PREVENTION BEYOND THE PIPELINE

UPCOMING DEADLINES

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

Letter of Intent
January 17, 2020

Invited Full Proposal
February 7, 2020

Letter of Intent
April 10, 2020

Invited Full Proposal
May 8, 2020

Letter of Intent
July 10, 2020

Invited Full Proposal
August 7, 2020

Letter of Intent
October 9, 2020

Invited Full Proposal
November 6, 2020

FUNDING OPPORTUNITY DESCRIPTION

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.

Specifically, the Prevention Beyond the Pipeline RFP supports:

1. **Studies Leveraging the 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**.
2. **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.

3. **Studies of 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 epidemiology or clinical trials. For clinical trial proposals, please see below detailed instructions and priorities under “Funding Priorities for Clinical Trial Proposals” and “Evaluation of Clinical Trial Proposals”.

Current target areas of interest include:

- Epigenetics
- Inflammation
- Mitochondria & metabolic function
- Neuroprotection
- Proteostasis
- Synaptic activity and neurotransmitters
- Vascular function
- Other aging targets (e.g. senescent cells)
- Other novel targets or pathways that are supported by compelling evidence demonstrating a rational biological connection to age-related cognitive decline or dementia risk

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AWARD INFORMATION

Average Award

- $50,000-$100,000 for epidemiological analyses
- Up to $3,000,000 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
- Payment structure will be negotiated and based on milestone achievements and recruitment

Average Duration

Multi-year
Potential for follow-on funding

Allowable Cost

Only direct costs are allowed. Please review our **Funding Policies**

ELIGIBILITY

Funding is open to researchers and clinicians worldwide at:

- **Academic medical centers and universities or nonprofits.**
- **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 FOR CLINICAL TRIAL PROPOSALS

For clinical trial applications, the ADDF prioritizes novel drug candidates with composition of matter intellectual property (IP) and repurposed and repositioned drugs with strategies to develop novel IP. Applications should include compelling preclinical packages with robust target engagement and efficacy data in relevant animal model(s) and demonstrate blood-brain barrier permeability for CNS targeted therapies.

For clinical trials, we prioritize applications that:

- Include data on dose optimization for the intended route of administration and treatment duration for the drug candidate
- 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
- Carefully select biomarkers that will measure target engagement and intermediate readouts that are proximal to clinical outcomes
- Demonstrate evidence of safety from earlier clinical studies, where available, and plans to address remaining safety concerns in the proposed clinical design
- For repurposing studies, a supplier that will provide sufficient quantities of the drug or compound to complete the study aims has been identified

EVALUATION OF CLINICAL TRIAL PROPOSALS

All clinical trial proposals will be evaluated for:

1. Rational biological connection of the target to the disease pathophysiology

- Is this a novel target? How is the target more compelling than other related targets that have been tested?
- Is there human genetic evidence linking the target to the condition?
- 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 disease 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?
- 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.

2. Strength of the preliminary data

- Are there compelling preclinical and clinical data to justify the proposed study?
- Does the application include data supporting target engagement?

3. Feasibility, research design, and methodology

- 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 where possible.
- 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?
- 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?

4. Justification for proposed clinical population

- Is the clinical population (age, co-morbidities, genotype) well-defined and justified?
- Is the clinical condition 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. high inflammation biomarkers for an anti-inflammatory agent)?

5. Investigative team, organizational capabilities, and project budget

- Do the PI(s) and collaborators have the appropriate experience to design and execute the project? Note: Clinical trials often require resources beyond those available at a single organization and

collaborations with other investigators and contract research organizations are encouraged.

- Do the investigators have complementary and integrated expertise?
- Is the budget appropriate for the proposed aims?

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.

ADDF FUNDING PORTAL

LOG IN OR **CREATE ACCOUNT**

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

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