Alzheon to Present ALZ-801 (Valiltramiprosate) Oral Tablet Program Update as Potential Treatment for Alzheimer's Disease in Adults with Down Syndrome at 4th International Trisomy 21 Research 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

Significant Effects of ALZ-801 on Beta Amyloid and Tau Biomarkers in Patients with Alzheimer's Support its Clinical Development in Genetically Determined Disorders of Brain Amyloidosis

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., June 7, 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 4th International Trisomy 21 Research Society Conference (T21RS conference) to be held on June 9-12, 2022 in Long Beach, California, USA.

Alzheon Vice President of Clinical Development & Medical Affairs, Patrick Kesslak, PhD, will give a podium presentation at the T21RS conference on Saturday, June 11, 2022, at 3:30-5:00 p.m. PT. This oral presentation will be included in the Scientific Session 5B: *Dialogues with Industry and Sponsors to Support Clinical Translation in Down Syndrome*.

The T21RS conference presentation: *Oral ALZ-801, an Amyloid Oligomer Inhibitor in Late-Stage Development: Clinical Profile and Potential for Down Syndrome,* will provide an opportunity to hear from Dr. Kesslak, who will give an overview of Alzheon's lead oral molecule ALZ-801 (valiltramiprosate) program and its potential as a treatment for Alzheimer's pathology in adults with Down syndrome. The presentation will also review the anti-amyloid oligomer mechanism of action of ALZ-801 and 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 well-differentiated approach to both treatment and prevention of Alzheimer's disease and related disorders. ALZ-801, administered orally as a tablet, acts on the same pathway as anti-amyloid antibodies, but works upstream to prevent the formation of neurotoxic soluble amyloid oligomers without disrupting the insoluble plaque deposits, avoiding the vascular complications of ARIA-E seen with anti-amyloid antibodies," said Susan Abushakra, MD, Chief Medical Officer of Alzheon. "Now, the results of our Phase 2 biomarker interim readout with ALZ-801, paired with favorable safety in over 2,000 AD patients, support the expansion into additional indications associated with high burden of beta amyloid pathology due to genetic predisposition, including Down syndrome and familial Alzheimer's disease. With increased accumulation of amyloid from a young age in the brains of persons with Down syndrome, ALZ-801 has the potential to become an effective oral treatment for a patient population with no approved drugs and growing unmet medical need."

Alzheon's pioneering approach of inhibiting the formation of neurotoxic beta amyloid oligomers in the brain of Alzheimer's patients continues to show potential as a viable treatment in several related neurological disorders. Importantly, rather than slowing the cognitive decline of patients as seen in trials with other agents, subjects treated with ALZ-801 in Alzheon's Phase 2 open-label trial demonstrated significant cognitive gain from baseline status on memory tests, showing improvement over the course of treatment.

Combined with a favorable safety profile and no events of vasogenic edema, new biomarker data and promising effects on cognitive measures support the disease modifying effect of ALZ-801 in Alzheimer's patients, and 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. The latest scientific discoveries, and the favorable safety profile of ALZ-801, further support its development in additional indications where amyloid toxicity plays a role, such as Alzheimer's disease in individuals with Down syndrome, familial AD, cerebral amyloid angiopathy, and dry age-related macular degeneration.

"We are thrilled that the scientific understanding of Down syndrome and concomitant Alzheimer pathology has advanced to the point where we can conduct drug trials for either treatment or prevention of disease progression and resulting cognitive decline," said William Mobley, MD, PhD, Professor of Neuroscience at UCSD and Director of the Down Syndrome Center for Research and Treatment. "I am glad to be chairing Alzheon's Advisory Meeting focused on ALZ-801 tablet and its promising potential for these indications." Dr. Mobley is the current President of the T21 Research Society and member of Alzheon's Scientific Advisory Board.

Individuals with Down syndrome suffer from life-long overproduction of amyloid, due to triplication of the amyloid precursor protein gene on chromosome 21. As the average lifespan of persons with Down syndrome increases, so does the likelihood of AD dementia. As a result of the substantially increased production of beta amyloid in persons with Down syndrome, it is projected that approximately 80% will develop dementia in their lifetime. With a focus on development of disease modifying treatments for Alzheimer's disease, Alzheon's small molecule

platform is well suited to treat Alzheimer's pathology in individuals with Down syndrome and patients with other amyloid-related disorders.

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 devastating neurodegenerative disorders. 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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