Alzheon to Present Industry-Leading Phase 2 Biomarker and Clinical Data with ALZ-801 (Valiltramiprosate) Oral Tablet at 2022 Alzheimer's Association International Conference

New Results Position ALZ-801 to Potentially Become the First Oral Agent that Can Slow or Even Stop and Prevent Alzheimer's Pathology in Patients and Healthy Individuals at Risk for the Disease

Several-Fold Greater Reduction on P-tau$_{181}$ Compared to Anti-Amyloid Antibodies Validates Superior Clinical Benefit from Prior Studies in Alzheimer's Patients

Significant Improvement on Memory Tests Consistent with P-tau$_{181}$ Biomarker Effects to be Further Confirmed in Ongoing APOLLOE4 Phase 3 Trial

Safety Profile in ALZ-801 Studies Remains Favorable and Consistent with Prior Safety Data in 2,000 Patients with No Evidence of Vasogenic Brain Edema

FRAMINGHAM, Mass., July 26, 2022 — Alzheon, Inc., a clinical-stage biopharmaceutical company developing a broad portfolio of product candidates and diagnostic assays for patients suffering from Alzheimer's disease (AD) and other neurodegenerative disorders, today announced that it will be presenting at the 2022 Alzheimer's Association International Conference (AAIC) to be held on July 31 – August 4, 2022 in San Diego, California, USA.

Alzheon Chief Medical Officer, Susan Abushakra, MD, will give a podium presentation at the AAIC conference on Sunday, July 31, 2022, at 8 a.m. PT or 11 a.m. ET. This oral presentation will be included in the Hybrid Developing Topics 1 Session.

The AAIC presentation: *Effects of Oral ALZ-801, an Amyloid Oligomer Inhibitor, on Plasma Biomarkers in APOE4 Carriers with Early Alzheimer's Disease: Results of Six-month Interim Analysis from a Phase 2 Biomarker Study*, will provide an opportunity to hear from Dr. Abushakra as she discusses the development strategy and path to New Drug Application (NDA) for the ALZ-801 (valiltramiprosate) program. The presentation will also review the anti-amyloid oligomer mechanism of action of ALZ-801, interim biomarker data from the 6-month interim analysis of

Alzheon's fully enrolled Phase 2 biomarker study, and updates on the ongoing pivotal APOLLOE4 Phase 3 trial evaluating ALZ-801 oral tablet in Alzheimer's patients.

"Alzheon has developed a novel, precision medicine approach to Alzheimer's disease by targeting neurotoxic amyloid oligomers. Now, very promising biomarker data with ALZ-801 in Early Alzheimer's patients, who are APOE4 carriers, provide further support for this approach and the potential for robust efficacy with the convenience of an oral tablet," said Susan Abushakra, MD, Chief Medical Officer of Alzheon. "ALZ-801 significantly reduced p-tau$_{181}$ levels in plasma over 6 months of treatment. Importantly, rather than simply slowing cognitive decline as seen with other anti-amyloid agents, subjects treated with ALZ-801 showed significant memory improvement from baseline over 6 months in parallel with the p-tau$_{181}$ reduction. Combined with a favorable safety profile and no events of vasogenic edema across the ALZ-801 studies, our new biomarker data, and promising cognitive benefits, support the disease modifying effect of ALZ-801 in Alzheimer's patients. These data and ongoing studies position ALZ-801 to potentially become the first oral agent that can slow or even stop and prevent Alzheimer's pathology in patients and healthy individuals at risk for the disease."

ALZ-801 (valiltramiprosate) is an oral agent in Phase 3 development as a disease modifying treatment for AD that blocks the formation of neurotoxic soluble amyloid oligomers that lead to cognitive decline in Alzheimer's patients. In mechanism of action studies, ALZ-801 has been shown to fully inhibit the formation of amyloid oligomers at the Phase 3 clinical dose. ALZ-801 has demonstrated potential for robust efficacy and favorable safety in the high-risk Alzheimer's population – patients with two copies of the apolipoprotein ε4 allele (APOE4/4).

"Alzheon has experienced tremendous progress in the past year, during which we launched the APOLLOE4 Phase 3 study, reported industry-leading disease modifying effects from our Phase 2 biomarker trial of oral ALZ-801 in Alzheimer's patients, and initiated a collaboration to commercialize a diagnostic that can measure the toxic forms of amyloid in human brain," said Martin Tolar, MD, PhD, Alzheon Founder, President, and Chief Executive Officer. "These advances attracted prominent investors to Alzheon and led to the completion of an oversubscribed Series D round, which, combined with the prestigious grants awarded by the National Institute on Aging totaling $51M, give us a strong financial position to rapidly complete these trials leading to NDA submission for oral ALZ-801, as well as the further expansion of our small molecule product platform for neurodegenerative disorders."

ALZ-801 is in a class of its own as an easy to administer oral tablet that has shown the potential for robust efficacy with a favorable safety profile, avoiding the vascular complications of brain edema seen with infusions of plaque-clearing anti-amyloid antibodies. The ongoing, fully enrolled Phase 2 biomarker study is evaluating oral ALZ-801 in Early AD patients, who carry either one or two copies of the ε4 allele of apolipoprotein E gene. Patients with these genotypes together constitute 65-70% of patients with Alzheimer's disease. APOE4 genotype, the leading risk factor for Alzheimer's after aging, is associated with a several-fold higher brain burden of neurotoxic amyloid oligomers.

About ALZ-801

ALZ-801 is an oral agent in Phase 3 development as a potentially disease modifying treatment for AD.[1,3] In mechanism of action studies, ALZ-801 has been shown to fully inhibit the formation of neurotoxic soluble 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 of cognitive symptoms and progression of AD.[1–4] ALZ-801 received Fast Track designation from the U.S. Food and Drug Administration in 2017. The clinical data for ALZ-801 and Alzheon's safety database indicate a favorable safety profile.[5–7,9] The initial Phase 3 program for ALZ-801 is focusing on Early AD patients with the APOE4/4 genotype, with future expansion to AD treatment and prevention in patients carrying one copy of the APOE4 gene and noncarriers.[1–4]

ALZ-801 APOLLOE4 Phase 3 Study

An Efficacy and Safety Study of ALZ-801 in APOE4/4 Early Alzheimer's Disease Subjects (NCT04770220): This ongoing study 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 the APOE4/4 genotype, 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 $47 million grant from the National Institute on Aging.

ALZ-801 Phase 2 Biomarker Study

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

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, is an oral agent in Phase 3 development as a potentially disease modifying treatment for AD. ALZ-801 is an oral small molecule that fully blocks formation of neurotoxic soluble amyloid oligomers in the brain. 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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