Alzheon to Present ALZ-801 (Valiltramiprosate) Phase 3 Program Update and Industry-Leading Disease Modifying Effects from Phase 2 Trial in Patients with Early Alzheimer's Disease at AD/PD and NDDS Scientific Conferences

New Results Position ALZ-801 Tablet 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., March 8, 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 16th International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD conference) to be held on March 15-20, 2022 in Barcelona, Spain, and the 10th Annual Neurodegenerative Drug Development Summit (NDDS conference) to be held on March 28-30, 2022 in Boston, MA, USA.

Alzheon Founder, President & CEO, Dr. Martin Tolar will give a podium presentation at the AD/PD conference on Thursday, March 17, 2022, at 6:45 p.m. local time or 1:45 p.m. ET. This oral presentation will be included in the Scientific Symposium: *APOE Mechanisms and Treatment Strategies* and can be accessed through the conference virtual portal or directly onsite. At the NDDS conference, Dr. John Hey, Chief Scientific Officer of Alzheon and Alzheon CEO, Dr. Martin Tolar will give oral presentations on Tuesday, March 29, 2022, at 12:30 p.m. ET and 4:00 p.m. ET, respectively.

The AD/PD conference presentation: *Interim Results from Phase 2 Biomarker Study with Oral Anti-Amyloid Agent ALZ-801: Plasma Biomarkers in APOE4 Carriers with Early Alzheimer's Disease,* will provide an opportunity to hear from Dr. Tolar, discussing the strategy and path to New Drug Application (NDA) for the ALZ-801 (valiltramiprosate) program, as well as the 6-month interim analysis from Alzheon's 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 pioneered precision medicine in Alzheimer's disease by targeting neurotoxic amyloid oligomers, and now very promising biomarker data with ALZ-801 provide further support for this approach and superior efficacy of our oral tablet. The APOLLOE4 Phase 3 trial and Phase 2 biomarker study, will contribute important insights into the pathogenesis of Alzheimer's disease and offer a new treatment paradigm in Alzheimer's," 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 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, our 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 NDDS conference will include two presentations from Alzheon:

- *Fluid & Imaging Biomarkers in ALZ-801 Development: A First-in-Class Oral Disease Modifying Agent for Alzheimer's Disease:* Dr. Hey will describe the science behind biomarkers in Alzheimer's, their importance in diagnosis and monitoring of therapeutic efficacy, as well as baseline data in APOE4 populations and longitudinal effects on core biomarkers in patients receiving ALZ-801 oral tablet.
- *ALZ-801 Phase 3 Program: Lessons & the Path Forward in Developing Targeted Therapies for Alzheimer's Disease:* Dr. Tolar will discuss the precision medicine approach Alzheon pioneered in Alzheimer's, the novel mechanism of action of ALZ-801 (valiltramiprosate), as well as the development strategy and timeline to NDA of the Phase 3 program in AD.

"Alzheon has developed a well-differentiated approach to both treatment and prevention of Alzheimer's disease with the small molecule oral tablet, ALZ-801, which 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," said John Hey, PhD, Chief Scientific Officer of Alzheon. "Now, the analysis of our Phase 2 biomarker interim data with ALZ-801 supports the promise of our disease-modifying mechanism and favorable brain penetration of ALZ-801, extending other key discoveries made by Alzheon scientists over the last 8 years. ALZ-801 is, therefore, 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. Because ALZ-801 is an oral treatment that has been shown to fully block formation of neurotoxic

amyloid oligomers, it could be used as a monotherapy or as a long-term maintenance treatment in combination with, or following, a treatment with monoclonal antibodies, which remove toxic amyloid from the brain."

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 one dose of 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 constitute 65-70% of Alzheimer's patients. The study also includes evaluation of clinical efficacy, safety, and tolerability of ALZ-801 over 104 weeks of treatment and will evaluate the extended pharmacokinetic profile of ALZ-801 over 8 hours in 24 subjects after 65 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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