

“Collaboration 4 Cure (C4C)”

Call for Proposals from San Diego Alzheimer’s Researchers: Alzheimer’s San Diego, in partnership with the Salk Institute (Salk), Sanford Burnham Prebys Medical Discovery Institute (SBP), The Scripps Research Institute (TSRI), University of California, San Diego (UCSD), and the J. Craig Venter Institute (Venter), are seeking proposals for the locally funded and managed “Collaboration 4 Cure (C4C)”, an innovative program to harvest the best research ideas and put them on a translational path towards identifying effective therapies for Alzheimer’s disease. The C4C program will primarily award investigators the drug discovery capabilities and services of SBP or TSRI through contracts managed by Alzheimer’s San Diego.

Background: Collaboration 4 Cure is a ground-breaking initiative led by Alzheimer’s San Diego, the City and County of San Diego, and San Diego’s premier research institutes to come together and combine resources to accelerate drug discovery projects to find a cure for Alzheimer’s disease right here in San Diego. The funding goal for the C4C is \$7 million over the next five years. San Diego has a uniquely dynamic, entrepreneurial and creative science and technology heritage, with a track record of achievement in the creation, commercialization and sustainment of disruptive technologies emanating from its medical science-based companies and leading research institutes and universities. C4C is an innovative partnership between Alzheimer’s San Diego and five local institutions, the Salk, SBP Discovery, TSRI, UCSD, and the Venter, to provide access to world-class translational drug discovery infrastructure and expertise for collaborative, open-source, pre-competitive, early-stage research towards identifying and validating starting points for the development of new therapeutic small molecules that can progress to the clinical treatment for Alzheimer’s disease and related dementias.

General Considerations:

Projects of interest will benefit from the development and optimization of high-throughput screening (HTS) assay(s), assay automation, and synthetic chemistry capabilities. Successful awardees will be provided access to the assay development & HTS teams at SBP or TSRI’s technology cores to enable the development of screens through access to their drug discovery infrastructure. These efforts will culminate in a preliminary HTS data package, to include a pilot screen that demonstrates robustness and operating characteristics of the developed assay, and development of follow-up assays needed to identify a valid “hit” compound. Projects that successfully achieve a robust “preliminary HTS data” package may be considered in subsequent years of this program for advancement through hit confirmation and validation to the screening of large chemical libraries of compounds. In parallel, it is anticipated that successful projects with robust HTS data packages may be used for joint applications to additional/alternate sources of funding (e.g. for HTS screening of large chemical collections such as the 385,000 NIH Molecular Libraries Small Molecules Repository (MLSMR) compounds through the NIH PAR-14-284 RFA, or additional grants from other agencies and foundations).

Important Deadlines: Letters of Intent (LOI) must be received by 5:00 PM Pacific Time on Friday, August 26, 2016. LOIs will not be accepted after this date. No exceptions will be made. Letters of intent (LOI) are submitted directly to c4c@alzsd.org with the subject line “**C4C LOI submission**”.

For those invited from their LOIs to submit a full proposal, these applications must be received by 5:00 PM Pacific Time on October 17, 2016. Scientific and technical review will be conducted between October to November 2016. The C4C program will make final announcements of selected recipients no later than December 15, 2016.

Important Deadlines Summary for this program are:

Friday, July 22, 2016	Letter of Intent (LOI) Opens
Friday, August 26, 2016	LOI deadline
Monday, September 12, 2016	Full applications invited
Monday, October 17, 2016	Full applications due
Monday, December 15, 2016	Anticipated award notifications

Eligibility: *Both academic, non-profit and small businesses with primary operations in San Diego are eligible.*

The C4C program is open to any principal investigator holding a faculty appointment at any accredited, greater San Diego area-based University, academic institution, hospital, medical practice or not-for-profit medical or life sciences research institution, inclusive of stakeholder institutes: Salk, SBP, TSRI, UCSD, and the Venter. All applicants will be required to obtain institutional endorsement of their research application from their respective home institutions. In addition, small business enterprise organizations (as defined by the Small Business Administration (SBA) [Table of Small Business Size Standards](#) under NAICS Codes 325412, 541711 and 541712 and also meet [NIH SBIR/STTR Eligibility Criteria](#)) are eligible to apply. Small businesses must submit documentation of net assets and annual earnings for consideration during the letter of intent process.

IMPORTANT: *Consultation with either the SBP or TSRI Drug Discovery centers is encouraged in developing the LOI.*

Application Procedures: Both letters of intent (LOI) and invited applications are submitted directly to the Alzheimer's San Diego contact email for this program: c4c@alzsd.org with the subject line "**C4C LOI submission**" or "**C4C Invited Application submission**".

The LOI will consist of a two (2) page (8.5" x 11", 0.5" margins all around, 11-pt ARIAL font) application that should address the following:

- Background/Rationale – why is the target important, indication, genetics, proof of concept and citations
- Preliminary Data – target modulation-phenotype & assays (use/cite figures from key publication(s); embedded figures should be legible with legends in 8 pt Arial font)
- Experimental plans (approach, assay concept, format and cascade of hit progression assays)
- Readiness of applicant's reagents and assays (necessary reagents created, qualified and available)

In addition, the applicant may include up to two (2) reference documents (in PDF format) to support their LOI. Each reference document may only include one paper, abstract or other documentation. Multiple references combined into one (1) PDF will not be accepted. LOIs will be evaluated and select investigators will be invited to submit full applications. Additional information regarding review evaluation for LOIs and applications is included in "Review Process" section below.

For those LOI applicants invited to submit full project proposals, it should be a 5-page proposal that should include the elements of the LOI with more specific details about:

- The research plan and clear and explicit definition of the hit progression cascade (including a flow chart of assays, go/no-go criteria, expected number of compounds, and clear definition of responsible party for each assay)
- Rationale and purpose for each secondary and tertiary assay on compounds that advance to that stage
- Availability of purchase, or path to scale up & produce key reagent(s) for the project (engineered or base cell lines, purified proteins, enzymes, antibodies) and estimates of their costs and time to

delivery

- In cases where the applicant's lab is the only available source of key reagent(s) and/or key secondary (2°) and tertiary (3°) assays, a brief budget and budget justification (table), with timelines for deliverables. (see "**Available Funding**" below)
- Applicants are expected to develop the research plan in consultation with either SBP or TSRI with input on feasibility. They will develop a 1-page quotation for services and cost of materials, and time to achieve each milestone: (1) reagent transfer and scale up, (2) 1° and 2° assay developed and validated w/ pilot HTS on a small (1,000 – 5,000) compound collection, (3) hit confirmation & validation from initial pilot hits through 1° and 2° by (SBP or TSRI) which will be part of the application.

Review Process: Letters of Intent (LOIs) will be reviewed by a Joint Review & Operations Committee (JROC) comprising representatives from Alzheimer's San Diego, representatives of San Diego Drug Discovery Consortium stakeholder institutions, and 3-5 representatives of local biotech or pharmaceutical companies. The criteria on which projects will be evaluated, with an emphasis on collaborative, translational research are:

- Plausibility of the project based on known biology of proposed target and therapeutic agent for Alzheimer's disease or related dementias.
- Status of intellectual property, "competition", freedom-to-operate or prior art of a process or reagent.
- Appropriateness of target for chemical modulation ("druggability") and pre- or clinical proof-of-concept (POC) studies.
- Technical feasibility of the project proposed, including the readiness of investigator-created reagents and current benchtop assays for screening.

Available Funding: The primary purpose of the C4C program is to provide access to early drug discovery capabilities rather than direct transfer of funds to individual investigator laboratories. Awards will provide services to investigators in the form of early drug discovery capabilities and is not a direct funding mechanism for individual investigator laboratories. Successful applicants will partner with, and obtain access to resources and services of the SBP Discovery or TSRI drug discovery centers including assay automation, HTS, and synthetic chemistry capabilities, which can be applied to the discovery and development of innovative first-in-class compounds that have the potential to be developed into therapeutics. The funds will be administered by Alzheimer's San Diego and used to remit against approved quotes for services to these partnered centers.

In very specialized cases, with approval of the Joint Steering Committee limited funds may be made available to a PI laboratory to enable, for example, scale-up production of unique critical reagents or key assays or services that only the PI's laboratory can perform. Investigators will submit invoices against pre-approved service quotes. Please note that the C4C program is a unique funding opportunity that provides access to resources or specific supplemental funding to achieve drug discovery and translational critical path items and is NOT meant to replace or augment an operating grant directed towards basic research or to recruit new research personnel, launch major new research directions, fund general operating support for the lab or purchase equipment with applications beyond the project.

Mechanism of award, reporting requirements and allowable costs: The mechanism of the award is to provide access to early drug discovery capabilities rather than direct transfer of funds to individual investigator laboratories. It is expected that successful applicants will confer monthly or as needed with the project team and JROC. Quarterly milestones will be evaluated for each awardee by the Joint Steering Committee and project continuation will be linked to the attainment of milestones. In addition, financial reports of expenditures will be required before additional funds are released. Continuation of the funding of the project's duration is contingent upon the timely receipt of scientific progress and financial reports. In such cases, where project have reached a scientific or technical impasse, the unspent, non-invoiced funds may be redeployed to

other projects in the overall C4C portfolio upon recommendation by the JROC and approval by the JSC. PI of such defunded or terminated projects may wish to reapply if they are able to demonstrate the prior impasse has been overcome (technically or new research) and that novelty and relevance are still valid.

Budget and Duration: The C4C program anticipates funding multiple awards with service quotations of \$35,000 - \$65,000 for each project, depending on assay complexity. Duration of awards is one (1) year and contingent upon attainment of specific milestones. It is envisioned that projects that successfully achieve a robust preliminary HTS data package may be advanced for funding of full-scale HTS, hit confirmation, validation and expansion in the subsequent year (year 2), through an expedited, competitive review. Projects LOIs that already demonstrate achievement of “HTS ready” status, may be reviewed, considered and awarded Y2 levels of funding to enable service providers to proceed immediately to HTS, hit confirmation and hit validation.

Confidentiality: Consistent with Alzheimer’s San Diego’s policies, members of all committees will not share the information provided by applicants through the registration and application process except with directors, officers and/or representatives of stakeholder institutions, as deemed necessary. Nonetheless, applicants should not provide confidential information, such as chemical structures, at the LOI stage.

Materials and Data Sharing: Awarded applicants will be required to provide necessary, unique reagents that are not commercially available and necessary for their proposal, such as cells expressing recombinant enzymes/proteins, primary and secondary antibodies, tagged peptide substrates, and available positive controls (e.g., a known inhibitor of the target) to the translational partners (SBP or TSRI) under an MTA for purposes related to this C4C pre-competitive program.

Intellectual Property: All pre-existing intellectual property will remain the exclusive property of the party that created it prior to or independent of the funded research. During the term of the funding period, new inventions will be subject to Alzheimer San Diego’s Patent Policy existing with or to be signed with the awardee’s institutions at the time of approving the award.

Disclaimer: Last year the National Alzheimer’s Association® voted to consolidate the independent chapters into a single nonprofit entity controlled from its Chicago headquarters. In late 2015, the Board of the San Diego/Imperial Chapter of the Alzheimer’s Association® decided to separate from the National Alzheimer’s Association®. Alzheimer’s San Diego, an independent local organization was formed in order to best serve those affected by Alzheimer’s and dementia in San Diego by ensuring a local governing board with local decision-making and that funds raised in San Diego remain in San Diego. Alzheimer’s San Diego is **NOT** affiliated with the Alzheimer’s Association®, the Alzheimer’s Association® San Diego/Imperial Chapter, the Alzheimer’s Drug Discovery Foundation, the Alzheimer’s Foundation of America (AFA) or the Bright Focus Foundation.

For more information about any of the grant schemes or the application process, please contact Alzheimer’s San Diego at c4c@alzsd.org and your email will be directed to the scientific and program staff, who will respond by email or phone within 2-3 days.

