Alzheon to Present Multiple Clinical, Neuroimaging and Modeling Results for Oral Valiltramiprosate/ALZ-801 from Phase 2 and 3 Studies at CTAD Conference in San Diego, December 1–4, 2025

Valiltramiprosate Demonstrates Potential as the First Oral Disease-Modifying Agent to Slow Alzheimer's Pathology, Indicated by Both Clinical and Volumetric MRI Data

Nine Posters Showcase Consistent Benefits of Oral Valiltramiprosate in Carriers Across Clinical Outcomes and Brain Integrity Measures

Valiltramiprosate Designed to Inhibit Amyloid Aggregation via Distinct Upstream Mode of Action to Slow Progression of Alzheimer's Disease

Precision Medicine Approach Supported by Valiltramiprosate's Favorable Safety in High-Risk APOE4 Carriers

FRAMINGHAM, Mass., November 19, 2025 — Alzheon, Inc., a clinical-stage biopharmaceutical company advancing innovative therapeutics and diagnostics for patients with Alzheimer's disease (AD), today announced it will present new efficacy and safety data from the Phase 2 study long term extension over 3 years, and quantitative systems pharmacology (QSP) analyses for its lead investigational therapy, valiltramiprosate/ALZ-801, during the 18th Clinical Trials on Alzheimer's Disease (CTAD) conference in San Diego, California.

Valiltramiprosate is an investigational oral therapeutic agent in Phase 3 trials that works upstream of anti-amyloid antibodies by preventing neurotoxic amyloid oligomer formation. As a prodrug of tramiprosate with improved pharmacokinetics and brain penetration, it targets early amyloid aggregation, which is key in Alzheimer's disease progression. Valiltramiprosate aims to preserve cerebral structure and function in individuals with early-stage Alzheimer's disease, with a particular emphasis on APOE4/4 homozygotes, who represent the highest genetic risk group and experience rapid disease progression with limited available treatment options.

"Positive clinical and structural brain outcomes from the APOLLOE4 Phase 3 program continue to strengthen the case for valiltramiprosate as a potential breakthrough oral treatment for the high-risk APOE4 population," said David Watson, PhD, Founder & Principal Investigator, Alzheimer's & Research Treatment Center. "Therapies that safely reduce the formation of toxic amyloid oligomers at the start of the disease process have the potential to shift how and when we treat Alzheimer's disease. ALZ-801 has shown that promise in clinical trials."

Quantitative Systems Pharmacology (QSP) analyses of long term valiltramiprosate clinical data to be presented at CTAD, predict preservation of hippocampal volume and broad reduction in neurodegeneration, consistent with meaningful slowing of clinical decline in early symptomatic AD. Studies show that valiltramiprosate binds monomeric beta amyloid, blocking the creation of harmful oligomers associated with synaptic toxicity and neuron loss. QSP analysis links reduced toxic oligomer formation to greater preservation of hippocampal volume, less neurodegeneration, and slower disease progression, especially in APOE4/4 individuals who have higher levels of neurotoxic amyloid. Favorable long-term safety results over 3 years with no ARIA events continue to differentiate valiltramiprosate from other potential treatment options.

"These new findings support our upstream approach in altering the course of Alzheimer's disease and highlight valiltramiprosate's potential as a safe, effective oral therapy for APOE4 patients," said John Hey, PhD, Alzheon Chief Scientific Officer. "Consistent clinical, imaging, and molecular modeling data provide a solid basis for regulatory discussions and precision medicine development of our lead product."

Details of Presentations at CTAD
Monday 3:00 p.m. – Tuesday 5:30 p.m.
Poster: *Effects of Oral Valiltramiprosate on Clinical Efficacy, Safety and Brain Volume Outcomes in APOE4/4 Homozygotes with Early AD: Topline Results of APOLLOE4 Randomized, Placebo-Controlled 78-Week Multi-Center Trial*

- **Presenter:** Dr. Susan Abushakra, Chief Medical Officer, Alzheon, Inc.
- **Poster #P-054**

Poster: *Clinical Stabilization in APOE4 Carriers with MCI over 3 Years Correlates with Reduced Hippocampal Atrophy in a Phase 2 Long-Term Extension Study with Oral Valiltramiprosate*

- **Presenter:** Dr. John Hey, Chief Scientific Officer, Alzheon, Inc.
- **Poster #P-056**

Poster: *Correlations of Valiltramiprosate Effects on Hippocampal Volume and Cortical Thickness with Clinical Outcomes in APOE4/4 Subjects with MCI: Prespecified Analysis from the 78-Week APOLLOE4 Phase 3 Trial*

- **Presenter:** Dr. Aidan Power, Chief Development Officer, Alzheon, Inc.
- **Poster #P-058**

Poster*: Effects of the Oral Anti-Amyloid Agent Valiltramiprosate on Measures of Microstructural Integrity: Diffusion MRI Results of the Phase 3 APOLLOE4 Trial in APOE4/4 Homozygotes with Early AD*

- **Presenter:** Dr. Earvin Liang, VP of Clinical Development, Alzheon, Inc.
- **Poster #P-060**

Poster*: The Safety and ARIA Effects of the Oral Anti-Amyloid Agent Valiltramiprosate from the Phase 3 APOLLOE4 Trial in APOE4/4 Homozygotes with Early AD*

- **Presenter:** Dr. David Watson, CEO, Alzheimer's Research & Treatment Center
- **Poster #P-086**

Poster*: Biomarker Positive APOE4 Carriers with MCI Show Stability on MMSE Over 208-weeks of Treatment with Oral Valiltramiprosate in a Phase 2 Multi-Center-Single-Arm Trial*

- **Presenter:** Dr. Patrick Kesslak, Senior Research Fellow, Alzheon, Inc.
- **Poster #P-085**

Wednesday 7:15 a.m. – 5:30 p.m.

Poster: *Valiltramiprosate/ ALZ-801 Inhibits Amyloid Oligomer Formation: Quantitative Systems Pharmacology Analysis of A-Beta Aggregation Dynamics & Impact on AD Progression*

- **Presenter:** Dr. John Hey, Chief Scientific Officer, Alzheon, Inc.
- **Poster #P-272**

Poster: *Valiltramiprosate Prevents Hippocampal Atrophy & Clinical Decline in An Early Symptomatic APOE4/4 AD Subpopulation in Phase 3 Study via Potential Neurogenesis/ Neuroplasticity Action*

- **Presenter:** Dr. Jeremy Yu, Senior Research Fellow, Alzheon, Inc.
- **Poster #P-277**

Poster: *Quantitative System Pharmacology Analysis of Oral Valiltramiprosate Natural Trajectory of Alzheimer's Disease Progression by APOE4 Genotype: Contribution of Anti-Amyloid Oligomer & APOE4 Corrector Modes of Action*

- **Presenter:** Jean Schaefer, VP of CMC & Project Management, Alzheon, Inc.
- **Poster #P-296**

About ALZ-801

Valiltramiprosate/ALZ-801 is an investigational oral agent currently in Phase 3 development as a potential first-in-class, disease-modifying treatment for Alzheimer's disease.[2-6,8,11] Valiltramiprosate is designed to inhibit the formation of neurotoxic soluble beta amyloid oligomers that contribute to cognitive decline in individuals with AD.[2-6,8,13] Preclinical mechanism-of-action studies have demonstrated that ALZ-801 can completely block the formation of these neurotoxic oligomers at the dosage used in Phase 3 clinical trials.[2,8,11,13] Valiltramiprosate employs an enveloping molecular mechanism of action intended to prevent the aggregation of soluble amyloid oligomers in the human brain, [13] which are associated with the onset and progression of

cognitive impairment in AD patients.[2,3,6,8,9] In recognition of its therapeutic promise, valiltramiprosate received Fast Track designation from the U.S. Food and Drug Administration in 2017 for the treatment of Alzheimer's disease.

Clinical trial data indicate that valiltramiprosate exhibits strong clinical efficacy at the MCI stage, and a favorable safety profile, with no observed increase in the risk of brain vasogenic edema.[4-9,12,14] The initial Phase 3 program for valiltramiprosate targets Early AD patients who are homozygous for the apolipoprotein ε4 allele (APOE4/4), with plans to expand future research to include AD treatment and prevention in individuals carrying one copy of the APOE4 gene.[2–9]

Valiltramiprosate APOLLOE4 Phase 3 Trial

An Efficacy and Safety Study of Valiltramiprosate in APOE4/4 Early Alzheimer's Disease Subjects (NCT04770220): This trial was designed to evaluate the efficacy, safety, biomarker and imaging effects of 265 mg twice daily oral dose of valiltramiprosate in Early AD subjects with two copies of the apolipoprotein ε4 allele (APOE4/4 homozygotes), who constitute approximately 15% of Alzheimer's patients. This double-blind, randomized trial compared oral valiltramiprosate to placebo treatment over 78 weeks. The APOLLOE4 trial was supported by a grant from the National Institute on Aging to Alzheon, with Susan Abushakra as the principal investigator.

Valiltramiprosate APOLLOE4 Long Term Extension Trial (Phase 3 LTE)

An ongoing long-term extension of the trial, APOLLOE4-LTE, evaluates valiltramiprosate in subjects who complete the core APOLLOE4 study for an additional 104 weeks of treatment for a total of 182 weeks or 3.5 years over the core and LTE study. This LTE study is currently ongoing in the US, UK, and Canada (NCT06304883).

Valiltramiprosate Phase 2 Biomarker Trial

Biomarker Effects of Valiltramiprosate in APOE4 Carriers with Early Alzheimer's Disease (NCT04693520): This trial was designed to evaluate the effects of 265 mg twice daily oral dose of valiltramiprosate on biomarkers of AD pathology in subjects with Early AD, who have either the APOE4/4 or APOE3/4 genotype and constitute 65-70% of Alzheimer's patients. The primary outcome was the change from baseline in plasma p-tau$_{181}$. The trial also included evaluation of clinical efficacy, safety, tolerability, and pharmacokinetic profile of valiltramiprosate over 104 weeks of treatment. A completed long-term extension of the trial evaluated the same dose of valiltramiprosate for an additional 104 weeks of treatment for a total of 208 weeks.[2,6,7]

About Alzheon

Alzheon, Inc. is a clinical-stage biopharmaceutical company dedicated to advancing a diverse portfolio of product candidates and diagnostic assays for individuals affected by Alzheimer's disease and other neurodegenerative disorders. The company is focused on innovating therapeutic solutions that directly target the underlying pathology of neurodegeneration. Its lead Alzheimer's clinical candidate, valiltramiprosate/ALZ-801, is a first-in-class oral agent currently in Phase 3 clinical development as a potentially disease-modifying treatment for Alzheimer's disease. Valiltramiprosate is an orally administered small molecule shown in preclinical studies to completely inhibit the formation of neurotoxic soluble amyloid oligomers. Leveraging clinical

expertise and a robust technology platform, Alzheon pursues drug discovery and development using a precision medicine approach that incorporates individual genetic and biomarker profiles, aiming to advance therapies with meaningful benefits for patients.

Alzheon Scientific Publications

[1]Abushakra S, et al: *Clinical Efficacy, Safety and Imaging Effects of Oral Valiltramiprosate in APOEε4/ε4 Homozygotes with Early Alzheimer's Disease: Results of the Phase III, Randomized, Double-Blind, Placebo-Controlled, 78-Week APOLLOE4 Trial*, **Drugs** 2025.

[2]Pearson D, et al: *Polymorph Analysis of ALZ-801 (Valiltramiprosate), a Valine-Conjugated Oral Prodrug of Tramiprosate in Late-Stage Clinical Development for Alzheimer's Disease,* Journal of **Chemical Crystallography** 2025.

[3]Hey JA, et al: *Clinical Pharmacokinetics of Oral ALZ-801/Valiltramiprosate in a Two-Year Phase 2 Trial of APOE4 Carriers with Early Alzheimer's Disease,* **Clinical Pharmacokinetics** 2025.

[4]Aye S, et al: *Point of View: Challenges in Implementation of New Immunotherapies for Alzheimer's Disease,* **The Journal of Prevention of Alzheimer's Disease** 2025;12(1):100022.

[5]Abushakra S, et al: *APOLLOE4 Phase 3 Study of Oral ALZ-801/Valiltramiprosate in APOE ε4/ε4 Homozygotes with Early Alzheimer's Disease: Trial Design and Baseline Characteristics,* **Alzheimer's & Dementia** 2024; 10(3): e12498.

[6]Tolar M, et al: *The Single Toxin Origin of Alzheimer's Disease and Other Neurodegenerative Disorders Enables Targeted Approach to Treatment and Prevention,* **International Journal of Molecular Sciences** 2024; 25(5), 2727.

[7]Hey JA, et al: *Analysis of Cerebrospinal Fluid, Plasma β Amyloid Biomarkers, and Cognition from a 2-Year Phase 2 Trial Evaluating Oral ALZ-801/Valiltramiprosate in APOE4 Carriers with Early Alzheimer's Disease Using Quantitative Systems Pharmacology Model,* **Drugs** 2024; 84(7), 825-839.

[8]Hey JA, et al: *Effects of Oral ALZ-801/Valiltramiprosate on Plasma Biomarkers, Brain Hippocampal Volume, and Cognition: Results of 2-Year Single Arm, Open Label, Phase 2 Trial in APOE4 Carriers with Early Alzheimer's Disease,* **Drugs** 2024; 84(7), 811-823.

[9]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(12), 6355.

[10]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(1): e12117.

[11]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(1): 95.

[12]Tolar M, et al: *The Path Forward in Alzheimer's Disease Therapeutics: Reevaluating the Amyloid Cascade Hypothesis*, **Alzheimer's & Dementia** 2020; 16(11):1553-1560.

[13]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.

[14]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.
[15]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.
[16]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.
[17]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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