

Alzheon nabs \$100M in series E to advance oral Alzheimer's drug

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Alzheon Inc. has raised \$100 million in a series E financing round to push its oral drug candidate for early Alzheimer's disease (AD), [ALZ-801 \(valiltramiprosate\)](#), through a late-stage, APOLLOE4 study.

On the brink of a data readout in the third quarter of 2024, Framingham, Mass.-based Alzheon is approaching regulatory filings in the U.S. this year, Martin Tolar, founder, president and CEO of Alzheon, recently told *BioWorld*.

"We are at the dawn of a [new era of Alzheimer's treatment](#)," Tolar remarked, "because we finally understand the underlying pathogenesis, what is the toxin, and how to [target] neurotoxic soluble amyloid oligomers – the trigger and driver of [AD]."

Prior to founding Alzheon in June 2013, Tolar had built and led several biotechs, like Knome Inc., Normoxys Inc. and Comentis Inc., after obtaining his medical degree from Charles University. A neurologist in training from Boston Medical Center, Tolar received his postdoctorate in neuroscience for his work on the apolipoprotein E4 (APOE4) protein in neurodegeneration.

Targeting early AD patients with APOE4/4 genotype

In life, conditions related to infection, stress and injury, among others, can cause proteins like beta-amyloid, tau and alpha synuclein (which normally play an important function for brain health) to accumulate and change shape, called misfolding. Those misfolded proteins form toxic aggregates, which in turn leads to neurodegenerative diseases like AD and Parkinson's disease.

"As we get older, we are not able to effectively clear toxins from our brain and ... start having neurodegenerative disorders," Tolar explained.

The multicenter randomized double-blind placebo-controlled phase III [APOLLOE4](#) trial of ALZ-801 is ongoing for 325 patients with early AD and two APOE4 alleles [linked to the genetic form of AD](#).

Considering AD symptoms are [known to be more aggressive](#) and have earlier onset in the population, these individuals can benefit from biomarker-based screening and early treatment, Tolar said. Results from Alzheon's phase II biomarker study showed early and sustained statistically significant reductions in plasma p-tau181 ranging from 31-43% over two years, suggesting alleviation of amyloid oligomer-driven brain neurodegeneration.

In mechanism-of-action studies, ALZ-801 fully blocked the formation of neurotoxic soluble beta-amyloid oligomers at the phase III clinical dose, with favorable safety showing no increased risk of vasogenic brain edema, the company said.

The FDA granted fast track designation to the amyloid protein deposition inhibitor for AD in October 2017.

If development is successful, ALZ-801 will inhibit the formation of soluble toxic amyloid aggregates and act upstream from all late-stage amyloid-targeting treatments, Tolar said. As an oral tablet, the therapy would also increase patient access and convenience.

“Our mission ... was always to develop an oral treatment that can be used broadly and early in the disease.” To date, Alzheon has raised \$185 million in financing. The company also received in August 2020 a \$51 million research grant, including an initial \$47 million plus another \$4 million, from the U.S. NIH’s National Institutes of Aging, as previously reported by *BioWorld*.

The latest series E funding round, led by Alerce Medical Technology Partners, is expected to pad the company’s cash runway to 2026 – until phase III program completion and aid the commercialization of ALZ-801.

Prevention, the key to bypass big pharma’s plight?

Meanwhile, Tolar noted that the industry “needs drugs with better, more meaningful efficacy.” The current efficacy rates of 20% to 30% are “on the threshold of being meaningful,” he said, but “we need drugs that do not cause brain hemorrhages, or amyloid-related imaging abnormalities (ARIA).”

Big pharma had [long sought, but failed](#), to develop a therapy for AD. [Renewed hope](#) came in the form of Biogen Inc. and Eisai Co. Ltd.’s Leqembi (lecanemab), which gained initial U.S. FDA approval under the accelerated approval pathway in January 2023.

Leqembi’s full approval came in July 2023, but not without a black box warning, indicating the highest level of risk, regarding ARIA, the most common and severe side effect of the drug class.

Others, like Eli Lilly and Co.’s donanemab, also faced [regulatory pushback](#) due to rising concerns of ARIA in March 2024, although an FDA advisory committee [swung votes](#) to back the therapy by June 10.

“[Big pharma’s] initial target, which was wrong, was targeting the insoluble amyloid plaque,” Tolar said.

Disturbing the plaque causes vasogenic brain edema and microhemorrhages, Tolar explained, since antibodies clear the plaque that accumulate on vessel walls and make vessels “leaky” for plasma and blood. “However, antibodies are not completely targeted to hit the plaque and also interact with neurotoxic amyloid oligomers and that drives their efficacy.”

Instead of directly targeting the toxic plaques, potentially causing fatal side effects, Alzheon’s approach has been to build an oral drug to prevent formation of neurotoxic oligomers that cause brain neurodegeneration.

Differentiating between early, late AD

Most people, when referring to AD, Tolar noted, think of symptoms occurring in the last, terminal stages of the disease, characterized by severe clinical symptoms of memory loss and cognitive and behavioral dysfunction.

But the reality is, “the disease is active and damaging the brains of patients for 20 years before the onset of clinical [symptoms],” he said.

The upside is that, even though the brain cannot “regenerate,” it has neuroplasticity, signaling potential to derail disease progression in individuals through early risk identification [via biomarkers](#) and early treatment.

The 20-some years leading up to severe impairment, therefore, is “the best opportunity to change the course of the disease,” he said.