Pre-clinical study to fulfill FDA requirements for the completion of AV-1959 IND

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Contact information of lead PI
Country

USA

Title of project or programme

Pre-clinical study to fulfill FDA requirements for the completion of AV-1959 IND

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 4,136,058.72

Start date of award

01/07/2015

Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Biotechnology... Brain Disorders... Dementia... Immune System... Immunization... Neurodegenerative... Neurosciences... Prevention... Translational Research... Vaccine Related

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer's disease (AD) is characterized clinically by progressive cognitive decline, eventually resulting in death, usually within 10 years of the diagnosis. The number of demented individuals worldwide is estimated to be 35.6 million people, and it is believed that it will reach 100 million by the year 2050. According to the Alzheimer's Association, in 2013, AD will cost the United States $203 billion. This number is expected to rise to $1.2 trillion by 2050. The main goal of the proposed U01 project is a translation to the clinic of the pharmaceutical-grade DNA epitope vaccine candidate (AV-1959D) developed by our team. Recently, our team reported on generating this novel, DNA-based AD epitope vaccine composed of a short immunogenic B cell epitope of amyloid (3 copies: 3A?1-11), fused with a platform of multiple universal foreign Th epitopes (designated as MultiTEP) that are known to be recognized by various human immune response genes (MHC class II). Delivered by an electroporation system, the AV-1959D vaccine generates robust cellular immune responses to foreign epitopes, eliminates activation of potentially harmful autoreactive T cells and induces strong and therapeutically potent anti-A? antibodies in mice, rabbits, and monkeys (4 papers published). As to the cellular immune responses, AV-1959D diminished the variability of immune responses due to MHC Class II diversity, in macaques, and activated Th cells specific to epitopes from MultiTEP platform in all vaccinated animals. Accordingly, in the frame of our U44 program funded by NINDS in 2009-2012 we manufactured our leading candidate DNA vaccine, AV-1959D and completed a pre-IND meeting with the FDA in Dec of 2012. In this U01 project we propose completing the pre-clinical efficacy, safety/toxicology and biodistribution studies in APP/Tg mice (3xTg-AD) using an AgilePulseTM in vivo Electroporation system modified for mouse studies. These studies, according to FDA recommendations will be performed in two groups of 3xTg-AD mice, possessing different stages of AD-like pathology. Additionally, a safety study evaluating the affect of the vaccine on neuropathology (such as meningeal-related inflammation, microhemorrhage, vascular degeneration, vasogenic edema, etc) will be performed in Tg-SwD/I mice with extensive CAA. At the completion of these studies our multidisciplinary team, including immunologists, vaccine researchers, neuroscientists/cognitive scientists, molecular biologists, toxicologists, clinical drug developers and investigators with extensive experience in AD early and late phase clinical trials, will obtain all of the necessary regulatory documents and an FDA- approved IND for AV-1959D Phase I trials.

Lay Summary

PUBLIC HEALTH RELEVANCE: According to the Alzheimer's Association, besides the fact that 5.2 million Americans, and about 25 million people worldwide live with Alzheimer's Disease (AD), in just the United States, AD will cost $203 billion in 2013, and $1.2 trillion by 2050, making its repercussions devastating. In this U01 project we propose to perform the pre-clinical efficacy, safety/toxicology and biodistribution/persistent studies in transgenic mice for our vaccine candidate (called AV-1959D). At the completion of these studies, the main goal of our multidisciplinary team is to obtain all of the necessary regulatory documents for an FDA-approved investigational new drug (IND) for AV-1959D clinical trials in AD patients.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A