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Alzheimer's prevention initiative marks milestone

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The Alzheimer's Prevention Initiative (API) trial in cognitively healthy individuals has reached a significant milestone with the first participants in Colombia receiving doses of an experimental anti-amyloid antibody, crenezumab designed to delay or prevent the onset of Alzheimer's disease.

The groundbreaking autosomal dominant Alzheimer's disease trial, designed to determine whether the investigational drug may delay or prevent the onset of symptoms of Alzheimer's disease in individuals with a genetic risk of Alzheimer's disease is described by the National Institutes of Health (NIH) as a cornerstone of the National Plan to Address Alzheimer's Disease. This study will include approximately 300 people from a large extended family in Colombia who share risk for a rare genetic mutation that typically triggers Alzheimer's symptoms around age 45. The trial targets those who are destined to develop Alzheimer's disease because of their genetic history.

The NIH, Banner Alzheimer's Institute (BAI), the University of Antioquia in Colombia, and Genentech, a member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY) originally announced the $100 million prevention trial in May 2012, with support from NIH's National Institute on Aging , BAI and Genentech. Since then, the researchers and their colleagues have developed the clinical trial design, enabled the infrastructure for conducting a clinical trial with amyloid brain imaging in Colombia, conducted preliminary brain imaging and other biomarker studies, and secured the government approvals needed to conduct the

trial. They have also established a registry of close to 3,300 members of the extended family, who have been medically and cognitively evaluated, setting the stage to enroll interested and eligible participants into the trial over the next 18 months.

"With participants now enrolled and beginning to receive doses, we are pleased to be one step closer to redefining Alzheimer's prevention research as we know it," said Dr. Pierre N. Tariot, BAI Director. "The trial is expected to end in 2020 and results will be made public soon after that."

Participants in the double-blind, placebo-controlled trial receive an injection of either crenezumab or a placebo at set intervals for up to five years. Crenezumab is an antibody therapy that Genentech in-licensed from Swiss biotech company AC Immune SA. The study is of sufficient size and duration to be able to address the question of whether the drug can reduce participants' chances of developing the disease's disabling and irreversible symptoms and preserve memory and thinking abilities. It will also explore whether treatment can slow the progression of Alzheimer's biomarkers, and whether these biomarkers could be used in the future to more rapidly test promising experimental prevention therapies. Researchers will use advanced imaging techniques, cerebrospinal fluid tests and sensitive cognitive measures to monitor whether the accumulation of amyloid and other tell-tale proteins in the brain is reduced, whether brain size and function is maintained, and, most importantly, whether mental performance is preserved.

This approach shifts the research paradigm from trying to reverse disease damage to exploring whether it is possible to attack and block its cause at the earliest point—which can be a decade or more before symptoms surface. If successful, it may allow accelerated evaluation and approval of drugs to fight Alzheimer's.

As a part of the international API, formed to accelerate the evaluation of experimental therapies, the study represents a significant shift in researchers' attempts to detect, treat and ultimately prevent Alzheimer's. It will also offer a robust test of what is often called the amyloid hypothesis. This yet to be proven hypothesis suggests that accumulation of the protein amyloid in the brain plays a key role in the progression of Alzheimer's disease and that anti-amyloid treatments may someday slow or even stop the progression if started before the disease has extensively damaged the brain.

In this groundbreaking public-private partnership, data and samples from the trial will be shared with the research community after the trial is over. The study design and data sharing agreement are intended to find faster ways to test the growing number of investigational treatments being tested to prevent the clinical onset of Alzheimer's.

Dr. Tariot and Dr. Eric M. Reiman from the Phoenix-based BAI lead API and are conducting this trial in close cooperation with Genentech's research and clinical team and a Colombian team, API Colombia, headed by Dr. Francisco Lopera of Grupo de Neurociencias de Antioquia at the University of Antioquia in collaboration with several local institutions as Hospital Pablo Tobón Uribe, IPS Universitaria, Hospital de Yarumal and Fundación Universidad de Antioquia.

"There is no guarantee that the investigational treatment will work, but there is only one way to find out," said Dr. Reiman. "We are excited about the opportunity to find faster ways to test prevention therapies and to help find one that works as soon as possible."

About 5.2 million Americans are living with Alzheimer's today, a number that could nearly triple to a projected 13.8 million by 2050. Globally, the disease and other dementias are expected to affect nearly 115 million by then.

"Our families have been waiting for this moment," said Dr. Lopera. "They are eager to participate in the fight against Alzheimer's and to be of help to the rapidly growing number of people around the world who are at risk of developing this terrible disease."

Provided by Banner Alzheimer's Institute