Alzheon to Present New Evidence of Neurovascular Protection and Preserved Brain Microstructure from Oral Valiltramiprosate Trials in APOE4/4 Alzheimer's Patients at AAIC 2026 Conference in London

Phase 3 and Phase 2 Studies in APOE4/4 Alzheimer's Patients Show Favorable Safety, Low Risk for Brain Bleed and Edema (ARIA), and Neurovascular Protection

Long-Term Phase 3 and Phase 2 Extension Data Support Precision Medicine Approach in High-Risk APOE4/4 Patients with Mild Cognitive Impairment (MCI)

Nine Posters Highlight New DTI, Volumetric MRI, and Plasma p-tau217 Findings Supporting Sustained Clinical and Brain Atrophy Benefits in MCI Patients

Valiltramiprosate Could Become First Oral Therapy to Slow Alzheimer's Pathology

FRAMINGHAM, Mass., July 6, 2026 — Alzheon, Inc., a clinical-stage biopharmaceutical company developing investigational therapies and diagnostic assays for Alzheimer's disease (AD) and other neurodegenerative disorders, today announced that it will present nine posters on its lead investigational therapy, valiltramiprosate/ALZ-801, at the 2026 Alzheimer's Association International Conference (AAIC) in London, United Kingdom. The presentations will feature expanded analyses from the Phase 3 APOLLOE4 and Phase 2 biomarker trials and their long-term extensions, including new evidence of neurovascular protection; diffusion tensor imaging (DTI) and volumetric MRI (vMRI) correlations with clinical outcomes; sustained long-term efficacy and safety; and a quantitative systems pharmacology (QSP) analysis evaluating valiltramiprosate as a potential oral maintenance therapy for AD following plaque clearance with anti-amyloid antibody treatments.

"Our AAIC presentations reflect more than a decade of disciplined execution in addressing one of the most urgent global unmet needs: Alzheimer's disease in APOE4/4 patients, who carry the greatest genetic risk and are most vulnerable to complications from anti-amyloid antibodies," said Martin Tolar, MD, PhD, Founder, President and CEO of Alzheon. "Across nine presentations covering Phase 3 efficacy and safety, imaging and plasma biomarkers, long-term safety, and a new analysis of valiltramiprosate as a potential oral maintenance therapy after anti-amyloid antibody treatment, we are positioning valiltramiprosate as a foundational oral therapy and strengthening

Alzheon's precision medicine platform. If approved, we are committed to making valiltramiprosate available to the patients who need it most, and to potentially extending its benefits to broader APOE4 populations in the years ahead."

Valiltramiprosate/ALZ-801 is an investigational oral agent in Phase 3 development as a potential first-in-class, disease-modifying treatment for Alzheimer's disease. It acts upstream of anti-amyloid antibodies by inhibiting the formation of neurotoxic soluble amyloid oligomers. The Phase 3 program targets patients with MCI who are homozygous for the apolipoprotein ε4 allele (APOE4/4), a group that represents approximately 15% of all Alzheimer's patients. Because APOE4/4 AD patients have a high prevalence of cerebral amyloid angiopathy (CAA), they are particularly vulnerable to brain edema and microhemorrhage complications associated with anti-amyloid antibody therapies, known as amyloid-related imaging abnormalities (ARIA). The AAIC presentations will report neurovascular and ARIA outcomes from the placebo-controlled APOLLOE4 trial. These findings in APOE4/4 patients may also have implications for treating CAA patients and adults with Down syndrome, who similarly have a high prevalence of underlying CAA.

The presentations will also include diffusion tensor imaging and volumetric MRI analyses of hippocampal microstructure; plasma p-tau217 findings; biomarker correlations with imaging and clinical endpoints; sustained efficacy and safety data from long-term extension studies of up to four years; and a quantitative systems pharmacology (QSP) evaluation of valiltramiprosate as a potential oral maintenance therapy following donanemab or lecanemab treatment.

"Although the Phase 3 trial did not meet its primary endpoint, we believe the new Phase 3 and long-term extension analyses being presented at AAIC reinforce valiltramiprosate's differentiated profile as one of the few oral anti-amyloid agents with the potential to slow disease progression while preserving vascular integrity in APOE4/4 Alzheimer's patients," said Susan Abushakra, MD, Chief Medical Officer of Alzheon. "The expanded Phase 3 analyses showed consistent neurovascular protection, including lower ARIA rates in the overall population versus placebo, together with clinically meaningful benefits on cognition and brain volume in the pre-specified MCI subgroup from the Phase 3 and Phase 2 long-term extension studies. New diffusion tensor imaging analyses further demonstrated preservation of hippocampal microstructure and correlations with clinical and brain volume outcomes. We believe these structural effects, together with a significant reduction in plasma p-tau217 in the overall population, support the disease-modifying potential of valiltramiprosate. Importantly, long-term extension findings in APOE4/4 and APOE3/4 carriers continue to show a favorable safety profile, with no symptomatic ARIA-E or ARIA-H observed through up to four years of treatment."

Details of Presentations at AAIC 2026 Conference

Sunday, July 12, 2026
Time: 7:30AM – 4:15PM GMT

Poster: *Significant Positive Correlations Between Microstructure and Efficacy/Brain Atrophy of Oral Valiltramiprosate in APOE4/4 MCI Subjects*

- **Presenter:** Earvin Liang, PhD, Vice President of Clinical Development, Alzheon, Inc.

Poster: *Valiltramiprosate on Plasma p-Tau217, p-Tau217/Ab42, vMRI and Clinical Correlations in Phase 3 APOE4/4 Early AD Subjects*

- **Presenter:** John A. Hey, PhD, Chief Scientific Officer, Alzheon, Inc.

Monday, July 13, 2026
Time: 7:30AM – 4:15PM GMT

Poster: *Valiltramiprosate Reduced ARIA Rates in APOE4/4 with Early AD: Results of Phase 3 APOLLOE4 Trial and CAA Implications*

- **Presenter:** Earvin Liang, PhD, Vice President of Clinical Development, Alzheon, Inc.

Poster: *Valiltramiprosate Improves Hippocampal Microstructure and Clinical Outcomes in APOE4/4: Phase 3 DTI and vMRI in Early AD*

- **Presenter:** Jeremy Yu, MD, PhD, Senior Research Fellow, Alzheon, Inc.

Poster: *Oral Valiltramiprosate Shows Sustained CDR-SB Benefit Over 2.5 Years in APOE4/4 MCI Subjects: APOLLOE4 Phase 3 Long-term Extension Results*

- **Presenter:** Susan Abushakra, MD, Chief Medical Officer, Alzheon, Inc.

Tuesday, July 14, 2026
Time: 7:30AM – 4:15PM GMT

Poster: *Safety of Oral ALZ-801 in APOE4/4 and APOE3/4 Subjects with Early AD in Long-term Extension Studies up to 4 Years*

- **Presenter:** Aidan Power, MB, BCh, MRCPsych, Chief Development Officer, Alzheon, Inc.

Poster: *Valiltramiprosate in Biomarker-positive APOE4/4 MCI Subjects Shows Clinical Stability and Slows Atrophy Over 4-years*

- **Presenter:** Patrick Kesslak, PhD, Senior Research Fellow, Alzheon, Inc.

Poster: *Valiltramiprosate Effects on Cerebellar Volume in APOE4/4 Early Alzheimer's Disease Subjects from Phase 3 APOLLOE4 Study*

- **Presenter:** Susan Abushakra, MD, Chief Medical Officer, Alzheon, Inc.

Wednesday, July 15, 2026
Time: 7:30AM – 4:15PM GMT

Poster: *Oral Valiltramiprosate Maintenance Therapy After Donanemab and Lecanemab Treatment: QSP Analysis of Amyloid Aggregation by APOE Genotype*

- **Presenter:** Jean F. Schaefer, Vice President of CMC & Project Management, Alzheon, Inc.

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.[3-7,9,12] Valiltramiprosate is designed to inhibit the formation of neurotoxic soluble beta amyloid oligomers that contribute to cognitive decline in individuals with AD.[4-8,10,15] 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.[3,9,12,14] Valiltramiprosate employs an enveloping molecular mechanism of action intended to prevent the aggregation of soluble amyloid oligomers in the human brain, [14] which are associated with the onset and progression of cognitive impairment in AD patients.[3,4,7,9,10] 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 suggest 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. [1-10,13,15] 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.[3–10]

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)

A long-term extension of the trial, APOLLOE4-LTE, evaluated 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 ended in January 2026 (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.[3,7,8]

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. Its well-differentiated follow-on candidate, ALZ-507, is a once daily oral therapy designed to inhibit the formation of amyloid oligomers while also correcting the high risk APOE4 gene. 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: *Hippocampal Atrophy on Magnetic Resonance Imaging as a Surrogate Marker for Clinical Benefit and Neurodegeneration in Early Symptomatic Alzheimer's Disease: Synthesis of Evidence from Observational and Interventional Trials,* **CNS Drugs** 2026; 40(2): 199-214.

[2]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; 85(11): 1455-1472.

[3]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; 55, 206-215.

[4]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; 64(3): 407-424.

[5]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.

[6]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.

[7]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.

[8]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.

[9]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.

[10]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.
[11]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.
[12]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.
[13]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.
[14]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.
[15]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.
[16]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.
[17]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.
[18]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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