PROGRAM TO ACCELERATE CLINICAL TRIALS (PACT)

FUNDING OPPORTUNITY DESCRIPTION

The PACT RFP supports IND-enabling studies and early-phase clinical trials that test promising pharmacological interventions and devices for Alzheimer's disease (AD) and related dementias. Both disease-modifying and symptomatic agents will be considered.

This funding opportunity prioritizes diverse drug mechanisms and modes of action related to the biology of aging and other emerging therapeutic areas for dementia. For this reason, amyloid targeted approaches and cholinesterase inhibitor proposals will not be considered for this RFP.

Stage of development:

1. Early-stage human clinical trials including:
   - Phase 0 micro- or sub-therapeutic-dosing studies
   - Phase 1 trials in healthy subjects
   - Biomarker-based proof-of-concept studies (generally phase 1b or phase 2a trials) designed to assess target engagement and downstream pharmacologic effects

2. Regulatory studies including:
   - Non-GLP and GLP pharmacology and toxicology studies, pre-formulation, and GMP manufacture required for investigational new drug (IND) and clinical trial authorization (CTA) preclinical packages. Funding is available for preparation of traditional and exploratory IND applications
   - Long-term toxicology studies to enable longer-term dosing in phase 2 trials
   - GMP manufacturing and testing of clinical grade drug required to move into phase 2 or phase 3 trials

For clinical trial applications, if IND-enabling work is in progress, funding for clinical studies would be contingent upon an IND (or equivalent) being granted and full review of the data package.

Type of therapy: Novel, repurposed and repositioned drugs, as well as natural products and devices will be considered. Therapeutic modalities of interest include small molecules, peptides, antibodies, gene therapies, antisense oligonucleotides, and stem cells. Other non-pharmacologic interventions, such as diet, meditation, and exercise, will not be considered. A detailed landscape analysis to compare competition related to the mode or mechanism of action is strongly encouraged.

Drug mechanisms or modes of action: Novel drug mechanisms and modes of action related to the biology of aging and other emerging therapeutic areas for dementia are considered high priority. These include, but are not limited to:

- Epigenetics
- Inflammation
- Mitochondrial & metabolic function
- Neuroprotection
- Proteostasis
- Synaptic activity and neurotransmitters
- Vascular function
- Other mechanisms and modes of action related to the biology of aging (e.g. senescent cells)

- Other novel mechanisms or modes of action that are supported by compelling evidence demonstrating a rational biological connection to the disease process
- **Please note:** Anti-amyloid approaches (e.g., anti-amyloid aggregation, beta-amyloid vaccines, beta- or gamma-secretase inhibitors) and cholinesterase inhibitor proposals will not be considered

UPCOMING DEADLINES

ELIGIBILITY

AWARD INFORMATION

EXPECTATIONS AND EVALUATION

The following guidance may assist you in developing a strong application that allows reviewers to better evaluate the science and merit of your proposal. The strongest proposals will contain many or all of the aspects listed below.

Please note: ADDF prioritizes novel drug candidates with composition of matter intellectual property (IP) and repurposed or repositioned drugs with strategies to develop novel IP.

Mechanisms or modes of action: Applicants are encouraged to provide a clear rationale and compelling evidence for targeting the proposed mechanism or mode of action in AD or related dementias and should specifically address these questions in the proposal:

- Is the mechanism or mode of action novel? How is the target biology more compelling than other related targets that have been tested for the disease?
- Is there human genetic evidence linking the target biology to the disease?
- Is the target expressed in disease-relevant regions of the brain (or where applicable, in the periphery) in humans and/or animal models?
- Are there changes in target mRNA/protein expression or activity in human disease specimens, and do they correlate with disease severity and cognitive functions?
- Does genetic and/or pharmacological manipulation of the target in disease-relevant in vitro (e.g., primary cultured neurons/glia or cells derived from patient iPSCs) or in vivo models alter disease phenotypes?
- If the molecular target is unknown, the strength of the evidence for the mode of action and its link to disease pathophysiology will be evaluated. The applicant should summarize the existing evidence in the proposal

Preliminary data: Applicants are encouraged to include data around the following:

- Supportive preclinical efficacy data in relevant animal models
- Evidence of blood-brain barrier penetration (for CNS targeted therapies)
- Preclinical and, if available, clinical PK/PD data on dose optimization for the intended route of administration and dosing regimen
- Preclinical, and if available, clinical safety data. Proposals should include plans to address remaining safety concerns if any are identified in earlier studies

Clinical population: Proposals including patients should provide justification for the selected clinical population and how enrollment criteria such as clinical subtype, stage of severity, known genetics (e.g. ApoE status), and neuropathology (e.g. amyloid positivity) relate to the proposed mode of action. Applicants must

provide information about recruitment of the target population to demonstrate that a sufficient number of patients are available to meet recruitment goals.

Expectations for biomarker-based proof-of-concept studies:

- Provide justification for the dose(s) selected
- Design studies to answer specific questions about a therapy's activity, including whether an intervention is safe, engages its target, induces expected downstream pharmacological effects, and leads to changes on disease-related measures
- Include biomarker outcomes that align with the proposed mechanism or mode of action and, where possible, are predictive of clinical efficacy
- Include clinical assessments that align with the appropriate domains of the clinical syndrome, stage of disease, and mechanism of action. Although these studies may not be powered to detect differences in clinical outcomes, the inclusion of cognitive and neuropsychological endpoints may be informative as exploratory outcomes. Expected directional changes that correlate with biomarker changes may be observed and can inform planning for subsequent studies
- Engage a biostatistician early in the development of the study design. Statisticians can help to determine the appropriate study design options and sample size calculations for these smaller biomarker-based studies, particularly when novel biomarkers without established effect sizes are used

Investigative team: Clinical trials often require resources beyond those available at a single organization and collaboration with other investigators and contract research organizations and consultants are encouraged.

Please note: All clinical trials receiving ADDF funding must register and submit results for "applicable clinical trials" on the **ClinicalTrials.gov Protocol Registration and Results System Information** website.

APPLICATION SUBMISSIONS

Review the **Application Instructions** for steps on applying.

LOG IN OR CREATE ACCOUNT

We encourage you to contact us if you would like to discuss your proposed project and receive initial feedback.

For scientific inquiries, please contact:

Alessio Travaglia, PhD, Interim Director, Scientific Affairs

atravaglia@alzdiscovery.org

For inquiries related to contracting and the online funding portal, please contact:

Mission Related Investments Team

grants@alzdiscovery.org