Alzheon to Present Phase 2 Biomarker Trial Results and Baseline Characteristics from APOLLOE4 Phase 3 Trial of Oral ALZ-801/Valiltramiprosate in Patients with Early Alzheimer's Disease at Alzheimer's Association International Conference

Fully Enrolled Pivotal APOLLOE4 Phase 3 Trial in Early Alzheimer's Patients on Track for Topline Data Readout in 2024

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

Robust and Sustained Plasma P-tau$_{181}$ Reduction Observed in Phase 2 Biomarker Trial, Combined with Preservation of Brain Volume and Correlations with Cognitive Effects, Reinforces Potential of ALZ-801 to Slow Alzheimer's Disease Progression

ALZ-801 Safety Results in APOE4 Carriers Remain Favorable & Consistent with Prior Formulation's Data Resulting in Safety Database of Over 3,000 AD Patients, Showing no Increased Risk of Vasogenic Brain Edema

FRAMINGHAM, Mass., July, 23 2024 — 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 Alzheimer's Association International Conference (AAIC) in Philadelphia, held from July 28 to August 1, 2024.

"Our scientific presentations at this year's AAIC conference demonstrate our commitment to advancing Alzheimer's research and developing treatments that can transform the standard of care for people living with Alzheimer's disease," said Susan Abushakra, MD, Alzheon's Chief Medical Officer. "Alzheimer's is devastating to patients and families, and we believe the data we are presenting reinforce the potential of our lead agent ALZ-801/valiltramiprosate as a first-in-class, oral disease modifying therapy that may simplify the patient journey and provide increased access. In addition to the presentations at AAIC, we look forward to the upcoming topline from our pivotal APOLLOE4 Phase 3 trial later this year. We believe these data may support ALZ-801 as the first oral treatment to slow the progression of Alzheimer's disease."

Alzheon will give four presentations at the conference, which include the following two oral sessions and two posters:

Late Breaker Podium Presentation: *"Phase 3 Trial of Oral Anti-Amyloid Agent ALZ-801/Valiltramiprosate in APOE4/4 Homozygotes with Early Alzheimer's Disease: Baseline Characteristics and Prevalence of Comorbid Cerebral Amyloid Angiopathy"*

- **Presenter:** Dr. Aidan Power, Chief Development Officer, Alzheon Inc.
- **Date and time:** Wednesday, July 31, 2024: 8:00 a.m. ET – 8:45 a.m. ET

Featured Research Symposium Presentation: *"Plasma Biomarkers, Hippocampal Volume and Cognitive Effects of Oral ALZ-801: The Phase 2 Biomarker Study and its Long-Term Extension in APOE4 Carriers with Early Alzheimer's Disease"*

- **Presenter:** Dr. Susan Abushakra, Chief Medical Officer, Alzheon Inc.
- **Date and time:** Wednesday, July 31, 2024: 9:00 a.m. ET – 10:30 a.m. ET

Poster: *"Use of External Comparator-Arm from ADNI-1 for the ALZ-801/Valiltramiprosate Phase 2 Study of APOE4 Carriers with Early Alzheimer's Disease: Regulatory Basis and Statistical Considerations"*

- **Presenter:** Dr. John Hey, Chief Scientific Officer, Alzheon Inc.
- **Date and time:** Monday, July 29, 2024: 7:30 a.m. ET – 4:15 p.m. ET

Poster: *"Low Incidence of Amyloid Related Imaging Abnormalities over 104 Weeks in a Phase 2 Study of Amyloid Anti-Oligomer Agent ALZ-801 (Valiltramiprosate) in Biomarker Positive APOE4 Carriers with Early Alzheimer's Disease"*

- **Presenter:** Dr. Patrick Kesslak, Senior Clinical Research Fellow
- **Date and time:** Tuesday, July 30, 2024: 7:30 a.m. ET – 4:15 p.m. ET

About ALZ-801

ALZ-801/valiltramiprosate is a potential first-in-class, investigational oral agent in Phase 3 development as a potentially disease modifying treatment for AD.[1-4,6,9] ALZ-801 is designed to block the formation of neurotoxic soluble beta amyloid oligomers implicated in cognitive decline in Alzheimer's patients.[1-4,6,11] In mechanism of action studies, ALZ-801 has fully inhibited the formation of neurotoxic soluble beta amyloid oligomers at the Phase 3 clinical dose.[6,9,11] ALZ-801 acts through a novel enveloping molecular mechanism of action to block formation of neurotoxic soluble amyloid oligomers in the human brain[11] associated with the onset and progression of cognitive decline in AD patients.[1,4,6,7] 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 potential for robust clinical efficacy and favorable safety results with no increased risk of brain vasogenic edema.[2-7,10,12] The initial Phase 3 program for ALZ-801 is focusing on Early AD patients with two copies of the apolipoprotein ε4 allele (APOE4/4 homozygotes), with potential future program expansion to AD treatment and prevention in patients carrying one copy of the APOE4 gene and noncarriers.[1–7]

ALZ-801 Phase 2 Biomarker Trial

Biomarker Effects of ALZ-801 in APOE4 Carriers With Early Alzheimer's Disease (NCT04693520): This ongoing trial was 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 included evaluation of clinical efficacy, safety, tolerability, and pharmacokinetic profile of ALZ-801 over 104 weeks of treatment (primary endpoint). An ongoing long-term extension of the trial evaluates ALZ-801 for an additional 104 weeks of treatment for a total of 208 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.

ALZ-801 APOLLOE4 Long Term Extension Trial

An ongoing long-term extension of the trial, APOLLOE4-LTE, evaluates ALZ-801 in subjects who complete the core APOLLOE4 study for an additional 52 weeks of treatment for a total of 130 weeks or 2.5 years over the core and LTE study (NCT06304883).

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 a first-in-class 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: *The Single Toxin Origin of Alzheimer's Disease and Other Neurodegenerative Disorders Enables Targeted Approach to Treatment and Prevention,* **International Journal of Molecular Sciences,** 2024; 25, 2727.

[2] Hey J, et al: *Analysis of Cerebrospinal Fluid, Plasma β-Amyloid Biomarkers, and Cognition from a 2-Year Phase 2 Trial Evaluating Oral ALZ-801/Valiltramiprosate in APOE4 Carriers with Early Alzheimer's Disease Using Quantitative Systems Pharmacology Model,* **Drugs** 2024.

[3]Hey J, et al: *Effects of Oral ALZ-801/Valiltramiprosate on Plasma Biomarkers, Brain Hippocampal Volume, and Cognition: Results of 2-Year Single-Arm, Open-Label, Phase 2 Trial in APOE4 Carriers with Early Alzheimer's Disease,* **Drugs** 2024.

[4] 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.

[5] 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.

[6] 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.

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

[8] 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.

[9] 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.

[10] 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.

[11] 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.

[12] 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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