Alzheon to Present Industry-Leading Biomarker, Brain Preservation, and Clinical Effects with Oral ALZ-801 (Valiltramiprosate) at 15th Annual Clinical Trials in Alzheimer's Disease 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 Plaque-Clearing Antibodies and Unprecedented Preservation of Hippocampal Volume Validate Superior Clinical Benefits from Prior Studies in Alzheimer's Patients

Significant Improvement from Baseline on Memory Tests at 3 and 6 Months, and Disease Stabilization Above Baseline at 1-Year Timepoint, to be Further Confirmed in Ongoing APOLLOE4 Phase 3 Trial

Safety profile in ALZ-801 Studies Remains Favorable & Consistent with Prior Data in Over 2,000 AD Patients, with no Evidence of Vasogenic Brain Edema

FRAMINGHAM, Mass., November 22, 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 new clinical trial data at the 15th Annual Clinical Trials on Alzheimer's Disease (CTAD) conference to be held from November 29 – December 2, 2022 in San Francisco, CA, USA.

Alzheon Chief Medical Officer, Susan Abushakra, MD, will give a podium presentation at the CTAD conference on Friday, December 2, 2022, at 11:45 a.m. PT or 2:45 p.m. ET. This oral presentation will be included in the Focus Session: Interim or Preliminary Data and Study Design.

The CTAD presentation: *Significant Effects of Oral ALZ-801 on Plasma Biomarkers of Alzheimer's Disease: 12-Month Interim Analysis of Phase 2 Biomarker Study in APOE4 Carriers with Early AD*, will provide an opportunity to hear from Dr. Abushakra as she discusses the statistically

significant and clinically relevant reduction in biomarkers of neurodegeneration, robust preservation of brain volume, and positive memory effects in Alzheimer's patients following 12 months of treatment with investigational agent ALZ-801 in the fully enrolled Phase 2 biomarker trial. Dr. Abushakra will also provide an update on the ongoing pivotal APOLLOE4 Phase 3 trial evaluating ALZ-801 oral tablet in Alzheimer's patients, and the path to New Drug Application (NDA) for the ALZ-801 (valiltramiprosate) program.

"Alzheon has pioneered precision medicine in Alzheimer's disease by targeting neurotoxic amyloid oligomers, and now very promising biomarker, imaging, and clinical data with ALZ-801 provide additional support for this approach. Across many trials of anti-amyloid treatments, p-tau$_{181}$ has emerged as a consistent plasma biomarker that correlates with clinical benefit. The several-fold greater reduction on the p-tau$_{181}$ biomarker in plasma compared to plaque-clearing anti-amyloid antibodies, combined with preservation of brain hippocampal volume and their positive correlations with cognitive benefits, validate the disease modifying effects of ALZ-801 in Alzheimer's patients," said Martin Tolar, MD, PhD, Founder, President, and CEO of Alzheon. "Importantly, rather than slowing the cognitive decline of patients as seen in trials with other agents, subjects treated with ALZ-801 demonstrated cognitive improvement from baseline status on memory tests and maintained their cognitive abilities over 1 year of treatment. These well-differentiated results combined with a favorable safety profile showing no events of vasogenic edema, 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 potentially disease modifying treatment for AD that blocks formation of neurotoxic soluble beta amyloid (Aβ) oligomers causing cognitive decline in Alzheimer's patients. In mechanism of action studies, ALZ-801 fully inhibited the formation of amyloid oligomers at the Phase 3 clinical dose. ALZ-801 has shown potential for robust efficacy in the highest-risk Alzheimer's population – patients with two copies of the apolipoprotein ε4 allele (APOE4/4 homozygotes), and favorable safety with no events of brain vasogenic edema seen in trials with plaque-clearing antibodies. This population is the focus of ongoing Alzheon's pivotal Phase 3 APOLLOE4 trial and has the highest likelihood of demonstrating successful efficacy outcomes.

Alzheon's Phase 2 AD biomarker study (NCT04693520) enrolled 84 patients with Early AD, who carry either the APOE4/4 or APOE3/4 genotype and received oral ALZ-801 265 mg twice daily. All analyses of plasma biomarkers were performed at the laboratory of Professor Kaj Blennow at University of Gothenburg in Molndal, Sweden, and were audited according to Good Laboratory Practice. A total of 75 patients (mean age 69 years, 52% female) completed the Week 52 visit and were included in the pre-specified analysis. In this population, ALZ-801 demonstrated a significant 41% reduction from baseline in plasma p-tau$_{181}$ (p=0.016) at 52 weeks. ALZ-801 also significantly reduced the plasma p-tau$_{181}$/Aβ42 ratio by 37% at 52 weeks (p=0.032). Given the importance of p-tau$_{181}$ and Aβ42 as biomarkers of core AD pathology, these results support the disease modifying effect of ALZ-801 in Alzheimer's patients.

"Trials with plaque-clearing antibodies continue to support Alzheon science of targeting neurotoxic soluble aggregates of beta amyloid, and our positive results represent the latest evidence confirming the promise of ALZ-801, extending other key discoveries made by Alzheon scientists over the past 9 years. The significant effect on plasma p-tau$_{181}$, combined with the hippocampal volume preservation and clinical stabilization after 12 months of treatment, validates the anti-amyloid oligomer action of ALZ-801 in Alzheimer's disease. This consistency across these three outcomes is very encouraging and supports the emerging disease modifying profile of ALZ-801 in Alzheimer's patients," said Susan Abushakra, MD, Chief Medical Officer of Alzheon. "Alzheon has developed a well-differentiated approach with small molecule ALZ-801, which acts upstream on the same pathway as anti-amyloid antibodies, preventing the formation of neurotoxic soluble amyloid oligomers without disrupting the insoluble plaque deposits in brain tissue and small vessels, thereby avoiding the vascular complications of brain edema and microbleeds seen with infusions of plaque-clearing antibodies. This data highlights the potential safety and efficacy advantages of ALZ-801 compared to plaque-clearing antibodies, while also offering a simplified patient journey towards an effective treatment."

With support from the National Institute on Aging in the form of a $47M grant to fund the APOLLOE4 Phase 3 study with ALZ-801, Alzheon's drug candidate is well positioned to become one of the first disease-modifying treatments approved for slowing and even preventing cognitive decline in Alzheimer's patients. Pioneering a precision medicine approach in Alzheimer's, the APOLLOE4 Phase 3 trial is enrolling the highest-risk homozygous APOE4/4 AD patients and incorporates the latest biomarker and volumetric MRI measures to track patient benefit – levels of p-tau$_{181}$ and beta amyloid in plasma and cerebrospinal fluid, hippocampal volume, and other volumetric brain measures, along with the gold-standard primary clinical endpoint, ADAS-Cog 13 (Alzheimer's Disease Assessment Scale-Cognitive Subscale).

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] In mechanism of action studies, ALZ-801 has been shown to fully inhibit 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 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 (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 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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