New Alzheimer trial to use epilepsy drug that calms brain activity

September 22 2015, by Scott Dance, The Baltimore Sun

What could be one of the first treatments to delay or prevent Alzheimer's disease received a big boost from the National Institute on Aging, which is putting up $7.5 million to help fund the next round of trials for the drug being developed by a Baltimore start-up and the Johns Hopkins University.

The clinical trial will evaluate a drug used to treat epilepsy that has shown signs in smaller doses of calming brain hyperactivity linked to dementia.

"What this could mean for thousands of patients is they may never cross over into full-blown Alzheimer's dementia," said Jerry McLaughlin,

CEO of AgeneBio, the Baltimore company founded by a Hopkins researcher who discovered that the drug might be useful in treating Alzheimer's. "We're very excited."

Alzheimer's is a degenerative brain disease that often begins with memory loss but accelerates over time, causing sufferers to lose other body functions and eventually killing them. The disease accounts for most cases of dementia, a general term for a loss in brain function.

While some treatments are available for Alzheimer's symptoms, such as memory loss or changes in behavioral or sleep patterns, the once-a-day pill that researchers will test is among a small number looking to address the brain disease itself.

The institute's money, which was awarded to Johns Hopkins, will be put toward the drug's so-called Phase 3 trial over the next five years, covering about a tenth of the project's cost, according to AgeneBio.

Phase 3 trials test the effectiveness and safety of a drug or its application across a pool of a few thousand people. If such trials are successful, approval by the Food and Drug Administration is typically the next step.

For AgeneBio, the trial, which could start as soon as early 2016, could be a big step toward FDA approval and sale of the drug, McLaughlin said. The researchers expect results in 2019, which could mean they file for FDA approval that year or in 2020.

With the partnership with Hopkins and the National Institute on Aging - a division of the National Institutes of Health - AgeneBio joins the likes of Eli Lilly, Genentech and Novartis, which are also working with the NIH on treatments to prevent or cure Alzheimer's.

The drug, known as AGB101, is composed of a proprietary low-dose

formulation of levetiracetam, an FDA-approved treatment for epilepsy. In the Alzheimer's trial, subjects will receive one-fifth to one-12th the amount of levetiracetam prescribed to patients with epilepsy.

Michela Gallagher, the Krieger-Eisenhower professor of psychological and brain sciences at Hopkins and director of the university's Neurogenetics and Behavior Center, conducted the research that suggested the drug could be applied to Alzheimer's.

Two decades ago, it was thought that brain overactivity observed in patients with dementia was the brain overcompensating for whatever was causing Alzheimer's. But Gallagher and colleagues' work showed that hyperactivity in the brain was instead causing it to atrophy.

"If you brought overactivity down and it was serving a beneficial function, you would expect their memory performance would get worse, but it didn't," Gallagher said of tests on animal subjects.

In rat trials, Gallagher tested various treatments to calm the brain activity. While most other epilepsy drugs didn't work, levetiracetam was effective. The drug is considered an "atypical" anti-epileptic because it doesn't dull broader central nervous system activity.

Those findings became the basis of AgeneBio, which Gallagher founded in 2008. While it was briefly based in Indiana, the company moved to Baltimore last year and now has offices at the Johns Hopkins at Eastern campus in Waverly.

An earlier study of the drug, published this year, found that low doses calmed the overactivity in the brain and improved memory performance in subjects who were experiencing memory loss and were considered to be pre-dementia.

Now, Hopkins researchers plan to test the drug on hundreds of patients around the world, focusing on those who are showing signs of unusual memory loss or confusion but who don't yet have Alzheimer's.

The grant pays a share of Hopkins' costs for running the trial, while AgeneBio will cover the bulk of the expenses and also must make its data public as part of the deal. The university is a minority investor in AgeneBio but does not otherwise benefit financially from the partnership, McLaughlin said.

AgeneBio, which employs four people and has so far raised $18 million in investment, will seek more investors or a partnership with a pharmaceutical company to help fund its Phase 3 efforts, McLaughlin said.

"We believe this news, this validation from the NIH, will provide a lot of value," he said.

The need for effective Alzheimer's treatment is great, said Elizabeth Li, a spokeswoman for the Greater Maryland chapter of the Alzheimer's Association.

Last year Alzheimer's was estimated to cost $214 billion, including $150 billion to Medicare and Medicaid, but the federal government allocated $566 million to Alzheimer's research, she said. The association bills itself as the largest private funder of Alzheimer's research, and it contributed $14 million to 88 research projects last year, she said.

"Right now there is no way to prevent, cure or slow Alzheimer's disease," Li said.

That presents an opportunity for AgeneBio.

"We feel excited about the opportunity to potentially bring this therapeutic to patients," McLaughlin said. "It has this real opportunity to delay the onset of Alzheimer's dementia."