Target Identification for Novel Small Molecule Therapeutic for Alzheimers disease

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USA

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1

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Research Abstract

ABSTRACT Traditional approaches to drug development for Alzheimer’s disease are becoming increasingly expensive and in many cases disappointingly unsuccessful. Based on preliminary in vitro and in vivo studies we have identified a novel small molecule (methyl 2,4-dimethyl-5-oxo-5,6- dihydrobenzo[c][2,7]naphthyridine-1-carboxylate; (UK-101)) that significantly decreases

A?1-42 production and pro-inflammatory (M1) cytokines while simultaneously inducing anti-inflammatory (M2a) cytokines. Although our preliminary data show UK-101 effectively modifies 2 critical neuropathologic features of AD with no apparent adverse effects, the drug target remains unclear. Based on preliminary in silico modeling and in vitro data that suggest UK-101 may modulate mGluR5 an allosteric glutamate receptor recently identified as a potential therapeutic target in AD, the aims of the current proposal are to verify that mGluR5 is the drug target of UK-101, to quantify the binding constant of UK-101, and to verify that there are no significant off target effects of the drug. If successful, the data obtained in this proposal will allow further structure activity studies and most importantly establish a specific target for UK- 101.

Further information available at:

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United States of America

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N/A

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