SORT1:PGRN blocking antibodies for Frontotemporal dementia

https://neurodegenerationresearch.eu/survey/sort1pgrn-blocking-antibodies-for-frontotemporal-dementia/

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Country

USA

Title of project or programme

SORT1:PGRN blocking antibodies for Frontotemporal dementia

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,369,081.65

Start date of award

30/09/2016

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)... Behavioral and Social Science... Biotechnology... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Rare Diseases

Research Abstract

? DESCRIPTION (provided by applicant): SORT1 blocking antibodies for Alzheimer’s disease and Frontotemporal dementia Alector’s objective is to develop therapeutic antibodies against the receptor Sortilin1 (SORT1) for the treatment of the devastating neurological disorders Frontotemporal Dementia (FTD) and Alzheimer’s Disease (AD). FTD is a progressive disease that causes incapacitating changes in behavior, language, movement and cognition, and is the most common of the pre-senile dementias, affecting ~50,000-60,000 people in the US. AD is the most common cause of dementia, which shares many pathological and phenotypic features with FTD. As AD affects an estimated 5M Americans, with the numbers increasing steadily, the disease represents a major public health issue. There is no effective treatment for FTD, which is typically diagnosed 3-4 years after symptom onset, with a median survival of 6-11 years. Furthermore, there are no available treatments that halt progression of AD. Ultimately, patients with FTD or AD will require round-the-clock medical care. Progranulin (PGRN) is a neurotrophin that has been identified as a risk factor for neurodegenerative diseases. PGRN haploinsufficiency is causal for 10% of all FTD cases, while other alleles are associated with the development of late onset AD. SORT1 is a transmembrane receptor that controls the extracellular level of PGRN by binding it at the cell surface and rapidly internalizing it for lysosomal degradation, while it is dispensable for PGRN signaling. We propose to generate a therapeutic that can elevate extracellular levels of PGRN by developing antibodies that bind SORT1, block the interaction with PGRN, and thus functionally elevate PGRN levels in vitro and in vivo. Effective lead antibodies will be optimized for affinity and other characteristics and advanced for confirmatory and preclinical testing as development candidates. Both the dataset and SORT1 antibodies produced in this project would allow us to secure the additional funds necessary for advancing the candidate to preclinical testing, to IND submission, and to the clinic. Trials with a SORT1 antibody in patients with PGRN mutations would conclusively determine whether therapeutic PGRN elevation could provide meaningful clinical benefit in FTD and AD patients as hypothesized.

Lay Summary

PUBLIC HEALTH RELEVANCE: The goal of the present project is the development of a therapeutic Sortilin antibody that would increase the levels of Progranulin (PRGN) whose deficiency is causal to Frontotemporal Dementia (FTD) and is a risk factor for Alzheimer’s disease (AD). FTD is a devastating progressive neurodegenerative disorder that causes debilitating behavioral and emotional changes, and it is the most common cause of pre-senile dementia. AD is a disease of aging that is the most common cause of dementia, afflicting more than 5M Americans with progressively incapacitating memory and behavioral impairments. There are currently no treatments for FTD, no treatments that arrest AD progression and no proven treatments that can therapeutically elevate PRGN in haploinsufficient subjects.

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