) conference in Boston, Massachusetts from October 24-27, 2023.

"The treatment landscape for Alzheimer's disease is beginning to take shape, and Alzheon's simplified approach has an opportunity to transform the standard of care and improve access to treatment for all Alzheimer's patients. We are pleased with the growing body of evidence that supports ALZ-801's potential as the first oral anti-amyloid disease modifying therapy for Alzheimer's disease," said Martin Tolar, MD, PhD, Founder, President, and CEO of Alzheon. "Our efficacy data combined with a favorable safety profile with no events of vasogenic edema underscore the differentiated clinical profile of ALZ-801 tablet. We look forward to discussing these data at the CTAD conference and to results from our ongoing APOLLOE4 Phase 3 trial in APOE4/4 homozygotes that is expected to read out in the third quarter of 2024."

The details of the four posters to be presented at CTAD conference are as follows:

Poster: *Effect of ALZ-801/Valiltramiprosate, an Oral Inhibitor of Amyloid Oligomer Formation, on Plasma Biomarkers, Volumetric Brain Imaging Biomarkers, and Clinical Outcomes of Alzheimer's Disease: 12-Month Results of Phase 2 Biomarker Study in Early AD APOE4 Carrier Subjects*

- **Presenter:** John Hey, PhD, Chief Scientific Officer, Alzheon, Inc.
- **Location:** P043

Poster: *Cerebral Amyloid Angiopathy and Comorbid Cardiovascular Risk Factors in APOE4/4 Homozygotes with Early Alzheimer's Disease: Baseline Results from APOLLOE4 Phase 3 Trial of Oral Anti-Amyloid Agent ALZ-801*

- **Presenter:** Rosalind McLaine, MBA, PA-C, Senior Clinical Trial Manager, Alzheon, Inc.
- **Location:** LP030

Poster: *Cerebral Amyloid Angiopathy in APOE4/4 Homozygotes with Alzheimer's Disease: Baseline Characteristics of Subjects Enrolled in APOLLOE4 Phase 3 Trial of Oral ALZ-801 in Early AD*

- **Presenter:** Rosalind McLaine, MBA, PA-C, Senior Clinical Trial Manager, Alzheon, Inc.
- **Location:** P054

Poster*: Analysis of Aß (1-42) Oligomers by Cyclic Ion Mobility Spectrometry in Spiked Human Cerebrospinal Fluid*

- **Presenter:** John Hey, PhD, Chief Scientific Officer, Alzheon, Inc.
- **Location:** P136

ALZ-801/valiltramiprosate is an investigational oral therapeutic candidate in Phase 3 development for the treatment of Early AD. In mechanism of action studies, ALZ-801 fully blocked the formation of neurotoxic soluble beta amyloid (Aβ) oligomers at the Phase 3 clinical dose. Oral ALZ-801 has shown treatment potential in the highest-risk and most fragile Alzheimer's population – patients with two copies of the apolipoprotein ε4 allele (APOE4/4 homozygotes), as well as positive safety results, with no increased risk of vasogenic brain edema. This population is the focus of Alzheon's pivotal 78-week APOLLOE4 Phase 3 trial, which is now fully enrolled, and topline data are expected in the third quarter of 2024.

Alzheon's open-label, multicenter, single-arm Phase 2 biomarker trial evaluated biomarker effects, clinical efficacy, and safety of ALZ-801 tablet in 84 Early AD patients, who carry either one or two copies of the ε4 allele of apolipoprotein E gene (APOE3/4 heterozygotes and APOE4/4 homozygotes, respectively), and who showed positivity for amyloid and tau in cerebrospinal fluid (CSF). APOE4 genotype, the leading risk factor for AD after aging, is associated with a several-fold higher brain burden of neurotoxic amyloid oligomers, and APOE4 carriers represent two thirds of the Alzheimer's patient population. In addition, Alzheon is collaborating with the Czech Institute of Organic Chemistry & Biochemistry (IOCB) to develop an assay to measure the neurotoxic amyloid oligomers in CSF.

"The magnitude of p-tau$_{181}$ biomarker reduction in plasma compared to plaque-clearing anti-amyloid antibodies, combined with preservation of brain hippocampal volume and its robust positive correlations with cognitive benefits, reinforces our conviction that ALZ-801 has the potential to disrupt the Alzheimer's treatment paradigm by slowing the progression of this relentless and debilitating disease. We look forward to engaging in scientific discussions at CTAD on our Phase 2 and Phase 3 trials and the progress we have made with our colleagues at the IOCB Institute in developing an assay to measure amyloid oligomers in the brain," said John Hey, PhD, Chief Scientific Officer of Alzheon. "Results from our pivotal APOLLOE4 Phase 3 trial and a 3rd year extension of our Phase 2 biomarker trial will set the stage for the potential NDA filing next year and commercial launch in 2025."

About ALZ-801

ALZ-801/valiltramiprosate is an investigational oral agent in Phase 3 development as a potentially disease modifying treatment for AD.[1,3] ALZ-801 is designed to block the formation of neurotoxic soluble beta amyloid oligomers causing cognitive decline in Alzheimer's patients. In mechanism of action studies, ALZ-801 has fully inhibited the formation of neurotoxic soluble beta amyloid oligomers at the Phase 3 clinical dose.[5,6] ALZ-801 acts through a novel enveloping molecular mechanism of action to fully block formation of neurotoxic soluble amyloid oligomers in the human brain[7] associated with the onset and progression of cognitive decline in AD patients.[1–4] ALZ-801 received Fast Track designation from the U.S. Food and Drug Administration in 2017 for Alzheimer's disease. In clinical trials, ALZ-801 has shown favorable safety results.[5–7,9] The initial Phase 3 program for ALZ-801 is focusing on Early AD patients with the APOE4/4 genotype, with potential future program expansion to AD treatment and prevention in patients carrying one copy of the APOE4 gene and noncarriers.[1–4]

ALZ-801 Phase 2 Biomarker Trial

Biomarker Effects of ALZ-801 in APOE4 Carriers With Early Alzheimer's Disease (NCT04693520): This ongoing trial is designed to evaluate the effects of 265 mg twice daily oral dose of ALZ-801 on biomarkers of AD pathology in subjects with Early AD, who have either the APOE4/4 or APOE3/4 genotype and constitute 65-70% of Alzheimer's patients. The trial also includes evaluation of clinical efficacy, safety, tolerability, and pharmacokinetic profile of ALZ-801 over 104 weeks of treatment. An ongoing long-term extension of the trial evaluates ALZ-801 for an additional 52 weeks of treatment for a total of 156 weeks.

ALZ-801 APOLLOE4 Phase 3 Trial

An Efficacy and Safety Study of ALZ-801 in APOE4/4 Early Alzheimer's Disease Subjects (NCT04770220): This ongoing trial is designed to evaluate the efficacy, safety, biomarker and imaging effects of 265 mg twice daily oral dose of ALZ-801 in Early AD subjects with two copies of the apolipoprotein ε4 allele (APOE4/4 homozygotes), who constitute approximately 15% of Alzheimer's patients. This is a double-blind, randomized trial comparing oral ALZ-801 to placebo treatment over 78 weeks. The APOLLOE4 trial is supported by a $51 million grant from the National Institute on Aging.

About Alzheon

Alzheon, Inc. is a clinical-stage biopharmaceutical company developing a broad portfolio of product candidates and diagnostic assays for patients suffering from Alzheimer's disease and other neurodegenerative disorders. We are committed to developing innovative medicines by directly addressing the underlying pathology of neurodegeneration. Our lead Alzheimer's clinical candidate, ALZ-801/valiltramiprosate, is an oral agent in Phase 3 development as a potentially disease modifying treatment for AD. ALZ-801 is an oral small molecule that has been observed to fully block the formation of neurotoxic soluble amyloid oligomers in preclinical tests. Our clinical expertise and technology platform are focused on developing drug candidates and diagnostic assays using a precision medicine approach based on individual genetic and biomarker information to advance therapies with the greatest impact for patients.

Alzheon Scientific Publications

[1] Tolar M, et al: *Neurotoxic Soluble Amyloid Oligomers Drive Alzheimer's Pathogenesis and Represent a Clinically Validated Target for Slowing Disease Progression*, **International Journal of Molecular Sciences**, 2021; 22, 6355.

[2] Abushakra S, et al: *APOE ε4/ε4 Homozygotes with Early Alzheimer's Disease Show Accelerated Hippocampal Atrophy and Cortical Thinning that Correlates with Cognitive Decline*, **Alzheimer's & Dementia**, 2020; 6: e12117.

[3] Tolar M, et al: *Aducanumab, Gantenerumab, BAN2401, and ALZ-801—the First Wave of Amyloid-Targeting Drugs for Alzheimer's Disease with Potential for Near Term Approval*, ***Alzheimer's Research & Therapy***, 2020; 12: 95.

[4] Tolar M, et al: *The Path Forward in Alzheimer's Disease Therapeutics: Reevaluating the Amyloid Cascade Hypothesis*, **Alzheimer's & Dementia**, 2019; 1-8.

[5] Hey JA, et al: *Discovery and Identification of an Endogenous Metabolite of Tramiprosate and Its Prodrug ALZ-801 that Inhibits Beta Amyloid Oligomer Formation in the Human Brain*, **CNS Drugs**, 2018; 32(9): 849-861.

[6] Hey JA, et al: *Clinical Pharmacokinetics and Safety of ALZ-801, a Novel Prodrug of Tramiprosate in Development for the Treatment of Alzheimer's Disease*, **Clinical Pharmacokinetics**, 2018; 57(3): 315–333.

[7] Abushakra S, et al: *Clinical Effects of Tramiprosate in APOE4/4 Homozygous Patients with Mild Alzheimer's Disease Suggest Disease Modification Potential*, **Journal of Prevention of Alzheimer's Disease**, 2017; 4(3): 149-156.

[8] Kocis P, et al: *Elucidating the Aβ42 Anti-Aggregation Mechanism of Action of Tramiprosate in Alzheimer's Disease: Integrating Molecular Analytical Methods, Pharmacokinetic and Clinical Data*, **CNS Drugs**, 2017; 31(6): 495-509.

[9] Abushakra S, et al: *Clinical Benefits of Tramiprosate in Alzheimer's Disease Are Associated with Higher Number of APOE4 Alleles: The "APOE4 Gene-Dose Effect,"* **Journal of Prevention of Alzheimer's Disease,** 2016; 3(4): 219-228.

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