

Preclinical Development of a Selective Suppressor of Neuroinflammation for MCI/AD

<https://www.neurodegenerationresearch.eu/survey/preclinical-development-of-a-selective-suppressor-of-neuroinflammation-for-mci-ad/>

Principal Investigators

VAN ELDIK, LINDA J

Institution

UNIVERSITY OF KENTUCKY

Contact information of lead PI

Country

USA

Title of project or programme

Preclinical Development of a Selective Suppressor of Neuroinflammation for MCI/AD

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,934,409.17

Start date of award

01/09/2015

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)... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer's disease (AD) is one of the largest global public health crises facing us today, and is predicted to increase dramatically over the next decades as the world population ages. There are no effective therapies available to prevent, cure, or slow the progression of disease, and new therapeutic strategies are urgently needed. Our strategy is to target the abnormal glial activation and neuroinflammation that arises early in AD progression and that is becoming of increased interest as a therapeutic target. Dysregulated neuroinflammation responses such as proinflammatory cytokine overproduction from abnormally activated glia are seen early in AD, and are thought to be a key contributor to downstream synaptic dysfunction and cognitive deficits. This raises the possibility that selective targeting of the dysregulated cytokine response may be a useful therapeutic approach. This application seeks three years of support to bring to IND status a novel experimental therapeutic (termed MW151) whose pharmacological mechanism of action is to attenuate disease- and injury-induced proinflammatory cytokine overproduction, thereby reducing downstream synaptic and cognitive dysfunction in multiple animal models of CNS disorders. MW151 is a water-soluble, orally bioavailable, CNS-penetrant, small molecule with outstanding chemical and metabolic stability. MW151 has been extensively de-risked through several non-GLP pharmacological and toxicology screens, and a GMP compatible production scheme has been developed. However, MW151 has not progressed into final GLP preclinical development. Our hypothesis is that MW151 will be a successful candidate for development as an oral formulation for the future treatment of individuals with mild cognitive impairment due to AD. With U01 funding, we will pursue three aims that are milestone-driven with clear Go/No Go decision criteria. Aim 1: Perform preclinical pharmacokinetics and safety assessment of MW151. Aim 2: Produce GMP drug substance (API) and oral drug product. Aim 3: Obtain an IND for future first-in-human clinical investigations. This project will advance development of a promising drug candidate with the potential to prevent the transition to or slow the progression of AD. In addition, successful development of MW151 could have broad clinical applications not only to AD but to a number of other CNS disorders where proinflammatory cytokine dysregulation is part of the pathophysiology progression mechanism.

Lay Summary

PUBLIC HEALTH RELEVANCE: The proposed preclinical campaign addresses the urgent and critical need to develop effective disease-modifying therapeutics to prevent, delay, and treat AD. We are proposing to develop a promising drug candidate that in animal models attenuates the overactive proinflammatory cytokine aspect of neuroinflammation, and prevents the downstream neuron dysfunction and cognitive impairment that characterizes neurodegenerative disease progression. The aims are focused on FDA guidelines for investigational new drug status.

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