

## ADCS Combination Therapy Initiative Letters of Interest (LOI)

### Introduction

The Alzheimer's Disease Cooperative Study (ADCS) at the University of California, San Diego (UCSD) is currently seeking letters of interest for combination therapy initiatives that address a spectrum of disease targets and mechanisms in Alzheimer's Disease (AD).

### Background

It is increasingly recognized that there is no single pathogenic mechanism in AD. While the recent approval of disease modifying treatment, targeting amyloid- $\beta$  ( $A\beta$ ), is promising, treatment that targets only one single pathogenic mechanism in AD will continue to be of limited effectiveness. Designing treatments that include a combination of pharmacological and lifestyle interventions that target multiple pathways could be an effective therapeutic approach, and aligns with the NIH Research Implementation Milestones ([AD+ADRD Research Implementation Milestone Database | National Institute on Aging \(nih.gov\)](#)) and the Alzheimer's Association (AA) Part the Cloud initiative. The need for advancing multiple targets includes recognition for novel adaptive trial designs that employ data-driven approaches and incorporate existing and new biomarkers to robustly test the efficacy of multi-modal interventions that combine pharmacological and/or lifestyle interventions. To achieve this, collaboration will be pivotal to progress in combined therapeutic approaches for AD.

### Objectives

This initiative focuses on cutting-edge projects primed for clinical trial. The intent of this program is to establish a collaboration with the ADCS to accelerate successful, external peer-reviewed NIH or AA grant applications to fund proof of concept multi-site combination therapy trials. Projects conducted under this initiative will leverage the expertise of the ADCS at UCSD to work in collaboration with investigators to select the best and most exciting combination candidates and design the proper protocols to conduct multi-site clinical trials. **Of particular interest are proposals that have promising single-site pilot or phase I data available to support the application.**

### Goals of the combination therapy trials include:

- Enhanced efficacy achieved via a combination approach
- Reaching optimized therapeutic mechanism of action
- Ensure inclusion of diverse populations
- Tracking person-specific trajectories of treatment response

**Major Strategic Priorities under this call for LOIs** include but are not limited to multi-modal interventions that include a **combination of any** of the following:

- Non-pharmacological lifestyle interventions (i.e. sleep, social engagement, exercise, cognitive training)

- Repurposed compounds
- Natural products
- Novel candidates
- Existing treatments for AD in combination with any of the above

Projects that include only a single drug or non-pharmacological candidate are welcome with the understanding that we will work to identify other promising candidates to evaluate in combination.

### **Budget Requirements**

*There are no pre-designated allocated funds for this program.* As such, this program does not have a predetermined budget limitation for individual proposals. Selected proposals will culminate into a grant application to NIH or AA to fund the trial. Funded trials will be coordinated by the ADCS in collaboration with the study investigators. We hope that 3-5 projects will be selected to advance to grant application.

### **Applicant Eligibility**

Faculty members and researchers at all levels from any university are eligible to apply.

### **Proposal Guidelines**

Interested applicants should submit a Letter of Intent (LOI) including the following elements:

- Project Title
- Principal Investigator Information
  - Name
  - Title
  - Primary Department Affiliation
  - Physical Address
  - Email Address
  - Phone
- Description of institutional/organization environment
- Overview of research success to date
- Outline of proposed work (2 page maximum) including:
  - Specific Aims
  - Preliminary data to support intervention
  - Brief project description

### **Submission Dates**

- Submission and Deadline
  - This call for LOIs is open until further notification. Feel free to verify with the Program Manager.
  - LOIs should be uploaded via our website at <https://www.adcs.org/adcs-combination-therapy-initiative-request-for-proposals/>

## **Evaluation Criteria**

Letters of intent will be reviewed and evaluated based on the following criteria:

- Potential impact and feasibility of the proposed work, including pilot or early phase data
- Alignment with the objectives, goals and major strategic priorities of the ADCS Combination Therapy Initiative

Following this review, applicants will receive additional information regarding next steps. Promising proposals will proceed to an evaluation by the Intervention Selection Committee. Accepted proposals will lead to future grant applications to NIH or AA, which will be submitted on a rolling basis based on standard cycle dates.

## **Contact information**

For questions regarding the requirements for submission of a proposal or to request additional information, please contact Michelle Herman, Program Manager, at [mherman@health.ucsd.edu](mailto:mherman@health.ucsd.edu).

## **Why Collaborate with the ADCS?**

At UC San Diego, the Alzheimer's Disease Cooperative Study (ADCS), founded in 1991 and currently co-directed by Howard Feldman, MD and Judy Pa, PhD, has accelerated the discovery, development, and testing of new pharmacological and lifestyle-based treatments for Alzheimer's disease. The ADCS is a leading and highly regarded component of the comprehensive research and treatment effort at UC San Diego. It coordinates trials across a national network of academic institutions and specialty centers dedicated to Alzheimer's prevention and treatment and is committed to the support and success of this Combination Therapy Initiative.