2015 Part the Cloud Request for Applications (RFA): Translational Research Funding for Alzheimer’s Disease

**Competition Objectives:** In its fourth iteration, the Alzheimer's Association is pleased to announce the Part the Cloud Translational Research Funding initiative to increase the research efforts in Phase I and Phase II (Proof of Concept) clinical trials directed towards Alzheimer's disease and related dementias in North America.

**Background:** There is no greater healthcare need than slowing or preventing Alzheimer's disease. The vast increase in understanding of the neurobiology of AD in recent decades, from genetic factors to amyloid accumulation, tangle formation, cellular dysfunction and synaptic failure, has led to the identification of highly promising targets for new therapies. Among the therapeutic strategies being pursued are beta and gamma secretase inhibitors to reduce amyloid production, immune-therapeutics to increase clearance of amyloid, immune-therapeutics targeting tau pathology, and various approaches to protecting brain cells from neurodegeneration. However, the process of developing candidate therapies is long and complex leading to the failure of many drug development programs. The steps from target identification to the clinic includes high-throughput screening, lead optimization, establishing target engagement in vitro and in vivo, assuring central nervous system penetration, animal toxicology and finally the three phases of human testing. The full process takes many years and substantial resources, and typically involves different groups of investigators at different stages.

While many academic investigators and companies have successfully discovered candidate therapeutics, and have succeeded in the preclinical stages of development, moving into human testing can be a major stumbling block. Most government and non-government grant mechanisms support preclinical development or mid to latter clinical trials testing drug efficacy in humans, but there are few mechanisms for supporting the critical earlier human phase studies. At present, the National Institute on Aging supports many phases of preclinical AD drug development, including basic research on target identification, animal model testing of candidate therapeutics, preclinical toxicology and proof-of-concept studies in humans. These latter human studies must be preceded by smaller, early phase studies but there are few appropriate funding mechanisms through the National Institute on Aging or other organizations to fund the next step, Phase I trials in humans.

Novel compounds are typically introduced into humans through a series of small Phase 1 studies: single and then multiple ascending dose studies in healthy adults to assess pharmacokinetics and safety/tolerability over a range of possible doses. Drugs that are being re-purposed from other indications, and nutriceuticals/supplements that are generally recognized as safe, may not require these Phase 1 studies, but usually do require preliminary human studies to establish penetration into the central nervous system and/or target engagement; these are sometimes referred to as Phase 1b studies. Only when the appropriate Phase 1 studies are successfully completed can a larger Phase 2 be approved.
**Potential themes:** This new grant mechanism aims to fill the gap in AD drug development by providing support for early phase studies of potential Alzheimer's therapeutics or validation of biological markers in of disease progression.

**General considerations and Eligibility:** Applications will be accepted from academic investigators and small companies with lead candidate therapeutic agents that require early stage testing prior to Proof of Concept (POC) Phase 2 or 3 efficacy studies, or with lead therapeutic agents that have already established human safety data and require a small-scale pilot Proof of Mechanism (POM) study to begin proving the scientific concept in humans. This award will support Phase 1 studies or pilot small-scale Phase 2a studies for repurposed drugs in normal individuals or individuals with preclinical or symptomatic Alzheimer’s disease (i.e. early human studies to set the stage for efficacy studies), including single and multiple dose studies to establish safety, brain penetration and/or target engagement and POM in preparation for larger proof of concept trials. In addition, proposals may be considered that are POC to validate biological marker(s) of disease progression in a clinical trial environment. Any proposal must have a clear focus on Alzheimer’s disease and related disorder and be translational in nature. All proposals should clearly and explicitly outline the measure to be investigated, the methods for study, and outcomes. Researchers from underrepresented groups are encouraged to apply.

**Eligibility:** Both non-profit and small for-profit agencies in North America are eligible. Small for-profit agencies must submit documentation of net assets and annual earnings for consideration during the letter of intent process. Not-for-profit organizations must submit documentation verifying status during the letter of intent process. Applications will only be accepted from organizations conducting studies in North America. Researchers with full-time staff or faculty appointments are encouraged to apply. Applications from post-doctoral candidates will not be accepted. For questions as to whether an investigator or organization is eligible, please contact the Alzheimer’s Association at grantsapp@alz.org.

**Funding and award period:** The Association anticipates funding up to two (2) Part the Cloud Research grants. Each award is limited to $600,000 (direct and indirect costs) for two or three years. However, in instances where a project may have a budget exceeding this value, please contact the Alzheimer’s Association at grantsapp@alz.org for possible special programmatic or budgetary considerations. Requests in any given year may not exceed $400,000 (direct and indirect costs). Indirect costs are capped at 10 percent (rent for laboratory/office space is expected to be covered by indirect costs paid to the institution).

**Deadlines and award dates:** Letters of intent must be received by 5:00 PM EASTERN STANDARD TIME, July 15, 2015 and must address the RFA both in scope and location. Late or incomplete letters of intent will not be accepted after this date (no exceptions).
Full applications must be received by 5:00 PM EASTERN STANDARD TIME, August 26, 2015. Scientific and technical review will be conducted from August-September 2015. The second-level review by the Medical and Scientific Advisory Council will be conducted during October 2015. Funding is anticipated to be awarded by November 30, 2015.

Reporting requirements: Awardees will be required to provide sixth month milestones, and have bi-annual discussions with the Alzheimer’s Association. Annual scientific progress and financial reports are required. Continuation of the grant over the awarded duration is contingent upon the meeting scientific milestones, and upon timely receipt of scientific and financial reports.

Budget: A “budget summary” for the proposed research project is required and must be submitted with the application and within the allowable page limits. However, if the application is to be awarded, a more detailed budget will be required and must be approved before the disbursement of funds. Your budget must not exceed the maximum amount of the award ($600,000) unless you have received special consideration by the Alzheimer’s Association. To be considered for a budget increase, please contact the Alzheimer’s Association at: grantsapp@alz.org.

Costs not allowed under this award include:
- Tuition
- Computer hardware or software for investigators
- Rent for laboratory/office spaces
- Construction or renovation costs

For more information: Contact grantsapp@alz.org or call 1.312.335.5747 or 1.312.335.5862.

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