



2024 Part the Cloud Translational (PTC) Research for Alzheimer's Disease Program

Competition Objectives: The Alzheimer's Association is pleased to announce the next offering of the Part the Cloud Translational Research Funding initiative to increase the research efforts in Phase I and Phase II (Proof of Concept) clinical trials evaluating novel or repurposed potential medications directed towards Alzheimer's disease and related dementias internationally.

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. 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. There are few appropriate funding mechanisms to fund the next step, Phase I trials in humans.

Potential themes: This new grant mechanism aims to fill the gap in Alzheimer's disease and related dementia clinical trials for advancing potential therapeutics forward by providing support for early phase studies (Phase 1 and Phase 2).

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 (Phase 1) 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 in humans 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 asymptomatic or symptomatic Alzheimer's and related dementia (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 disorders and be translational in nature. All proposals should clearly and explicitly outline the measure to be investigated, the methods for study, the study population, and outcomes. Researchers from underrepresented groups are encouraged to apply.

Studies funded by Part the Cloud with results justifying further development (e.g. Phase 2b, or 3) may be eligible to apply to the Alzheimer's Clinical Trials Consortium (ACTC) (U24 AG057437). ACTC provides comprehensive infrastructure and expertise on ADRD clinical trials. ACTC and the proposer will work in collaboration to develop a grant application to National Institute on Aging, NIH. If funded, ACTC will conduct the trial. Mentorship and Principal Investigator training in Alzheimer's Clinical Trials is provided by ACTC. Read more at: <https://www.actcinfo.org/submit-a-proposal/>.

Eligibility: Both non-profit and small for-profit organizations are eligible. Open to International Applicants. Small for-profit organizations must submit documentation of net assets and annual earnings during the letter of intent process as a part of the review process. Not-for-profit organizations must submit documentation verifying status during the letter of intent process.

Applications will be accepted from organizations conducting studies around the world. 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.

Note: Alzheimer's Association grants are generally open to scientists and researchers across the globe; however, as a U.S.-based charity, the Alzheimer's Association is subject to, and complies with, U.S. law. As a result, the Alzheimer's Association cannot award, and will not award, grants in violation of applicable U.S. statutes and regulations. This means, among other things, that the Alzheimer's Association cannot, and will not, fund any individual or entity (i) that is subject to U.S. comprehensive or targeted sanctions or if awarding funding would result in a violation of such sanctions, (ii) that is on the U.S. List of Specially Designated Nationals or entities owned or controlled by such persons, or (iii) when doing so is otherwise prohibited by U.S. laws related to combating terrorism.

Funding and award period: We anticipate funding up to four Part the Cloud Research Awards. Each grant is limited to \$1,000,000 (direct and indirect costs) over two or three years. Indirect costs are only allowed for not-for-profit institutions, and are capped at 10 percent (rent for laboratory/office space is expected to be covered by indirect costs paid to the institution).

Letter of Intent (LOI) Review Procedures:

All LOIs will be evaluated prior to invitation to submit a full application. Only LOIs that meet program specific guidelines as outlined in this request for applications will be invited to submit full applications.

Deadlines and award dates: Letters of Intent (LOI) must be received by 5:00pm EST, November 15, 2023. Letters of Intent will not be accepted after this date. No exceptions will be made. All LOIs must be completed and submitted online through our interactive system Proposal Central at <http://proposalcentral.com>. (No hardcopies or emails will be accepted)

The on-line LOI is approved and invited to submit a full proposal, an email notification will be sent from Proposal Central granting access to the on-line application. The online system must be used to submit a grant application—hard copies of the application will not be accepted.

Each LOI is evaluated with attention to:

- Demonstrable innovation/novelty of the proposed project (especially in the context of the PIs recently funded work)
- Alignment with the research priorities of the PTC request for applications and the Alzheimer’s Association
- Impact of project on Alzheimer’s and all other dementia research
- Evidence of methodological rigor that address the research question(s) being proposed

For those invited to submit, Full applications must be received by 5:00pm EST, January 31, 2024.

The full grant application consists of the following:

1. Problem Statement – 1 page
2. Work Plan – 5 pages; Efficacy should not be the primary outcome for studies at phase 1 and phase 2; however, it may be an exploratory outcome. All applications should have clear Go/No Go criteria to the next phase of clinical development of the therapy, which should be clearly outlined in the application. The application must demonstrate how data from the proposed study will inform future trials.
3. Available Resources & Budget Justification – 2 pages; If awarded, a full budget of planned expenses will be required.
4. Data Management and Sharing Plan – 3 pages; we recommend using the provided amended NIH template. When data sharing may be limited, applicants must explain such limitations at the time of application.
5. Recruitment Plan - 1 page; the Association expects all trials to match or exceed the diversity of their local population at a minimum. **Award must maintain at least 20% minimum representation of minoritized participants. The Association reserves the right to withhold payments if recruiting does not achieve this level of diversity.**
6. Reference and Citations – 1 page
7. Response to review comments – For resubmissions only – 1 page
8. Therapeutic Rationale – 1 page
9. Gantt Chart – 1 page (Optional)

10. Biosketch (PI/Co-PI/Key Personnel) – 5 pages max for each
11. Research Project Leadership Plan – 5 pages max
12. Key Milestones that align with proposed budget

Applications will be reviewed with special attention to:

- Significance of the question being studied & rationale of the target being pursued
- Applicant information
- Quality of the proposed trial design
- Quality and adequacy of available resources and budget
- Impact-Risk

Scientific and technical review will be conducted from **February – March 2024**. The second-level review by the Alzheimer's Association and subject matter experts in April 2024 and funding is anticipated to be awarded by **April 15, 2024**.

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 meeting the scientific milestones, achieving participant recruitment of 20% minimum representation of minoritized participants, and upon timely receipt of scientific and financial reports. Representation of study participants should be reflective of the communities that are being engaged for this study.

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, \$1,000,000 (inclusive of direct and indirect) over two or three years.

Costs associated with the management and sharing of research data are allowable

Costs related to participant remuneration should follow the recommendations proposed by the National Alzheimer's Coordinating Center (NACC) located here: <https://files.alz.washington.edu/documentation/remuneration-guidelines.pdf>

Allowable costs include:

- Small pieces of laboratory equipment and laboratory supplies
- Computer software if used strictly for data collection (requires prior approval)
- Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including laboratory technicians and administrative support directly related to the funded grant); there is no salary cap
- Membership to scientific association
- Professional development / communication training
- Support for travel to scientific and professional meetings not to exceed \$2,500 in any given year

- Training costs to visit and perform research related to the awarded project on another laboratory/facility (this is not to be included in the travel costs)
- Participant travel expenses for projects involving human participants is not included in the travel and is allowable expenses that can be captured under other expenses (itemized) in the budget.

Costs not allowed under this award include:

- Computer hardware or software for investigators (e.g. Microsoft Office, mouse, monitor, computer parts)
- Laboratory equipment such as freezers, ultracentrifuges, RT-PCR, Microscopy/imaging equipment
- Service contract fees of equipment
- Construction or renovation costs
- Tuition
- Rent for laboratory/office spaces
- Expenses such as Data Network Recharges and Computing and communication device support services
- General liability insurances, such as GAEL
- Wire and currency exchange fees
- Salary and/or compensation for Alzheimer's Association Staff or current members of the Alzheimer's Association Medical and Scientific Advisory Group (MSAG) and the International Research Grant Program (IRGP) Council. A complete list of MSAG and IRGP Council members can be found on our website alz.org/grants.

For more information: Contact grantsapp@alz.org

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Part the Cloud, benefiting the Alzheimer's Association.***