PROGRAM TO ACCELERATE CLINICAL TRIALS

UPCOMING DEADLINES

Must be received by 5:00 pm ET on the deadline date.

Letter of Intent
January 18, 2019

Invited Full Proposal
February 8, 2019

Letter of Intent
April 12, 2019

Invited Full Proposal
May 10, 2019

Letter of Intent
July 12, 2019

Invited Full Proposal
August 9, 2019

Letter of Intent
October 11, 2019

Invited Full Proposal
November 8, 2019

Average Duration

Varies (multi-year) with potential for follow-on funding.

Average Award

Up to $5 million based on stage and scope of research. Depending on the availability of funds, in certain cases, well-justified larger budgets may be considered. For studies requiring additional support, co-funding from other funding agencies or investors is encouraged.

Eligibility

Funding is open to researchers and clinicians worldwide at:

- **Academic medical centers and universities or nonprofits.** Industry partnerships are strongly encouraged.
- **Biotechnology companies.** Funding is provided through mission-related investments that require return on investment based upon scientific and/or business milestones. Existing companies and new startups are both eligible.

FUNDING PRIORITIES

The goal of this RFP is to increase the number of innovative pharmacologic interventions tested in clinical studies for Alzheimer's disease and related dementias. The PACT RFP supports clinical trials, experimental medicine, and regulatory studies for novel drugs (small molecules and biologics including antibodies, peptides, gene therapies), repurposed drugs (existing drugs that are approved for other diseases and conditions), repositioned drugs (existing drugs that have entered clinical trials for other indications and have not yet been approved), and natural products.

Specifically, the PACT RFP supports:

Early-stage human clinical trials:

- Phase 0 micro- or sub-therapeutic-dosing studies
- Phase 1 single ascending dose and multiple ascending dose studies

- Phase 2a biomarker-based proof-of-concept or proof-of-mechanism studies. These studies can validate novel molecular targets in humans and de-risk novel therapeutic approaches earlier in clinical development by assessing the potential efficacy of therapeutic interventions using pharmacodynamic outcomes

Regulatory studies:

- Non-GLP and GLP pharmacology and toxicology studies, and scale-up, 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, if not completed prior to phase 1 studies
- GMP manufacture and testing of clinical grade drug required to move into phase 2 or phase 3 trials

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Drug Targets

Current target areas of interest include, but are not limited to:

- Neuroprotection
- Inflammation
- Vascular function
- Mitochondria & metabolic function
- Proteostasis
- ApoE
- Epigenetics
- Synaptic activity and neurotransmitters
- Other aging targets (e.g. senescent cells)

Other novel targets and pathways that are supported by compelling evidence demonstrating a rational biological connection to the disease process are encouraged.

NOTE: This RFP does not support anti-amyloid approaches (e.g., anti-amyloid aggregation, beta-amyloid vaccines, beta- or gamma-secretase inhibitors) or cholinesterase inhibitors.

EXPECTATIONS

For all PACT programs, the strongest applications will possess composition of matter patents (for novel drug candidates) or strategies for developing intellectual property (for repurposed and repositioned drugs), and include preclinical packages with: i) robust target engagement and efficacy data in relevant animal model(s) and ii) demonstrated blood-brain barrier permeability (CNS targeted therapies).

For phase 1 and phase 2 programs, applications should include data on dose optimization for the intended route of administration and treatment duration for the drug candidate.

For phase 2 programs, the strongest applications will:

- Carefully select biomarkers that will measure target engagement and intermediate readouts that are proximal to clinical outcomes
- Provide strong rationale for the proposed clinical population based on the drug candidate's mode of action
- Outline strategies for successful recruitment, retention and protocol adherence, with evidence of prior success for recruitment of the proposed number and population

- Demonstrate evidence of safety from earlier clinical studies and plans to address remaining safety concerns in the proposed clinical design

ClinicalTrials.gov: All clinical trials receiving ADDF funding must register and submit results information for certain "applicable clinical trials" on the ClinicalTrials.gov Protocol Registration and Results System Information Website.

EVALUATION

All proposals will be evaluated for:

- Rational biological connection of the target to the disease pathophysiology
- Strength of preclinical data package and any available preliminary human data
- Feasibility, study design, and methodology
- Rational selection of outcome measures and clinical population
- Investigator, organizational capabilities, and project budget

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Targets

The following criteria will be used to assess the proposed drug target(s):

- 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?
- Are there pharmacodynamic readouts of target engagement available that can be incorporated into clinical studies?
- How is the target more compelling than other related targets that have been tested for the disease?

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.

Clinical Trial Design

The following criteria will be used to assess the clinical trial design:

- Are the intervention modalities (arms, allocation, dosing frequency and route) well-defined and justified?
- Are outcomes/endpoints that measure target engagement, tolerance and responsiveness included? The inclusion of direct and indirect measures of target engagement are strongly recommended for phase 2 trials.
- Have the outcome measures been validated to detect changes in the defined clinical population?
- Is the study appropriately powered to detect changes in the primary outcome in the defined clinical population?
- Is the clinical population (age, co-morbidities, genotype) well-defined and justified?
- Is the stage of disease appropriate for the drug candidate's mode of action?

- Is the clinical population enriched to exhibit the appropriate phenotype for the proposed study (e.g. positive amyloid PET for an anti-amyloid therapy)?
- Are the procedures for data collection, management and analysis well-defined? For multi-site clinical trials, have the methods for standardization of procedures been described and justified?

APPLICATION SUBMISSIONS

Review the Application Instructions for steps on applying.

ADDF FUNDING PORTAL

LOG IN OR **CREATE ACCOUNT**

The ADDF considers its application process an iterative one, and we would be happy to talk to you about your program.

For program-related inquiries, please contact:
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For application submission inquiries, please contact:
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Alzheimer's Drug Discovery Foundation

A GuideStar-Rated Charity

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