NEUROIMAGING AND CSF BIOMARKER DEVELOPMENT PROGRAM

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 with potential for follow-on funding. Multi-year proposals can be considered.

Average Award

$150,000-$600,000 based on stage and scope of research. Larger amounts will be considered for PET ligand development for regulatory or clinical work. 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

Given the pathological heterogeneity of Alzheimer's disease and related dementias, new biomarkers are needed to more accurately characterize specific underlying pathophysiology.

This RFP seeks to support the development of CSF and neuroimaging biomarkers for multiple contexts of use (see below) that include but are not limited to:

1. **Clearly demonstrate target engagement for novel therapeutics**
   The development of biomarkers that can serve as measures of target engagement for novel targets such as neuroinflammation features (e.g. microglial activity, cytokine production, astrocytic activity), synaptic damage, metabolic activity, mitochondrial dysfunction, vascular health and epigenetic changes, among others, are of particular interest. High priority will be given to projects developing biomarkers that can be used in combination with therapies currently in development and serve as companion biomarkers.

2. **Detect signs of disease earlier and monitor progression**
   We are seeking programs developing sensitive biomarkers that can detect disease earlier than currently available tests. This includes biomarkers that can predict and monitor conversion from cognitively healthy to mild cognitive impairment (MCI) or MCI to Alzheimer's disease. We also seek prognostic markers that can predict rates of cognitive decline.
3. **More accurately diagnose and distinguish between dementia subtypes**
   Many types of dementias can present with similar clinical features, and patients often show overlapping pathologies. At present, it is challenging to distinguish between dementia subtypes. Biomarkers that can distinguish between subtypes and stratify patients in clinical trials are of high priority.

Biomarker Targets

Novel biomarkers of **neuroinflammation** and **synaptic integrity** are considered high priority. Other target areas of interest include, but are not limited to:

- Neurodegeneration
- Vascular injury or blood-brain barrier integrity
- Mitochondria & metabolic function
- Protein misfolding/proteostasis
- Oxidative stress
- White matter changes

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

EXPECTATIONS AND EVALUATION

Cerebrospinal fluid (CSF) biomarkers should be able to differentiate between dementia subtypes, increase diagnostic accuracy, be used for early detection before clinical onset, or serve as a companion diagnostic to a therapeutic in development. The biomarker can be a single analyte or panel of analytes; however, the proposed signature should have proof-of-concept data in human patient samples and the specific analyte combination should be well justified.

The ADDF has limited interest in CSF measures of amyloid and tau.

Neuroimaging:

- **Positron emission tomography (PET):** These projects should focus on ligands for target engagement and pharmacodynamic measurements of novel and repurposed therapeutics. This RFP will support pharmacokinetics, safety, and synthesis, as well as clinical development of novel PET ligands. The investigative team should include individuals with experience in developing PET ligands for human use.
- **Magnetic resonance imaging (MRI):** The proposed structural or functional approach should already have proof-of-concept data in human patients and be translatable for clinical use. Approaches that can measure novel targets and are significant improvements on what is currently available in MR techniques are a priority.
- **Magnetic resonance spectroscopy (MRS):** The ability to detect specific molecules or proteins relevant to the disease or a specific drug candidate should be demonstrated in the preliminary data section of the application.

Functional activity measures applicable to this RFP include electroencephalogram (EEG), magnetoencephalography (MEG), and transcranial magnetic stimulation (TMS). Only highly novel techniques or analyses for EEG, MEG, and TMS will be considered. These proposals should meet the following criteria:

- The proposed approach is a marked improvement on already existing functional measures used in clinical practice for diagnosing and monitoring dementias
- The biomarker and its biological connection to the disease should be established and clearly described
- Proof-of-concept data should be completed in human patients

Other novel approaches:

The biomarker should already be identified and validated in at least a small number of human samples. It should be clear how the approach is an improvement upon currently existing biomarkers.

All proposals should address the following:

- **Potential for Commercial Translation**
  The path to commercialization should be considered for all applications, and it should be clear how the proposed biomarker would fit into the current clinical landscape. The applicant should articulate where in the path to commercialization the study falls and what is the proposed plan forward. Clear milestones and go/no-go decision points should be provided. Identification of potential future commercial partners is encouraged.
- **Context of Use**
  This RFP will consider context of use categories that will advance drug development for Alzheimer's and related dementias. These categories, as defined by the FDA, include diagnostic, monitoring, predictive, prognostic, pharmacodynamic/response, and susceptibility/risk biomarkers. The expected context of use, which defines a biomarker's intended use clinically as a diagnostic or in drug development, should be described in the application.
- **How the Proposed Biomarker Compares to Currently Available Biomarkers**
  Currently available imaging and CSF markers of amyloid and tau can distinguish between Alzheimer's disease and healthy control individuals with high specificity and sensitivity. The applicant must demonstrate the advantage of their approach with these tests in mind (cheaper, easier to use, less invasive, etc.), and how it compares to the sensitivity/specificity of what is currently available (CSF Aβ, CSF tau, PET scans, MMSE, etc.).

In addition, all proposals will be evaluated for:

- Biological plausibility linking the biomarker to disease pathophysiology
- Scientific and technical merit of the proposed approach
- Biomarker's context of use
- Strength of preliminary data using the proposed biomarker
- Level of innovation
- Investigator, organizational capabilities, and budget for the project

The ADDF has limited interest in funding measures of cognition and function. Peripheral biofluids and digital approaches are not eligible through this RFP.

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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