



The brain of a person with Alzheimer's (left) is shrunken, compared with a normal brain (right), from nerve cell death, and a new drug has failed to stem such neurodegeneration.

Another Alzheimer's drug flops in pivotal clinical trial

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Scratch yet another Phase III Alzheimer's drug hopeful.

Merck announced late Tuesday that it is shuttering its EPOCH trial for the BACE inhibitor verubecestat in mild-to-moderate Alzheimer's after the external data monitoring committee concluded that the drug was a bust, with "virtually" no chance of success. A separate Phase III study in prodromal patients, set to read out in two years, will continue as investigators found no signs of safety issues.

This is one of Merck's top late-stage drugs, and news of the failure drove down the pharma giant's shares in after-market trading by 2.45%.

BACE drugs essentially seek to interfere in the process that creates amyloid beta, a toxic protein often found in the brains of Alzheimer's patients. As the top amyloid beta drugs like bapineuzumab and solanezumab — which sought to extract existing amyloid beta loads — ground their way to

repeated failures, developers in the field turned increasingly to BACE therapies as an alternative mechanism that could provide the key to slowing this disease down.

Merck's effort was the most advanced in the pipeline, but Eli Lilly and others are still in hot pursuit with their own persistent BACE efforts. Teams from Biogen/Eisai and Novartis/Amgen are also beaver away on BACE.

"Alzheimer's disease is one of the most pressing and daunting medical issues of our time, with inherent, substantial challenges to developing an effective disease-modifying therapy for people with mild-to-moderate disease. Studies such as EPOCH are critical, and we are indebted to the patients in this study and their caregivers," said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. "While we are disappointed that a benefit was not observed in this study, our work continues with APECS, which is studying verubecestat in people with less advanced disease."

Lilly recently decided to go ahead and stop its own prodromal Phase III for solanezumab after concluding that there was no logical reason to believe it could succeed after the study in patients with a mild form of the memory-wasting disease ended in disaster.

No significant new drug for Alzheimer's has been approved in the past 14 years, despite massively expensive trials aimed at tackling the disease. The pipeline has been littered with big failures, which have come in a steady drumbeat of defeat and discouragement.

Curiously, the next Phase III in Alzheimer's to read out will belong to Axovant, a startup from Vivek Ramaswamy, who bought in a failed drug from GSK and put it back into the clinic. Their 5-HT6 therapy follows a series of failures in the field for drugs that aimed at amping up cognition. The next big drug in the clinic — aducanumab — belongs to Biogen, which has stirred some significant expectations for a therapy that also has a troubling safety history.

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