

Alzheon receives \$47M NIH grant funding its phase III Alzheimer's study

By Lee Landenberger, Staff Writer

Privately held [Alzheon Inc.](#) picked up a \$47 million grant from the NIH's National Institute on Aging that will last over five years to support a phase III clinical trial of its oral brain-penetrant small molecule [ALZ-801](#) to treat Alzheimer's disease.

Alzheon CEO Martin Tolar, who has been leading the company since its 2013 inception, told *BioWorld* that the company's approach could well become the first safe and oral Alzheimer's drug that is a treatment and a preventative, an approach he said that has always been part of Alzheon's thinking.



Martin Tolar, founder, president and CEO, Alzheon

The data that validated the target was determined just in the past year, he said, adding that the delivery method is also a revelation.

"Oral delivery is a game changer," Tolar said. "Think about injectable treatments. They require a several-hour infusion, which is made even worse with COVID-19. It's not easy to administer and it's once or twice a month, often with a negative side effect profile."

Early Alzheimer's disease patients with two copies of the apolipoprotein ε4 allele (APOE4/4) will be enrolled. Those patients

have a higher risk of rapid disease progression and have been shown to respond to agents that block the formation of neurotoxic soluble amyloid oligomers. Tolar said the company is going to patients with no symptoms to measure biomarker changes. Neurotoxic beta amyloid oligomers, part of the search, are thought to be key triggers of cognitive worsening in those with early Alzheimer's.

"The disease starts in our brains 20 years before the symptoms," he said. "That's the window you want to intervene and prevent brain damage."

The study is based on independent research showing APOE4/4 patients with higher brain levels of toxic beta-amyloid oligomers than those who without APOE4/4. The Alzheon research shows ALZ-801 fully blocks formation of soluble neurotoxic amyloid oligomers in the brain with a favorable long-term safety profile.

The study, set to begin in the first quarter of 2021, will evaluate the cognitive endpoint, Alzheimer's Disease Assessment Scale-cognitive subscale, as the primary clinical outcome, and other functional, behavioral and global clinical endpoints. The 300 patients expected to enroll in the study will be those with early Alzheimer's disease and the APOE4/4 genotype. Randomized

patients are set to receive 265 mg tablets or placebo twice daily for 18 months.

Tolar said the company can tap into the grant for the phase III when needed over the next five years, adding that the study is "rather small" compared to those by Biogen Inc and other large companies that are spending billions of dollars for their studies. He said he expects a readout by the middle of 2021.

ALZ-801 is a prodrug of the active agent tramiprosate. It received fast track designation from the FDA in 2017.

Alzheon was born in October 2013 when it picked up ALZ-801 from Neurochem Inc., which later became Bellus Health Inc. In January 2019, Alzheon withdrew its S-1 filing to conduct an IPO to raise up to \$30 million. It was the second time the company had terminated the venture. In April 2018, the company announced plans for an offering of 5 million shares of its common stock priced between \$13 and \$15 each, which was subsequently withdrawn that May.

The competitors

On a similar track to Alzheon is Aribio Co. Ltd., of Seongnam, South Korea, which has AR-1001 in a phase II study. The multitarget drug is designed to remove beta-amyloid oligomers in circulation, inhibit neuronal cell death and restore synaptic loss in mild to moderate Alzheimer's disease. In June, Aribio completed enrollment in the 210-patient study comparing two doses of the drug to placebo. Primary endpoints are the change in the Alzheimer's Disease Assessment Scale-cognitive subscale and change in Alzheimer's disease Cooperative Study-Clinical Global Impression of Change. Aribio said it expects top-line expected by early 2021.

Eisai Co. Ltd., of Tokyo, and Bioarctic AB have BAN-2401, a beta-amyloid antagonist for treating Alzheimer's disease, in a phase IIb study. The companies released data in late July from the open-label extension showing a decrease in brain amyloid levels measured at 3, 6 and 12 months in those who received placebo during active study, with observed effect comparable to results in those randomized initially to highest dose of study drug.

On [Aug. 11](#), U.S. regulators accepted the BLA from Biogen Inc. and Eisai related to aducanumab for Alzheimer's disease and assigned it a priority review. The two companies restarted the clinical program in October 2019 with aducanumab, which had failed a futility analysis, after ransacking a larger dataset to find that the drug may have important activity in AD, the most frequently seen type of amyloidosis in humans and the commonest form of dementia.