Alzheon Announces that United States Federal Circuit Affirmed Decision of U.S. Patent Office Invalidating Risen (Suzhou) Pharmaceutical Technology Co., Ltd.'s Patent on Isotopically Enriched Forms of ALZ-801/Valiltramiprosate

U.S. Federal Circuit Affirmed Without Discussion Final Decision of U.S. Patent Office Invalidating Risen (Suzhou) Pharma Tech's U.S. Patent No. 10,472,323 on Isotopically Enriched Forms of ALZ-801

Fully Enrolled APOLLOE4 Phase 3 Pivotal Trial Evaluating ALZ-801 in Early Alzheimer's Patients on Track for Topline Data Readout and Potential NDA Submission in 2024

FRAMINGHAM, Mass., April 8, 2024 — 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 that the United States Court of Appeals for the Federal Circuit affirmed the U.S. Patent Office decision invalidating Risen (Suzhou) Pharmaceutical Technology Co., Ltd.'s patent on isotopically enriched forms of ALZ-801/valiltramiprosate. The decision was affirmed without discussion by the Federal Circuit Court (Case No. 22-2232).

In 2020, Alzheon petitioned the Patent Trial and Appeal Board (PTAB) of the U.S. Patent Office (USPTO) to institute an Inter-Parties Review (IPR) of Risen's U.S. Patent No. 10,472,323 (IPR2021-00347). This patent claimed deuterated and other isotopic derivatives of Alzheon's Alzheimer's disease investigational drug candidate, ALZ-801/valiltramiprosate, along with other isotopically enriched prodrugs of tramiprosate. Alzheon's IPR petition was granted and ultimately resulted in the PTAB's July 12, 2022 Final Written Decision finding that all claims in the '323 patent were unpatentable.

In 2022, following the PTAB's unanimous decision against the Risen patent, Risen petitioned the PTAB to institute invalidation proceedings against two of Alzheon's granted U.S. patents relating to ALZ-801/valiltramiprosate (IPR2022-01200 and PGR2022-0051). The PTAB denied both of Risen's petitions in January 2023. That decision was not appealed by Risen.

Risen appealed the PTAB's decision to the United States Court of Appeals for the Federal Circuit. On March 7, 2024, the Federal Circuit heard oral arguments in the case, and on March 11, 2024, it issued a Rule 36 judgment in favor of Alzheon, affirming the PTAB's decision without comment.

"Alzheon is pleased that the U.S. Federal Circuit affirmed the Patent Trial and Appeal Board's decision to invalidate all claims of Risen's patent. Alzheon will continue to vigorously defend our ALZ-801/valiltramiprosate franchise from parties seeking to copy or design around our asset," stated John Hey, PhD, Chief Scientific Officer of Alzheon, Inc. "In addition, the Patent Office's denial of Risen's attempts to attack our granted patents further reinforces the validity and strength of our patent protection for the investigational drug candidate ALZ-801. Topline data from pivotal APOLLOE4 Phase 3 trial evaluating ALZ-801 will set the stage for the potential NDA submission this year and commercial launch in 2025."

About ALZ-801

ALZ-801/valiltramiprosate is a potential first-in-class, investigational oral disease-modifying therapy in Phase 3 development for the treatment of early Alzheimer's disease. In mechanism-of-action studies, ALZ-801 fully blocked the formation of neurotoxic soluble beta amyloid (Aβ) oligomers at the Phase 3 clinical dose. ALZ-801 has shown potential for robust clinical efficacy in the highest-risk AD population – patients with two copies of the apolipoprotein ε4 allele (APOE4/4 homozygotes), and favorable safety with no increased risk of brain vasogenic edema. This population is the focus of Alzheon's pivotal Phase 3 APOLLOE4 trial, which is now fully enrolled and will be completed in mid-2024.

ALZ-801 Phase 2 Biomarker Trial

Biomarker Effects of ALZ-801 in APOE4 Carriers With Early Alzheimer's Disease (NCT04693520): This ongoing trial was designed to evaluate the effects of 265 mg twice daily oral dose of ALZ-801 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 ALZ-801 over 104 weeks of treatment. An ongoing long-term extension of the trial evaluates ALZ-801 for an additional 52 weeks of treatment for a total of 156 weeks.

ALZ-801 APOLLOE4 Phase 3 Trial

An Efficacy and Safety Study of ALZ-801 in APOE4/4 Early Alzheimer's Disease Subjects (NCT04770220): This ongoing trial is designed to evaluate the efficacy, safety, biomarker and imaging effects of 265 mg twice daily oral dose of ALZ-801 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 ALZ-801 to placebo treatment over 78 weeks. The APOLLOE4 trial is supported by a $51 million grant from the National Institute on Aging.

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, ALZ-801/valiltramiprosate, is a first-in-class oral agent in Phase 3 development as a potentially disease modifying treatment for AD. ALZ-801 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

[1] 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, 2727.

[2] 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, 6355.

[3] 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: Translational Research & Clinical Interventions**, 2020; 6: e12117.

[4] 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: 95.

[5] Tolar M, et al: *The Path Forward in Alzheimer's Disease Therapeutics: Reevaluating the Amyloid Cascade Hypothesis*, **Alzheimer's & Dementia**, 2019; 1-8.

[6] 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.

[7] 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.

[8] 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.

[9] 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.

[10] 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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