Alzheon Announces Closing of Oversubscribed $50 Million Series D Financing Round to Accelerate Completion of APOLLOE4 Phase 3 Trial and Expansion of Product Portfolio

Proceeds Will Accelerate Both Completion of APOLLOE4 Phase 3 Study Evaluating Oral Tablet ALZ-801 (Valiltramiprosate) and Regulatory Filings for Patients with Early Alzheimer's Disease

Initiation of Clinical Studies with ALZ-801 to Treat Additional Alzheimer's Populations as well as Healthy Individuals at Risk for the Disease

Expansion and Advancement of Product Platform of Highly Brain-Penetrant Small Molecules for Neurodegenerative Disorders

FRAMINGHAM, Mass., April 14, 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 has completed an oversubscribed $50 million Series D round from private and institutional investors.

"The recent announcement of industry-leading disease modifying effects from our Phase 2 biomarker trial of oral ALZ-801 in Alzheimer's patients provided validation of Alzheon's pioneering precision medicine approach in blocking formation of amyloid oligomers and attracted enthusiastic investor support," said Martin Tolar, MD, PhD, Alzheon Founder, President, and Chief Executive Officer. "Alzheon has developed a well-differentiated solution to both treatment and prevention of Alzheimer's disease with a broad platform of small molecules, which act on the same pathway as anti-amyloid antibodies but work upstream to prevent the formation of neurotoxic soluble amyloid oligomers, without disrupting the insoluble plaque deposits – which may account for brain swelling and microbleeds. Series D financing and recent validating data will accelerate development of ALZ-801 to potentially become the first oral agent that can slow or even stop and prevent Alzheimer's pathology in all 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).

Recently announced positive results from Alzheon's Phase 2 study demonstrated leading biomarker and clinical efficacy data with ALZ-801, which support Alzheon's approach to inhibiting formation of amyloid oligomers and the superior efficacy of ALZ-801. 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. 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.

"Alzheon has experienced tremendous progress in the past 12 months, during which we launched the APOLLOE4 Phase 3 study, completed robust data readouts from the Phase 2 biomarker study, and initiated a collaboration to commercialize a diagnostic that can measure the toxic forms of amyloid in human brain," said Ken Mace, Chief Financial Officer of Alzheon. "These successes attracted prominent investors to Alzheon, and now the funding from our Series D round, combined with the prestigious grant awarded by the National Institute on Aging, gives us a strong financial position to rapidly complete both these critical trials leading to NDA submission for oral ALZ-801, as well as the further expansion of our unique product platform."

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, 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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