PREVENTION BEYOND THE PIPELINE

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

- One year for epidemiological analyses
- Varies (multi-year) for clinical trials

Average Award

- $50,000-$100,000 for epidemiological analyses based on scope of research
- Up to $3 million for clinical trials based on stage and scope of research. For studies requiring additional support, co-funding from other funding agencies or investors is encouraged.

Eligibility

Funding is open to researchers, clinicians, and postdoctoral fellows in the U.S. and worldwide working in:

- **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.

INTRODUCTION

The ADDF seeks to support comparative effectiveness research, prevention clinical trials, and epidemiological studies that probe whether the use or choice of drugs alters the risk for dementia or cognitive decline.

FUNDING PRIORITIES

Consortium of Cohorts for Alzheimer's Prevention Action (CAPA): Epidemiological studies contribute unmatched information on whether the risk of dementia or cognitive decline may be influenced by long-term exposure to specific foods or supplements. However, high-powered studies are needed, ideally with dose, duration, and responder profiles, in order to translate

epidemiological research into actionable interventions for testing. Through the CAPA Consortium, the ADDF funds collaborative analyses on dementia prevention using a minimum of five longitudinal cohorts, either harmonized or analyzed through parallel analysis of cohorts using a shared analysis script. More information here. More information here.

Comparative Effectiveness Research: For many health conditions, physicians have a choice of clinically equivalent drugs. Some of these drugs are being investigated for repurposing to treat Alzheimer's or related dementias, due to potential disease-modifying properties that go beyond the treatment of their approved disease indication. The ADDF will consider funding research to generate an evidence base on whether choices in the routine clinical care of pre-existing conditions could protect from dementia. Priority will be given to the comparison of drugs that are otherwise clinically equivalent for the pre-existing condition (see Box 1 in the ADDF 2016 position paper). Methods may include randomized trials or epidemiology.

Cognitive Decline and Cognitive Reserve: Cognitive decline through aging and health conditions has been linked to an increased risk of dementia. The ADDF will consider funding programs to prevent and treat these conditions, including cognitive aging, menopause-related cognitive symptoms, postoperative delirium and postoperative cognitive decline, mild and/or repetitive traumatic brain injury, and chemotherapy-induced decline. Methods may include clinical trials or epidemiology.

EXPECTATIONS FOR CLINICAL TRIAL PROPOSALS

The strongest clinical trial 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 OF CLINICAL TRIAL PROPOSALS

Clinical trial proposals will be evaluated for:

- Rational biological connection of the target to the pathophysiology of the condition
- 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 regions of the brain relevant to the condition (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 the severity of the condition and cognitive functions?
- Does genetic and/or pharmacological manipulation of the target in relevant preclinical models alter phenotypes of the condition?
- 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 condition?

If the molecular target is unknown, the strength of the evidence for the mode of action and its link to 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 well-defined and justified?
- 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:
Yuko Hara, PhD, Director, Aging & Alzheimer's Prevention
yhara@alzdiscovery.org

For application submission inquiries, please contact:
Grants and Mission-Related Investments Team
grants@alzdiscovery.org

Alzheimer's Drug Discovery Foundation

A GuideStar-Rated Charity

57 West 57th Street, Suite 904
New York, NY 10019
info@alzdiscovery.org
212.901.8000