Alzheon Reports Plasma Biomarker Results from Phase 3 and 2 Studies of Valiltramiprosate/ALZ-801, Validating Its First-in-Class Mechanism of Action and Underscoring Benefits in Cognition, Function, and Brain Volume Protection in Alzheimer's Patients

Early and Consistent Decreases in P-tau$_{217}$ Plasma Levels Were Associated with Improvements in Cognition, Function, and Brain Atrophy Measures

MCI Subjects Receiving Valiltramiprosate Showed Significant Correlations Between Decreases in Plasma P-tau$_{217}$ and Improvements on ADAS-Cog (r = 0.28, p = 0.039), CDR-SB (r = 0.38, p = 0.005), and Hippocampal Volume (r = 0.35, p = 0.013)

High Rates of Alzheimer's Disease Positivity Were Confirmed Across Phase 3 and 2 Trials Using FDA-Approved P-tau$_{217}$/Aβ1-42 Biomarker Threshold

Results Validate Upstream Molecular Mechanism of Inhibiting Formation of Neurotoxic Soluble Amyloid Oligomers – A Key Driver of Alzheimer's Pathology

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

FRAMINGHAM, Mass., February 3, 2026 — Alzheon, Inc., a clinical-stage biopharmaceutical company developing a broad portfolio of investigational therapies and diagnostic assays for patients with Alzheimer's disease (AD) and other neurodegenerative disorders, today announced plasma biomarker analyses from its APOLLOE4 Phase 3 and Phase 2 clinical studies of valiltramiprosate/ALZ-801. New results offer robust evidence supporting the biological activity of valiltramiprosate's, its novel mechanism of action, and effects in therapeutic studies, while validating the Alzheimer's disease pathology in trial participants through FDA-approved plasma biomarker thresholds.

"Valiltramiprosate has emerged as the only late-stage oral treatment with a potential to materially change the Alzheimer's therapeutic landscape in the near future, and this data

completes the picture showing how valiltramiprosate's action leads to positive effects on cognition, daily function, and brain protection against atrophy," said Martin Tolar, Founder, President, and CEO of Alzheon. "In 2026, we will move forward with our plans for the next Phase 3 study based on analyses from the APOLLOE4 Phase 3 trial and its long-term extension. These efforts put us in a strong position as we focus on expanding the valiltramiprosate platform, developing new candidates, and investigating additional target groups."

Alzheon will continue to use these biomarker insights to advance the valiltramiprosate platform, improve patient selection, and guide clinical development for genetically defined and high-risk Alzheimer's disease groups.

"These findings underscore the usefulness of plasma biomarkers in connecting Alzheimer's disease pathology with clinically relevant outcomes," stated Robert Rissman, PhD, Professor of Physiology and Neurosciences at the University of Southern California. "The robust associations between decreases in plasma p-tau$_{217}$, benefits on cognition and function, and protection from brain atrophy, offer valuable insights into disease mechanisms and further justify the advancement of valiltramiprosate as a potential disease-modifying therapy."

Across both studies, the majority of participants satisfied criteria for AD positivity in accordance with the recently FDA-approved plasma p-tau$_{217}$/Aβ1-42 ratio. In the Phase 3 APOLLOE4 trial involving APOE4/4 homozygotes, 94% of enrolled subjects were confirmed as AD positive, and in the Phase 2 trial targeting APOE4 carriers that utilized CSF biomarkers as inclusion criteria, 97% of homozygote and 96% of heterozygote patients met the AD positivity threshold. These results demonstrate substantial enrichment for amyloid-driven disease across both clinical trials.

Biomarker analyses of Phase 3 and 2 studies examining the effects of valiltramiprosate revealed consistent and early decreases in plasma p-tau$_{217}$, which is a biomarker linked to beta amyloid and early tau pathology. In the Phase 3 trial, participants who received valiltramiprosate for 78 weeks showed reductions in p-tau$_{217}$ starting at 26 weeks that continued throughout the treatment period, with even greater benefits seen in patients at the Mild Cognitive Impairment (MCI) stage.

For those with MCI in the placebo group, p-tau$_{217}$ *increased* by about 17% from baseline over 78 weeks, while those given valiltramiprosate experienced a *decrease* in p-tau$_{217}$ of approximately 36%, translating to a 53% difference vs. placebo. Among the MCI group receiving valiltramiprosate, there were significant and meaningful relationships between decreases in plasma p-tau$_{217}$ and benefits on clinical outcomes ADAS-Cog ($r = 0.28$, $p = 0.039$), CDR-SB ($r = 0.38$, $p = 0.005$), as well as protection of hippocampal volume ($r = 0.35$, $p = 0.013$).

Baseline plasma p-tau$_{217}$ levels were strongly correlated with both clinical and neuroimaging outcomes throughout the Phase 3 study, providing further biological support for the discovery that valiltramiprosate benefits are tied to treatment at the appropriate disease stage. Within the Phase 3 MCI cohort, baseline p-tau$_{217}$ demonstrated significant and consistent associations in valiltramiprosate–treated participants with ADAS-Cog at baseline ($r = 0.31$, $p = 0.019$), CDR-SB (r

= 0.40, p = 0.002), hippocampal volume (r = -0.532, p <0.0001), and cortical thickness (r = -0.60, p <0.0001). Notably, significant correlations were also identified in the overall Phase 3 population, including both active and placebo arms.

"Our new biomarker results offer robust biological validation for valiltramiprosate's upstream molecular mechanism, designed to inhibit formation of neurotoxic soluble amyloid oligomers, which are considered pivotal drivers of Alzheimer's disease pathology," said John Hey, Chief Scientific Officer of Alzheon, Inc. "The consistent demonstration of Alzheimer's positivity, early and sustained reductions in p-tau$_{217}$, and strong correlations with cognitive, functional, and imaging outcomes highlight the importance of p-tau$_{217}$ as a marker for disease progression and treatment efficacy, particularly in patients at earlier stages of Alzheimer's disease."

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.[5-1-10,13,15] 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)

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.[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. 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

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[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.
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Media Contact
Yasemin Khakian, Alzheon, Inc.
508.808.2301
yasemin.khakian@alzheon.com

Investor Contact

Erwan de Naurois, Alzheon, Inc.
802.735.8789
erwan.denaurois@alzheon.com