Target Engagement Biomarkers for Alzheimers Therapeutics

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Country

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Title of project or programme

Target Engagement Biomarkers for Alzheimers Therapeutics

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1

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Research Abstract
Abstract – Project Summary Cognition Therapeutics Inc. (CogRx) has discovered CT1812, a novel oligomer receptor antagonist that is the only drug candidate demonstrated to prevent and displace binding of Abeta oligomers to receptors on brain cells. By stopping the initiating event

in the Abeta oligomer cascade, this first-in–class drug candidate completely blocks downstream synaptotoxicity and restores memory to normal in aged transgenic mouse models of Alzheimer's disease. CT1812 displaces receptor-bound Abeta oligomers by allosterically antagonizing the sigma-2/PGRMC1 receptor (Izzo et al., 2014a, b). CT1812 thus represents the first disease-modifying therapeutic that will test the oligomer hypothesis of Alzheimer's disease. Such a drug candidate would significantly impact the lives of the 35 million patients worldwide suffering from AD and MCI, for whom no disease-modifying treatment exists. This proposal seeks to identify biomarkers of CT1812 functional target engagement. The project proposes 1) measuring changes in expression levels of proteins regulated by sigma- 2/PGRMC1 in the presence of Abeta oligomers that are blocked by CogRx's sigma-2/PGRMC1 antagonists in neurons and 2) determining if such changes are observed in the brains, CSF or serum of transgenic mice treated with CT1812. The proposed studies will also conduct unbiased proteomic investigations on biofluids from wild type and transgenic AD mice treated with CT1812 or vehicle to identify patterns of altered protein expression associated with drug engagement with target in settings of disease. With this data, we propose to construct a pathway from CT1812 target engagement to peripherally available biomarker using targeted reaction monitoring (MRM) proteomics data. The successful outcome of this project is the development of an assay to measure candidate biomarkers in humans for exploratory investigation in the clinic.

Further information available at:

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