# Alzheon to Present at H.C. Wainwright Annual Global Investment Conference on September 13, 2021

*Alzheon CEO Dr. Martin Tolar Will Provide Overview of Company Business and Update on Oral Anti-Amyloid ALZ-801 Phase 3 Program in Alzheimer's Disease*

FRAMINGHAM, Mass., September 13, 2021 — 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 Martin Tolar, MD, PhD, company's Founder, President and Chief Executive Officer will present at the H.C. Wainwright Annual Global Investment Conference on September 13th. Presentation will be available live on-demand from 7:00 AM EST until the end of the conference on September 15th.

The virtual conference will provide an opportunity for investors to engage in one-on-one meetings with Dr. Tolar and the Alzheon team, and to hear about recent developments in Alzheon's research including the APOLLOE4 Phase 3 trial (NCT04770220) for oral anti-amyloid treatment ALZ-801 that started enrolling patients earlier this year, and the Phase 2 biomarker trial (NCT04693520) that recently completed enrollment. Dr. Tolar will also discuss upcoming data readouts and inflection points in Alzheon's product platform.

"Recent developments in Alzheimer's have transformed the perception of the disease as being unstoppable and provided a clear path to approval for drug candidates targeting toxic amyloid," said Dr. Tolar. "Alzheon is at the forefront of these advances with ALZ-801 tablet, which acts on the same pathway as infusions of anti-amyloid antibodies but works to prevent formation of toxic amyloid fragments upstream. ALZ-801 is, therefore, in a class of its own as a small-molecule oral drug that has shown potential for robust efficacy with a favorable safety profile, by avoiding the vascular complications of brain edema and microbleeds seen with the infusions of anti-amyloid antibodies. The ALZ-801 program will bring critical biomarker data readouts in 2022, and the rapidly advancing APOLLOE4 Phase 3 trial positions ALZ-801 to potentially become the first oral disease-modifying agent for patients and healthy people at risk for Alzheimer's disease."

Dr. Tolar's presentation will provide an overview of Alzheon's Phase 3 program with its lead oral drug candidate, ALZ-801, as well as the anti-amyloid drug platform, which prevents formation of neurotoxic soluble amyloid oligomers that drive onset and progression of AD and other neurodegenerative disorders. ALZ-801 is a small molecule drug blocking formation of neurotoxic

amyloid oligomers, and has shown potential for robust efficacy and favorable safety in the high-risk population of patients with two copies of the apolipoprotein ε4 allele (APOE4/4).

With endorsement and Phase 3 support from the National Institute of Aging in the form of a $47 million grant, Alzheon has advanced its oral drug ALZ-801 into Phase 3. Applying a precision medicine approach, APOLLOE4 Phase 3 will initially enroll the highest-risk AD patient group of APOE4/4 subjects and will incorporate the latest biomarkers to track patient benefits — phosphorylated tau in cerebrospinal fluid and blood, synaptic and inflammatory biomarkers, hippocampal volume and cortical thickness measures, and positron emission tomography of tau and neurofibrillary tangle pathology in a subset of enrolled subjects.

"The degree of amyloid oligomer selectivity appears to be the key factor that, together with pharmacokinetic properties, determines the magnitude of the benefit and risk profile for each anti-amyloid agent," said Dr. Tolar. "By incorporating the latest fluid and imaging biomarkers in our development program, we will generate robust data regarding efficacy and patient benefit throughout our studies. Combined with our genetics-based precision medicine approach to target individuals most likely to develop Alzheimer's, these biomarkers will maximize the likelihood of a successful Phase 3 trial to support a New Drug Application submission in 2024."

**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 is an optimized prodrug of tramiprosate that has shown promising results in analyses of Phase 3 clinical data,[7,9] and has a novel anti-amyloid oligomer mechanism of action.[5,8] ALZ-801 received Fast Track designation from the U.S. Food and Drug Administration in 2017. The clinical data for ALZ-801 and its active agent, tramiprosate indicate long-term clinical efficacy in AD patients with the APOE4 genotype and a favorable safety profile.[5–7,9] 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] The cognitive improvements observed in the tramiprosate Phase 3 studies may also be attributed in part to the therapeutic effects of 3-sulfopropanoic acid (3-SPA), an endogenous anti-oligomer substance found in the human brain discovered by Alzheon scientists that, like tramiprosate, inhibits formation of toxic amyloid oligomers.[5] 3-SPA is the primary metabolite of ALZ-801 and its discovery helps explain the beneficial pharmaceutical attributes of ALZ-801, including favorable safety profile, high selectivity for amyloid, and excellent brain penetration.[3,5,6] ALZ-801 treatment increases levels of 3-SPA in the brain and augments the body's natural mechanism to inhibit formation of toxic amyloid oligomers.[5,6] 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.[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 prodrug of tramiprosate that fully blocks formation of neurotoxic soluble amyloid oligomers in the brain. ALZ-801 is an easy-to-take tablet that builds on the safety and efficacy profile of its active compound tramiprosate, which has been evaluated in clinical trials involving over 2,000 Alzheimer's patients. 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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