



Banner
Alzheimer's
Institute

EMBARGOED UNTIL Tuesday, July 15 AT 12:00 am EDT or 6 am CEST

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**Banner Alzheimer's Institute Announces Partnership with Novartis
in New Study of Alzheimer's Prevention Treatments**

Two drugs to be studied in North America and Europe in volunteers at high risk for disease

Copenhagen, Denmark (July 15, 2014) —Researchers from the Banner Alzheimer's Institute (BAI) today announced a partnership with Novartis in a pioneering medical trial to determine whether two investigational anti-amyloid drugs—an active immunotherapy and an oral medication—can prevent or delay the emergence of symptoms of Alzheimer's in people at particularly high risk for developing the disease at older ages.

The five-year APOE4 trial will involve more than 1,300 cognitively healthy older adults, ages 60 to 75, at high risk of developing symptoms of Alzheimer's because they inherited two copies of the apolipoprotein E (APOE4) gene—one from each parent. About 2 percent of the world's population carries two copies of this gene and one in four people carry one copy of the APOE4 gene, which is strongly linked to late-onset Alzheimer's. One in four people carry one copy of the APOE4.

The trial—subject to regulatory authority approval—will begin in 2015 at approximately 60 sites in Europe and North America, including BAI's headquarters in Phoenix, Ariz. Participants will receive either the active immunotherapy or the oral medication or a placebo.

The study is partially funded by a \$33.2 million grant commitment from the National Institutes of Health (NIH), part of the U.S. Department of Health and Human Services, awarded in 2013, and more than \$15 million in philanthropic and in-kind contributions by Banner Alzheimer's Foundation. It is part of the Alzheimer's Prevention Initiative (API), an international collaboration led by BAI to accelerate the evaluation of promising prevention therapies.

Today's announcement of the partnership with Novartis, a Swiss pharmaceutical company, and the selection of the drugs to be studied, represent a dramatic investment in novel approaches to Alzheimer's prevention research.

“We hope Novartis’s substantial investment of resources and expertise will lead to a significant breakthrough in Alzheimer’s research,” said Dr. Pierre N. Tariot, study director for BAI, an arm of Banner Health, one of the largest nonprofit healthcare systems in the United States. “We are taking clinical trials to a critical new stage. This approach shifts the research paradigm from trying to reverse disease damage to attacking and preventing its cause, years before symptoms could surface.”

The active immunotherapy is aimed at triggering the body’s immune system to produce antibodies that attack different forms of the amyloid protein, which many researchers have suggested plays a critical role in the development of Alzheimer’s. The oral medication is a BACE (beta-secretase1) inhibitor, designed to prevent the production of different forms of the amyloid protein.

The two drugs, which will be tested separately, are intended to stop the accumulation of amyloid in ways that differ from the anti-amyloid antibody therapies now being tested in API’s Autosomal Dominant Alzheimer’s Disease (ADAD) trial in Colombia, and in two other prevention trials. The drugs are being introduced even before amyloid accumulates in some of the participants’ brains. The trial will increase the chance of finding treatments that will prevent, slow or delay the loss of memory and other cognitive abilities associated with Alzheimer’s.

The new study marks the second major trial associated with API. In 2012, NIH announced the long-term ADAD study of cognitively healthy individuals who are destined to develop Alzheimer’s at an unusually early age because of their genetic history. The \$100 million study—funded by NIH, BAI and Genentech, a biotechnology company—is focused on approximately 300 members of an extraordinarily large family from Colombia who share a rare genetic mutation that typically triggers Alzheimer’s symptoms around age 45.

The ADAD study, a partnership of BAI, Genentech and the University of Antioquia in Colombia, is evaluating the amyloid antibody agent crenezumab.

“There are no guarantees that any of these investigational treatments will prevent the clinical onset of Alzheimer’s disease,” said Dr. Eric M. Reiman, one of the study directors for BAI. “But we are grateful for these opportunities to find out.”

The APOE4 and ADAD trials will be critical in determining whether anti-amyloid treatments are likely to show benefit for Alzheimer’s. Both trials include the best-established cognitive and biological measures of the disease, and a strategy that might make it possible to substantially shorten the time needed to conduct future prevention trials. Both trials also include precedent-setting agreements for the sharing of study data and biological samples after the studies conclude.

Volunteers for the APOE4 study will receive either active immunotherapy injections or a BACE inhibitor in pill form or a placebo. Participants will be recruited via multiple venues, including the Alzheimer’s Prevention Registry website created by BAI in 2012. The registry

www.endALZnow.org) currently has more than 37,000 potential volunteers and is aiming to recruit more than 250,000.

The APOE4 study's new website, which will launch in 2015, will create a platform to explain the study, register potential participants and provide disclosure information and consent forms. Volunteers who meet the study criteria will be asked to mail a sample of their genetic material (such as a cheek swab) to a laboratory. The volunteers will learn the results of that test in the context of possibly enrolling in the trial.

"This web research platform creates a powerful tool for any additional Alzheimer's research," said Jessica Langbaum, Ph.D., co-director of the study at BAI. "This infrastructure enables us to create more than just a single drug trial, but rather a template for testing a variety of treatments for many years to come."

Volunteers who are selected will receive genetic counseling, as will others who are not chosen but who seek more information on their vulnerability. "We are keenly aware of the extreme sensitivity and emotional impact of disclosing genetic information," Dr. Langbaum said. Volunteers accepted into the trial will already know they are at high risk, while others may learn of a lesser but still increased risk. For both of these groups, BAI will be providing more detailed information and genetic counseling in person, by phone or possibly through video-conferencing or telemedicine.

"We are excited about the chance to partner with Novartis, which has a longstanding commitment to the fight against Alzheimer's and promising investigational treatments. They will conduct this study in a way that will be helpful to all stakeholders in the field," said Dr. Tariot.

"We are now coming to believe that attacking Alzheimer's disease, before clinical signs of memory loss and cognitive impairment become evident, may provide our best chance for effective therapies," says Dr. Neil Buckholtz, Director of the Division of Neuroscience at the NIA. "These studies will be important in helping to determine if and how that can be done."

Alzheimer's is a debilitating and incurable disease that affects as many as 5 million Americans age 65 and older, according to a number of estimates. Without the discovery of successful prevention therapies, the number of U.S. cases is projected to nearly triple by 2050.

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About Banner Alzheimer's Institute

Banner Alzheimer's Institute (BAI) is a nonprofit organization dedicated to the goal of ending Alzheimer's disease without losing another generation. It is helping to launch a new era of Alzheimer's research—detection, treatment and prevention at the pre-symptomatic stage—and to establish a comprehensive model of care that can be the national standard. BAI was founded in 2006 by Phoenix-based Banner Health, one of the country's largest nonprofit healthcare systems. For more information, go to www.banneralz.org.

About Alzheimer's Prevention Initiative

The Alzheimer's Prevention Initiative (API) is an international collaborative formed to launch a new era of Alzheimer's prevention research. Led by the Banner Alzheimer's Institute, the API will conduct prevention trials in cognitively healthy people at increased genetic risk for Alzheimer's disease. It will continue to establish the brain imaging, biological and cognitive measurements needed to rapidly test promising prevention therapies and provide registries to support enrollment in future prevention trials. API is intended to

provide the scientific means, accelerated approval pathway and enrollment resources needed to evaluate the range of promising Alzheimer's prevention therapies and find ones that work without losing another generation. For more information, go to www.banneralz.org.