



**Alzheon Announces Two New Scientific Papers Ahead of APOLLOE4 Phase 3 Trial  
Topline Symposium at ADPD Conference in Vienna on April 1<sup>st</sup>, Marking 15  
Pathbreaking Peer-Reviewed Publications from Alzheon**

*Topline of APOLLOE4 Phase 3 Evaluating Valiltramiprosate/ALZ-801 Will be  
Presented at Dedicated Symposium at ADPD Conference in Vienna on April 1<sup>st</sup>, 2025*

*Publication in Journal of Prevention of Alzheimer’s Disease Highlights Challenges  
of Immunotherapies, Calling on Stakeholders to Prepare for Emerging Treatments  
Including Valiltramiprosate*

*Publication in Clinical Pharmacokinetics Demonstrates Favorable Pharmacokinetic  
Properties of Valiltramiprosate, an Investigational Oral Disease-Modifying  
Therapy for Treatment of Early Alzheimer’s Disease*

*Valiltramiprosate Has Potential to Become the First Oral Agent to Slow Alzheimer’s  
Pathology in Patients*

FRAMINGHAM, Mass., February 25, 2025 — [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 the publication of two new peer-reviewed scientific papers focused on advancement of understanding of AD and need for new treatments.

Alzheon Founder, President, and CEO, Martin Tolar, MD, PhD, was invited to present at the 2024 Nobel Forum at the Karolinska Institute in Sweden, where top researchers and drug developers were brought together to discuss the challenges of implementing new immunotherapies for AD and the need for oral agents with improved safety, efficacy, and access. The symposium discussed appropriate patient selection, early patient identification, and practical application of new treatments. Following the symposium, a peer-reviewed paper, where Dr. Tolar was a co-author, was published in *The Journal of Prevention of Alzheimer’s Disease*. The article can be viewed at [Point of View: Challenges in Implementation of New Immunotherapies for Alzheimer's Disease](#).

“I was honored to present the valiltramiprosate/ALZ-801 program at the 2024 Nobel Forum symposium. Immunotherapies for Alzheimer’s disease have advanced our field. Valiltramiprosate was discussed as a promising therapy that could improve the standard of care in Alzheimer’s with its potential efficacy, safety, and ease of oral administration,” said Martin Tolar, MD, PhD, Founder, President, and CEO of Alzheon and co-author of the publication. “However, significant hurdles remain with currently available treatments, including appropriate patient identification, safety monitoring, access and cost effectiveness. Furthermore, due to safety concerns and restrictions, these disease-modifying therapies are not optimal for APOE4/4 homozygotes, the most vulnerable Alzheimer’s patient population. At Alzheon we strive to address these challenges with our investigational oral molecule, valiltramiprosate, which could become the first oral agent to slow Alzheimer’s pathology in patients.”

The second Alzheon manuscript, “Phase 2 clinical Pharmacokinetics of valiltramiprosate,” was published in the scientific journal *Clinical Pharmacokinetics*. The full text can be accessed at: <https://link.springer.com/article/10.1007/s40262-025-01482-8>. This publication summarizes the pharmacokinetic profile of valiltramiprosate in apolipoprotein E4 (APOE4) carrier subjects from a Phase 2 trial in early AD.

“Despite the progress in approved therapies for Alzheimer’s disease, there remains a major unmet need for disease-modifying treatments with improved safety, efficacy and access. The favorable pharmacokinetic profile and consistent tablet properties, combined with low inter-subject variability in APOE4 homozygous and heterozygous patients, devoid of interactions with sex, race, age, or body weight, support the continued development of oral valiltramiprosate as a potential next generation disease-modifying treatment for Alzheimer’s disease,” said John Hey, PhD, Chief Scientific Officer of Alzheon and lead author of the study.

“Alzheon has now published 15 peer-reviewed scientific papers on key discoveries in Alzheimer’s disease that defined the toxic agent, patient population, biomarkers and key genetic risks,” said Dr. Tolar. “Importantly, Alzheon continues to advance the pathbreaking valiltramiprosate program and its backups and define a new path for developing precision medicine therapies directed at the right patients, at the right stage of disease, and with the right biological target, leveraging a unique mechanism that enables oral delivery.”

Alzheon will present the topline results of the pivotal APOLLOE4 Phase 3 trial at a dedicated symposium titled “*Inhibition of Beta Amyloid Oligomer Neurotoxicity with Oral Valiltramiprosate in APOE ε4/ε4 Homozygotes with Early Alzheimer’s Disease: Results of APOLLOE4 Phase 3 Trial*” at 9:45 AM Central European Time (CET) on the opening day of the Alzheimer’s Disease and Parkinson’s Disease (ADPD) conference, a major scientific meeting focused on neurodegenerative disorders. Symposium presentations will be made by multiple experts including Phillip Scheltens MD, PhD, Murali Doraiswamy, MD, Anton Porsteinsson, MD, David Watson, PsyD, and others.

The APOLLOE4 study was a first-of-its-kind Phase 3 trial focusing on APOE4/4 homozygotes and included 325 patients in the early stages of AD. APOE4/4 homozygotes represent a high-risk

patient population as they are 8-12 times more likely to develop AD and more likely to progress quickly into severe stages of disease. Furthermore, the approved disease-modifying therapies for AD have a boxed warning for treating APOE4/4 homozygotes, as they are more likely to develop brain swelling and bleeding. Data from Alzheon's Phase 3 topline show promising clinical and biomarker effects for this population with a severe unmet medical need.

### **About ALZ-801**

[Valiltramiprosate/ALZ-801](#) is a potential first-in-class, investigational oral agent in [Phase 3 development](#) as a potentially disease-modifying treatment for AD.<sup>1-5,7,10</sup> Valiltramiprosate is designed to block the formation of neurotoxic soluble beta amyloid oligomers implicated in cognitive decline in Alzheimer's patients.<sup>1-5,7,12</sup> In mechanism of action studies, ALZ-801 has fully inhibited the formation of neurotoxic soluble beta amyloid oligomers at the Phase 3 clinical dose.<sup>1,7,10,12</sup> Valiltramiprosate acts through a novel [enveloping molecular mechanism of action](#) to block formation of neurotoxic soluble amyloid oligomers in the human brain<sup>12</sup> associated with the onset and progression of cognitive decline in AD patients.<sup>1,2,5,7,8</sup> Valiltramiprosate received Fast Track designation from the U.S. Food and Drug Administration in 2017 for Alzheimer's disease. In clinical trials, valiltramiprosate has shown potential for robust clinical efficacy and favorable safety results with no increased risk of brain vasogenic edema.<sup>3-8,11,13</sup> The initial [Phase 3 program for valiltramiprosate](#) is focusing on Early AD patients with two copies of the apolipoprotein ε4 allele (APOE4/4 homozygotes), with potential future program expansion to AD treatment and prevention in patients carrying one copy of the APOE4 gene and noncarriers.<sup>1-8</sup>

### **Valiltramiprosate APOLLOE4 Phase 3 Trial**

An Efficacy and Safety Study of Valiltramiprosate in APOE4/4 Early Alzheimer's Disease Subjects ([NCT04770220](#)): This trial is 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 is a double-blind, randomized trial comparing oral valiltramiprosate to placebo treatment over 78 weeks. The APOLLOE4 trial is supported by a \$51 million [grant from the National Institute on Aging](#) to Alzheon, with Susan Abushakra as the principal investigator.

### **Valiltramiprosate APOLLOE4 Long Term Extension Trial (LTE)**

An ongoing long-term extension of the trial, APOLLOE4-LTE evaluates valiltramiprosate in subjects who complete the core APOLLOE4 study for an additional 52 weeks of treatment for a total of 130 weeks or 2.5 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 trial also included evaluation of clinical efficacy, safety, tolerability, and pharmacokinetic profile of valiltramiprosate over 104 weeks of treatment (primary endpoint). An ongoing long-term

extension of the trial evaluates the same dose of valiltramiprosate for an additional 104 weeks of treatment for a total of 208 weeks.

### 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 neurodegeneration. Our lead Alzheimer's clinical candidate, valiltramiprosate/ALZ-801, is a first-in-class oral agent in Phase 3 development as a potentially disease-modifying treatment for AD. Valiltramiprosate is an oral small molecule that has been observed to fully block the formation of neurotoxic soluble amyloid oligomers in preclinical tests. 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

<sup>1</sup>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.

<sup>2</sup>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.

<sup>3</sup>Abushakra S, et al: *APOLLOE4 Phase 3 Study of Oral ALZ-801/Valiltramiprosate in APOE  $\epsilon$ 4/ $\epsilon$ 4 Homozygotes with Early Alzheimer's Disease: Trial Design and Baseline Characteristics*, **Alzheimer's & Dementia** 2024; 10(3): e12498.

<sup>4</sup>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.

<sup>5</sup>Hey JA, et al: *Analysis of Cerebrospinal Fluid, Plasma  $\beta$  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.

<sup>6</sup>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.

<sup>7</sup>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.

<sup>8</sup>Abushakra S, et al: *APOE  $\epsilon$ 4/ $\epsilon$ 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.

<sup>9</sup>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.

<sup>10</sup>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.

<sup>11</sup>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.

<sup>12</sup>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.

<sup>13</sup>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.

<sup>14</sup>Kocis P, et al: *Elucidating the A $\beta$ 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.

<sup>15</sup>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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