Phase 1 clinical studies with the gamma-secretase modulator, NGP 555 to establish safety, pharmacokinetics, and biomarker efficacy

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Contact information of lead PI
Country

USA

Title of project or programme

Phase 1 clinical studies with the gamma-secretase modulator, NGP 555 to establish safety, pharmacokinetics, and biomarker efficacy

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,396,438.53

Start date of award

01/08/2015

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... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Neurodegenerative... Neurosciences... Translational Research

Research Abstract
? DESCRIPTION (provided by applicant): Currently, there is no cure for AD; however, it is widely accepted that inhibiting amyloid plaque formation would be beneficial for the prevention of Alzheimer’s disease. Although there are many mechanistic approaches for the treatment of AD, one novel and innovative approach is to modulate the activity of the key enzyme complex involved in Aß42 production (a primary component of amyloid plaques), ¿- secretase. Because of the potential for serious side-effects associated with inhibition of ¿-secretase, modulation of its activity was targeted in order to avoid non-specific effects. The failure of ¿-secretase inhibitors has mostly been attributed to side-effects caused by other ¿-secretase substrates such as Notch, an essential element for normal cellular development, and the buildup of the amyloid precursor protein carboxyl-terminal fragments (APP-CTFs), toxic fragments which likely cause loss of neuronal function. Our scientific approach resulted in the discovery and preclinical development of the clinical candidate, NGP 555, which is mechanistically devoid of these non-specific activities. Under NeuroGenetic Pharmaceuticals’ (NGP) current SBIR-fast track award with NINDs we have completed the final nonclinical studies necessary to file an IND and have prepared our IND for electronic filing, expected July, 2014. In our application to NIA (PAR 14-089), we propose to initiate Phase 1 clinical trials and accomplish single ascending dose (SAD) and multiple ascending dose (MAD) trials with safety and pharmacokinetic (PK)/pharmacodynamic (PD) readouts in normal healthy/elderly volunteers and in mild AD patients. In addition to the standard safety determinations, including showing NGP 555 is devoid of gastrointestinal and skin toxicity, we expect to determine drug effectiveness with Aß biomarker measurements in plasma and cerebrospinal fluid (CSF) along with neuronal health measurements of tau in the CSF. These data should be compelling enough to mitigate risks for entering into longer term trials with additional safety, bio-imaging, and cognitive endpoints of clinical efficacy for Ph 2a and 2b trials.

Lay Summary
PUBLIC HEALTH RELEVANCE: Alzheimer’s disease (AD) is a progressive, neurodegenerative condition that causes memory loss, confusion, cognitive decline, and behavioral changes. AD is the most common form of dementia in the elderly burdening as many as 1 in 8 people above the age of 65. Based on the large number of affected Americans- estimated currently at more than 5.4 million — and the enormous cost to society– in the billions– the need for effective preventin and treatment is compelling.

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