



Alzheon to Present Evidence of Neurovascular Protection from Trials with Oral Valiltramiprosate in APOE4/4 Alzheimer’s Patients Leading to Reduced Brain Edema and Microhemorrhage Risk at 2026 American Academy of Neurology Meeting in Chicago, Illinois

Valiltramiprosate Shows Favorable Safety Outcomes with Low ARIA Risk and Evidence of Neurovascular Protection in APOE4/4 Alzheimer’s Patients

Precision Medicine Approach Supported by Phase 3 and Phase 2 Results in High-Risk APOE4/4 Patients with Mild Cognitive Impairment (MCI)

Presentations Highlight Consistent Effects of Valiltramiprosate on Clinical Outcomes, Brain Volume Preservation, and Long-Term Disease Stability in MCI

Valiltramiprosate Targets Toxic Amyloid Oligomers Upstream of Antibodies, Offering Potential Disease Modification Without Increased Risk of Vascular Injury

FRAMINGHAM, Mass., April 14, 2026 — [Alzheon, Inc.](#), a clinical-stage biopharmaceutical company developing investigational therapies for patients with Alzheimer’s disease (AD) and related neurodegenerative disorders, today announced it will present new clinical, safety, imaging, and biomarker findings, as well as brain edema (ARIA-E) and brain microhemorrhage (ARIA-H) for its lead investigational therapy, valiltramiprosate/ALZ-801, at the American Academy of Neurology (AAN) Annual Meeting in Chicago, Illinois.

"Valiltramiprosate is currently the only remaining oral candidate with promise to improve patient outcomes in the foreseeable future. In our studies, valiltramiprosate demonstrates a distinct profile, as an oral anti-amyloid therapy with potential to slow disease progression while maintaining vascular integrity in early-stage Alzheimer's patients APOE4/4 patients, who are particularly susceptible to brain edema and microhemorrhage complications associated with anti-amyloid antibodies," stated Susan Abushakra, MD, Chief Medical Officer at Alzheon. "The data presented at AAN will outline the reduced incidence and delayed onset of ARIA-H observed in the Phase 3 study involving 298 APOE4/4 AD subjects, alongside brain volume benefits that show significant correlations with clinical outcomes within the pre-specified MCI subgroup. These

findings, together with supportive results from the four-year Phase 2 study, showcase the potential of valiltramiprosate to provide clinically meaningful benefits without elevating ARIA risk and while decreasing microvascular injury."

In the Phase 3 study, valiltramiprosate showed favorable safety and neurovascular results over 78 weeks, with low and balanced ARIA-E incidence (3% in both treatment and placebo arms). Across all ARIA subtypes, the active arm showed consistent reductions in the incidence of new events. In the placebo arm, 29% of subjects had new ARIA-H or ARIA-E vs. 19% in active arm, a significant 35% reduction ($p=0.031$). In addition, there was a delay to onset of new ARIA-H or ARIA-E events in the active arm ($p<0.02$). Incidence of concurrent microhemorrhages and siderosis was reduced by 89% ($p=0.01$) and their onset was delayed by 41% ($p=0.02$) in the active arm. Across both Phase 3 and Phase 2 studies, all ARIA-E and ARIA-H events were asymptomatic.

"The consistency we are seeing between clinical outcomes and brain volume preservation is particularly compelling," said Marwan N. Sabbagh, MD, FAAN. "These correlations suggest that targeting amyloid oligomers upstream of amyloid antibodies may meaningfully impact the underlying biology of the disease and slow brain neurodegeneration. The favorable and differentiated safety results, especially the low ARIA-E risk in APOE4/4 patients with reduced incidence of ARIA-H, further supports valiltramiprosate as a promising and differentiated oral treatment for early-stage Alzheimer's disease."

These findings suggest that valiltramiprosate may provide protective effects on cerebral microvasculature through reduction of vascular amyloid burden and/or by inhibiting inflammatory responses. This is particularly relevant in APOE4/4 patients, who have high prevalence of cerebral amyloid angiopathy with exaggerated inflammatory responses, leading to heightened risk of ARIA. The observed neurovascular effects in the overall Phase 3 study population are also consistent with findings from diffusion tensor imaging, showing significant preservation of microstructural integrity in white matter tracts that connect the hippocampus to cortical areas including the default mode network, as well as significantly reduced ventricular expansion and whole brain atrophy.

Details of Presentations at AAN Annual Meeting

Oral Presentation:

Sunday, April 19, 2026

Session: New Perspectives on Alzheimer's Therapeutics

Safety and ARIA Analyses of Oral Anti-amyloid Oligomer Agent Valiltramiprosate in APOE4/4 Homozygotes with Early Alzheimer's Disease (AD): Results of the Phase 3 78-week APOLLOE4 Trial

- Presenter: Susan Abushakra, Chief Medical Officer, Alzheon, Inc.
- Lecture Time: 2:36 PM – 2:48 PM CDT

Poster Presentations:

Sunday, April 19, 2026

Time: 8:00 AM – 9:00 AM CDT

Effects of Oral Valiltramiprosate on Clinical Efficacy, Safety, and Brain Volume Outcomes in APOE4/4 Homozygotes with Early Alzheimer’s Disease (AD): Topline Results of the 78-week Phase 3 APOLLOE4 Trial

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

Monday, April 20, 2026

Time: 8:00 AM – 9:00 AM CDT

Biomarker-positive APOE4 Carriers with MCI Show Cognitive Stability over 4 Years of Oral Valiltramiprosate/ALZ-801 Treatment: MMSE Responder Analysis from the ALZ-801 Phase 2 Long-term Extension Study

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

Monday, April 20, 2026

Time: 5:00 PM – 6:00 PM CDT

Clinical Effects of Oral Valiltramiprosate Treatment in APOE4 Carriers with Mild Cognitive Impairment (MCI): Results of the Phase 2 Study Long-term Extension over 3 Years

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

Correlations between Clinical and Brain Volume Effects of Oral Valiltramiprosate in APOE4/4 Homozygotes with MCI: Pre-specified Analyses of the Phase-3 APOLLOE4 78-Week Trial

- Presenter: Marwan N. Sabbagh, MD, FAAN

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 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.^{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-tau₁₈₁. 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

- ¹Abushakra 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, 199-214.
- ²Abushakra S, et al: *Clinical Efficacy, Safety and Imaging Effects of Oral Valiltramiprosate in APOE ϵ 4/ ϵ 4 Homozygotes with Early Alzheimer's Disease: Results of the Phase III, Randomized, Double-Blind, Placebo-Controlled, 78-Week APOLLOE4 Trial*, **Drugs** 2025; 85, 1455-1472.
- ³Pearson 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.
- ⁴Hey 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, 407-424.
- ⁵Aye 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.
- ⁶Abushakra S, et al: *APOLLOE4 Phase 3 Study of Oral ALZ-801/Valiltramiprosate in APOE ϵ 4/ ϵ 4 Homozygotes with Early Alzheimer's Disease: Trial Design and Baseline Characteristics*, **Alzheimer's & Dementia** 2024; 10(3): e12498.
- ⁷Tolar 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.
- ⁸Hey 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.
- ⁹Hey 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.
- ¹⁰Tolar 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.
- ¹¹Abushakra S, et al: *APOE ϵ 4/ ϵ 4 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.
- ¹²Tolar 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.
- ¹³Tolar M, et al: *The Path Forward in Alzheimer's Disease Therapeutics: Reevaluating the Amyloid Cascade Hypothesis*, **Alzheimer's & Dementia** 2020; 16(11):1553-1560.
- ¹⁴Hey 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.

¹⁵Hey 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.

¹⁶Abushakra 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.

¹⁷Kocis P, et al: *Elucidating the A β 42 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.

¹⁸Abushakra 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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