Part the Cloud Translational Research for Alzheimer's Disease Program: Enable the Molecule for Artificial Intelligence-Discovered Programs (PTC-EM-AI) Funding Program

Program Objective:

The Alzheimer's Association is pleased to announce a new funding initiative under Part the Cloud (PTC): Part the Cloud - Enable the Molecule for Artificial Intelligence-discovered Programs (PTC-EM-AI). This first-of-its-kind program is designed to bridge the gap between artificial intelligence (AI)-driven therapeutic discovery and the experimental work required to advance AI-generated hits into viable, translational lead candidates for Alzheimer's disease and related dementias (AD/ADRD). PTC-EM-AI will identify and invest in therapeutic programs that specifically emerge from artificial intelligence and machine learning (AI/ML) approaches, supporting them at the critical lead-optimization and investigational new drug (IND)-enabling stage.

Background:

Part the Cloud has been a driver of innovation in the clinical trials space since its inception. In partnership with the Alzheimer's Association, PTC is committed to accelerating the development of treatments that can alter the course of Alzheimer's disease and related dementias (AD/ADRD). In parallel, advances in AI and machine learning (ML) are reshaping how therapeutic hypotheses are generated, how targets are prioritized, and how new chemical matter is proposed. Yet, across the biopharmaceutical ecosystem, a persistent and well-documented translation gap exists between discovery-stage innovation and the availability of a therapeutic candidate that is sufficiently optimized, developable, and supported by data to advance into IND-enabling studies and early clinical testing.

AI-enabled discovery approaches have advanced rapidly and now include methods that integrate multi-omics and disease data, generative models that propose novel small molecules, and structure-based approaches that improve protein and biologics design. A recent peer-reviewed analysis of AI-native biotech clinical pipelines reported rapid growth in the number of AI-discovered molecules entering clinical trials and provided early evidence that AI methods can identify or design molecules with better clinical success rate. Specifically, the analysis reported that out of 24 AI-discovered molecules had completed Phase I trials; 21 were successful – a success rate of 80–90%. Industry standard success rates historically range from ~40–65% demonstrating the potential power of this approach.

Despite these advances, many AI-derived programs still face the hurdle of transitioning between *in silico* discovery outputs and an optimized, development-ready candidate. This translation work includes rigorous *in vitro* and *in vivo* pharmacology, pharmacokinetics (PK) and pharmacodynamics (PD), and biodistribution, central nervous system (CNS) exposure, off-target and safety liability assessment, developability and formulation considerations, and generation of a clear target product profile and evidence package that can support subsequent IND-enabling development. Historically, this gap is under-resourced and seen as high risk.

This first-of-its-kind funding mechanism aims to bridge this gap by de-risking and accelerating optimization of AI-originated therapeutic leads. PTC-EM-AID is positioned so that promising AI-derived insights do not stall at discovery but instead advance into the AD/ADRD therapeutic pipeline. The program prioritizes projects where AI/ML was central to the generation, selection, or optimization of the lead series and where a clear experimental plan will deliver a translationally credible lead candidate, supported by rigorous data packages, defined milestones, and a clear path to subsequent IND-enabling work and clinical development.

Entry Criteria:

Applicants must demonstrate readiness to execute a milestone-driven lead optimization program (hit-to-

lead complete or late hit-to-lead), with the following in place at the time of application:

- Documented AI-discovered origin: Evidence that AI/ML methods were central to target identification and or hit/lead generation and prioritization, with clear records sufficient for verification and reproducibility.
- Qualified hit or lead series: At least one hit or lead series with experimentally confirmed activity in disease-relevant assays, plus an assay cascade suitable for SAR-driven optimization.
- Clear AD/ADRD biological rationale: A mechanistic link between target or pathway and AD/ADRD, with a rationale for disease modification or clinically meaningful benefit.
- Early selectivity or specificity: Preliminary evidence of selectivity or specificity, or a validated plan and assays to establish it early in the project.
- Initial developability and liability profile: Early data appropriate to modality (for example, solubility, stability, permeability, metabolic stability for small molecules; stability, aggregation, expression feasibility for biologics) and a defined plan to address known liabilities.
- Preliminary PK feasibility plan: Either initial PK data or a defined, near-term plan with appropriate assays and analytical methods to establish exposure and guide optimization.
- Preliminary Target Product Profile: Draft TPP defining intended patient population, route of administration, key attributes for a development candidate, and differentiation hypothesis.
- Project feasibility and resourcing: A credible chemistry or engineering plan, access to required platforms (CRO or internal), and a milestone plan with clear go/no-go criteria.

Entry Criteria Option B: IND-Enabling Track

Applicants must demonstrate readiness to execute IND-enabling studies and activities that support an IND (or international equivalent) submission, with the following in place at the time of application:

- Documented AI-discovered origin: Evidence that AI/ML methods were central to target identification and or hit/lead generation and prioritization, with clear records sufficient for verification and reproducibility.
- Candidate nomination readiness: A nominated development candidate, or a clearly bounded short list with candidate selection criteria and a plan to lock the candidate early in the award period.
- Robust pharmacology package: Confirmed potency and mechanism in relevant systems, with target engagement evidence and a defined translational biomarker strategy.
- Selectivity and safety de-risking: A defined safety liability profile and off-target risk assessment appropriate to modality and target class, with mitigation strategy where needed.
- PK and exposure foundation: *In vivo* PK supporting dose and exposure rationale, including brain exposure or CNS-relevant distribution where appropriate, plus PK/PD linkage when feasible.
- Developability and formulation foundation: Data supporting feasibility for formulation and stability consistent with the intended route of administration and dosing paradigm.
- CMC readiness: A feasible CMC plan including route/process feasibility, analytical methods plan, stability approach, and a plan for producing material suitable for IND-enabling studies.
- Finalized Target Product Profile and development plan: A finalized TPP and a stage-appropriate regulatory strategy aligned to IND-enabling requirements, including planned studies and timeline.
- IP and freedom-to-operate plan: A clear IP position and plan suitable for advancing into IND-enabling and early clinical development.

Supported Activities (Lead Optimization and IND-Enabling):

A. For Lead Optimization and Candidate Selection

- Iterative medicinal chemistry or biologics engineering, SAR development, and compound or variant triage.
- *In vitro* ADME and developability profiling (for example, solubility, permeability, metabolic stability, CYP and transporter interaction risk, plasma protein binding; for biologics, stability, aggregation, viscosity, expression and purification feasibility).
- *In vivo* pharmacokinetics, biodistribution as relevant, and preliminary brain exposure studies, including establishment of PK/PD relationships where feasible.
- Target engagement and mechanism-of-action studies, including development and validation of translationally relevant biomarker assays.
- Early safety and tolerability de-risking (non-GLP), including selectivity panels and *in vitro* liability screens (for example, ion channel, genotox screens as appropriate, cytokine release risk where relevant).
- Proof-of-concept efficacy studies in disease-relevant models appropriate to the mechanism and modality.
- Early formulation feasibility and developability risk reduction (non-cGMP), including stability and compatibility assessments.
- CRO activities and specialized assays required to execute the milestone plan.

B. IND-Enabling Activities (for IND-Enabling Track proposals)

- IND-enabling pharmacology and safety pharmacology studies required for regulatory progression.
- IND-enabling toxicology studies, including dose range finding and GLP toxicology as appropriate.
- Biodistribution and tissue cross-reactivity studies relevant to modality and target.
- CMC activities required to support IND-enabling studies, including analytical method development, stability studies, and manufacturing of material suitable for IND-enabling and early clinical needs (includes cGMP where required).
- Formulation development to support IND-enabling studies and initial clinical dosing.
- Regulatory documentation and IND preparation activities when directly tied to completion of the IND-enabling package and planned submission.

Activities Not Supported

- Those focused on purely computational methodology or algorithm development without experimental validation of the therapeutic lead (i.e. rationale for the selected target and/or biological relevance of the target).
- Activities unrelated to lead optimization, candidate selection, or IND-enabling readiness.
- Platform development or general AI tool building that is not directly tied to advancing a specific AI-discovered therapeutic program.
- Drug repurposing projects focused on approved or previously clinically tested drugs.
- Clinical trial execution.

Eligible Therapeutic Mechanisms:

All therapeutic modalities will be considered, including but not limited to small molecules, PROTACs, antibodies, antisense oligonucleotides (ASOs), gene therapies, and other novel biologics. Applications may target a wide range of validated or emerging disease mechanisms relevant to Alzheimer's disease

and related dementias, such as amyloid, tau, neuroinflammation, synaptic dysfunction, or other neurodegenerative pathways. Only approaches with the potential for disease modification will be considered; symptomatic treatments without disease-modifying potential are not within the scope of this RFA.

Applicants should clearly specify the entry point for their proposed project within the IND-enabling timeline and provide a well-justified rationale for how the proposed work will directly support clinical advancement. Funded projects must remain strictly within the IND-enabling stage; applications that include activities from earlier discovery phases or later clinical trials will not be considered.

Funding and award period:
Each PTC award is limited to a total award amount of $1,000,000 (direct and indirect costs) for a duration of up to three years. Indirect costs are only allowable for non-profit organizations, and are capped at 10 percent of total direct costs, inclusive of indirect costs for any subcontracts. For-profit organizations are not permitted indirect costs.

Detailed guidelines on allowable and not allowable costs are included below.

The Alzheimer's Association reserves the right to not allow unbudgeted expenses.

Key Dates:
LOI and application submissions must be received by 5:00 pm Eastern time by their respective deadlines. Late submissions will not be accepted - *no exceptions.*

Letter of Intent Launch	**By August 31, 2026**
Letter of Intent Deadline*	**October 20 2026, 5:00 pm ET**
Letter of Intent Deadline* ISTAART MEMBER	**October 22, 2026, 5:00 pm ET**
Application Deadline	**January 5, 2027, 5:00 pm ET**
Application Deadline ISTAART MEMBER	**January 7, 2027, 5:00 pm ET**
Application Review	**December 2026–February 2027**
Award Notifications	**By March 15, 2027**

*** Note, due to the high number of submissions, specific feedback and reviewer comments are not provided at the LOI stage.**

Eligibility and Ineligibility Considerations:
To avoid disqualification, investigators are encouraged to carefully consider these eligibility and ineligibility requirements before applying. The Alzheimer's Association reserves the right to find an investigator ineligible to submit to a particular program, based on the guidelines below. This section describes general inclusion and exclusion criteria. Specific requirements and additional exclusions to eligibility are noted in some detailed competition descriptions.

- Eligibility (Applicant):
  - **The Alzheimer's Association recognizes the need to increase the number of scientists from underrepresented groups to strengthen the research enterprise for Alzheimer's and related dementia. Scientists from these groups are encouraged to apply**.

- Applicants must be considered full-time employees based on the organization/ institution definition of full-time.
- Applicants must hold a full-time position at their organization that is equivalent to the level of Assistant Professor or above. Postdoctoral fellows are not eligible to apply, however, they can be listed on the proposal as key personnel.
- The Alzheimer's Association reserves the right to request further documentation to confirm eligibility of an applicant.
- Only one primary PI per application. Multiple PI projects are not allowed. However, collaborators may be included as key personnel on the project.

- Eligibility (Organization/ Institution):
  - In general, public, private, research laboratories, medical centers, hospitals and universities are eligible to apply. For profit organizations are eligible to apply.
    - State and federal government-appropriated laboratories in the U.S. and abroad are prohibited from serving as the applicant institutions for this program. However, state and federal government scientists can participate as collaborating scientists with research teams from other eligible applicant institutions.
  - For the Letter of Intent (LOI), you will be required to either of the following:
    - a W-9 that is signed and dated within the past five years by the signing official for US entities
    - a W-8 or W-8-BEN that is signed and dated within the past five years by the signing official
    - The form must include the EIN, TIN or VAT number
  - For non-profit organizations (non-academic), additional documentation may be required to confirm your organization has segregation of duties between transaction execution and transaction recording.

- Ineligibility (Applicant):
  - Individuals currently enrolled as a student in an undergraduate, master or doctoral program are not eligible, regardless of prior degree status.
  - Postdoctoral fellows or staff below the rank of Assistant Professor (or equivalent) are not eligible.
  - Temporary, part time, or acting faculty are not eligible.
  - Investigators who are delinquent in reporting to the Alzheimer's Association. The Alzheimer's Association will not accept new grant applications from investigators currently awarded an Association grant who are delinquent in submitting required reports and other deliverables on active grants. Investigators that have previous Alzheimer's Association awards closed as 'Incomplete' are not eligible to apply without exception. This policy will be strictly adhered to with no exceptions.
  - Overlapping funding of more than one Alzheimer's Association grant is not allowed. Investigators with Association awards in programs from specific program announcements may still apply to a program listed in this call, but the project must be distinct from their current award. Overlap with research or clinical fellowship programs or this program are not allowed.
  - Applications that represent the same aspects of a project should not be submitted to different programs of the Alzheimer's Association. There are some exceptions so please contact grantsapp@alz.org if you have questions.
  - Current Medical and Scientific Advisory Group (MSAG) and International Research Grant Programs (IRGP) Council members of the Alzheimer's Association cannot serve as principal investigators in any award. They may serve as key personnel or collaborators, provided there is no financial benefit and/or salary allocated to them.

- Ineligibility (Organization/ Institution):
  - State and federal government-appropriated laboratories in the U.S. and abroad are

prohibited from serving as the applicant institutions for this program.

- Applications will not be accepted if the institutional official responsible for fiscal oversight of the award also serves as the Principal Investigator (PI) on the project. Additionally, no familial relationship may exist between the PI and the institutional official with fiscal authority.
- Applicants CANNOT submit more than one proposal to any of the programs in the current grant competition—even if the proposals cover distinctly different topics (i.e. only one application is allowed regardless of the distinct areas of focus). It is allowed for members of the same team to submit different aspects of a project to different programs, as long as they are complementary and not the same project.
- Applicants may revise and resubmit an application that was previously submitted for an earlier grant cycle; however, a new LOI is required each year. A current LOI corresponding to the application year must accompany each application. Revisions of previous submissions will be treated as new applications. Efforts will be made to provide some continuity in reviews. The resubmission of an approved LOI does not guarantee that you will be invited to resubmit a full application in a future cycle. Resubmissions may be submitted to a different program in this call and still be a resubmission. Resubmissions are reviewed holistically again, and merely responding to reviewer critiques is not enough to be funded on resubmission.

Note: *Alzheimer's Association grants are generally open to scientists and researchers across the globe; however, as a U.S.-based charity, the Alzheimer's Association is subject to, and complies with, U.S. law. As a result, the Alzheimer's Association cannot award, and will not award, grants in violation of applicable U.S. statutes and regulations. This means, among other things, that the Alzheimer's Association cannot, and will not, fund any individual or entity (i) that is subject to U.S. comprehensive or targeted sanctions or if awarding funding would result in a violation of such sanctions, (ii) that is on the U.S. List of Specially Designated Nationals or entities owned or controlled by such persons, or (iii) when doing so is otherwise prohibited by U.S. laws related to combating terrorism.*

Letters of Intent:
LOIs are a required component of the application process. No application will be considered without an approved LOI, including resubmitted applications. LOIs must be submitted online by the stated deadline. Late submissions will not be considered. Additional details about the LOI components, review criteria and process are included below.

All LOIS will be evaluated prior to invitation to submit a full application. Only LOIs that meet specific guidelines as outlined herein will be invited to submit applications.

LOI Components: Applicants must complete the required sections and upload any required documents. Some of these required fields are described below:

- **Principal Investigator name & contact information**
- **Lead Institution**
  - Applicant must be a full-time employee at time of submission
  - Institution/organization name must be in English
- **Current academic rank/position**
  - Must be current at the time of submission; pending promotions are not allowed
- **Proposal title**
- **Area of focus: Specific options will be available from a dropdown menu**
- **Brief project description (limited to 10,000 characters, including spaces)**

- **AI Centrality Statement (required, maximum 2 pages)** Applicants must provide a clear, evidence-based statement showing that AI was central to the discovery of the target and/or lead series. Applicants must include:
    - Workflow map (one figure acceptable): A simple step-by-step depiction of the discovery workflow identifying where AI was used and where conventional methods (for example docking, similarity search, rule-based filters, database queries) were used.
    - Decision trace: A short narrative describing how the AI system's output directly drove experimental decisions (for example, AI generated ranked targets or molecules that were advanced to experimental testing).
    - Baseline comparator: At least one practical comparison showing the AI component provided meaningful lift beyond a non-AI baseline, using a metric appropriate to the step (for example enrichment, hit rate, novelty or diversity, potency progression, property improvement trajectory, or prioritization accuracy). Aggregate results are acceptable.
- **Minimal Provenance and Auditability Package (required, maximum 2 pages)**
    - Model summary: Model type (for example GNN, transformer, Bayesian optimization, multimodal model), input data types, output format, and the specific decision task it supported.
    - Data categories and rights: High-level description of training and inference data categories (for example public bioactivity data, internal assay data, structural data, omics).
- **Employer Identification Number (EIN) or TIN**
    - This number must match the non-profit documentation
    - This is information specific to the *institution* not the applicant.
- **ORCID ID**
- **Institutional financial verification**
    - W-9 (US entities) signed and dated within the past five years by an authorized institutional signing official and must include the EIN number
    - W-8-BEN (non-US entities) signed and dated within the past five years by an authorized institutional signing official and must include the EIN/TIN or VAT number
- **Biosketch**
    - For Principal Investigator only, applicants will be able to provide biosketches for other members of the project team at the full application stage
    - The Alzheimer's Association highly recommends using the latest NIH biosketch format (excluding Section D. Scholastic Performance), but any format will be accepted. Hyperlinks are allowed in biosketch only for individual research projects.

LOI Review Criteria and Process:

LOIs will be evaluated with attention to:

- Innovation/novelty of the proposed project (especially in the context of the PI's recently funded work)
- Alignment with the research priorities of this PTC request for applications and the Alzheimer's Association
- Impact of project on Alzheimer's and all other dementia research
- Evidence of methodological rigor that addresses the research question(s) being proposed

A proposal may be considered non-responsive the approach is limited to standard computational methods alone (for example docking-only, similarity search-only, rules-only, or database mining-only) with no evidence AI drove selection decisions and/or if the applicant cannot provide a basic decision

trace and minimal provenance identifiers linking AI outputs to the nominated target and or lead series.

LOIs will be reviewed by 2-3 reviewers with expertise in the area of the application. Due to the number of LOIs received, individual feedback or comments from reviewers will not be shared. A fraction of LOIs will be invited for full application.

If the on-line LOI is approved and invited to submit a full proposal, an email notification will be sent from Proposal Central granting access to the on-line application. The online system must be used to submit a grant application; hard copies of the application will not be accepted.

Application Details:
Following the LOI review, some of these projects are invited to submit full applications. The PI who submits the application must be the same PI who submitted the approved LOI. The application does not need to be completed in one session; a partially completed application can be saved and completed at any time before the deadline. It is imperative that you proofread your application before submission; you will not be allowed to make any changes to the application after the deadline or once applications are under review.

The application must be submitted by the receipt date/time deadline. Once submitted, you will receive a confirmation e-mail from proposalCENTRAL that your application was successfully submitted. If you do not receive a confirmation, click the Proposals tab and under the "Status" column make sure it says **Submitted** and not **In Progress** which indicates you have not yet submitted your application. It is the applicant's responsibility to make sure that the application is complete and accurate before submission. Only a single copy of an application will be accepted.

Signatures are not required at the time of submission by the Association, however, the signature page provided is for use should your institution/organization require signatures; the Association does not override any institutional policies and/or procedures. Please do not submit the signature page with your application.

Applicants may use LLMs and other generative AI tools in the preparation of their LOIs and full applications. Applicants are fully responsible for the content of their proposal, even those parts produced by an AI tool. Using one of these tools will not affect the review of your application.

Key Considerations for Proposal Development:
Applicants are encouraged to clearly address the following key aspects in their proposal to enhance clarity and facilitate comprehensive evaluation:

- *Therapeutic Target and Biological Mechanism* - Clearly identify the biological target and/or pathway your therapeutic aims to modify. Explain briefly how this target or pathway is implicated in Alzheimer's disease or related dementias.
- *Innovative Aspects and Differentiation* - Provide a clear description of the unique aspects of your proposed therapeutic approach. If similar treatments or therapies exist, specify how your candidate differs in terms of mechanism of action, potential efficacy, safety profile, or other distinguishing features.
- *Scientific Rationale and Supporting Evidence* - Describe the scientific evidence including genetic, biochemical, pharmacological, or other relevant data supporting your hypothesis that modulating your chosen target or pathway will positively impact disease progression. Include evidence from preclinical models and explain how your chosen animal models closely reflect human Alzheimer's pathology.
- *Biomarkers and Clinical Translation*: Describe any established biomarkers or clinical assessments that can reliably predict therapeutic efficacy or clinical outcomes. Indicate how these biomarkers have been or will be validated for use in your proposed preclinical or eventual clinical studies.
- *Intellectual Property (IP) Status:* Detail the intellectual property landscape of your therapeutic candidate or related technology, including issued patents, filed applications, or other relevant

protections. If patents exist, provide relevant patent numbers or application references. Describe any IP constraints or barriers that might influence future commercialization or licensing.
- *Anticipated Safety and Risk Management:* Identify foreseeable safety concerns related to your therapeutic target, molecule, anticipated dose, or delivery method. Outline your plan to evaluate, mitigate, or manage potential risks, including immunogenicity, toxicity, or other liabilities.
- *Pathway to IND and Commercialization:* Outline the next key steps necessary to move your candidate towards IND submission and eventual commercialization.

Additional details for the application process are described below.

If you are invited to submit a full application, the required materials including the application format, templates, and instructions, will be available online at proposalCENTRAL after your LOI has been approved in the system.

Full applications will not be accepted without an approved LOI from the current cycle. If you did not receive an email from an Alzheimer's Association staff member about your approval to submit a full application for the current cycle you should not submit an application, even if one is available in your proposalCENTRAL Account.

Applicants must complete the required sections and upload required documents as listed. Some fields are identical to the LOI. Some of these required fields are described below:

- Executive Summary (maximum 1 page): Concisely describe the project's objectives, significance, proposed activities, and anticipated outcomes. Clearly indicate the stage of the project within the IND-enabling timeline.
- Detailed Research Strategy and Work Plan (maximum 6 pages). Provide a robust scientific justification for the chosen therapeutic approach, including in-depth background information linking the therapeutic target or mechanism to Alzheimer's disease or related dementia pathology. Clearly outline project goals and specific aims, methods, experimental design, and expected outcomes. Discuss potential pitfalls and present alternative strategies for overcoming these challenges. Provide compelling preliminary data validating the biological target, mechanism of action, and efficacy in the relevant *in vitro* or *in vivo* models. Include relevant figures, graphs, or images that support scientific rigor and feasibility.
- Comprehensive Target Product Profile (TPP) (Maximum 2 pages): Provide a detailed TPP specifying clinical objectives, intended patient population, dosage forms, route of administration, therapeutic dosing regimen, safety profile, and efficacy benchmarks. Clearly link the proposed activities and milestones to achieving the defined TPP goals.
- Data and Statistical Analysis plan (maximum 1 page).
- Available Resources & Budget Justification (maximum 2 pages) – A budget justification for the proposed research project is required and must be submitted with the application and within the allowable two-page limit. However, if the application is awarded, a more detailed budget will be required and must be approved before the disbursement of funds. Indicate any additional sources of complementary funding that will enhance or supplement this project's goals.
- Data Management and Sharing Plan (maximum 3 pages): The Association recommends using the amended NIH template provided. When data sharing may be limited, applicants must explain such limitations at the time of application.
- Detailed Milestone Plan and Timeline (e.g. Gantt Chart) (maximum 3 pages): Clearly delineate project stages and milestones, specifying critical decision points and go/no-go criteria. Milestones must be quantifiable and tied to specific, measurable outcomes. Include anticipated timeframes for each milestone, clearly showing progression toward IND submission or next developmental phase.
- Intellectual Property (IP) Status and Commercialization Plan (maximum 2 pages): Clearly describe the current IP status related to the project, including patent filings, issued patents, or any existing IP constraints. Outline a strategy for securing, protecting, and potentially licensing intellectual property. Provide a commercialization strategy, including the potential pathway for

future clinical trials, manufacturing, and collaboration with industry partners.

- Research Project Team Qualifications and Roles (maximum 5 pages): Provide detailed information about the Principal Investigator(s), co-investigators, and collaborators. Outline the experience, expertise, and previous success relevant to drug discovery and development, Alzheimer's research, regulatory processes, and commercialization. Clearly define roles, responsibilities, and interactions among team members, consultants, and CROs (if applicable).
- Reference and Citations – maximum 1 page.

Budget Considerations: It is required that most of the funds awarded under this program be used for direct research support. For non-profit organizations, no more than 10% of the total direct costs may be included as indirect costs; this is inclusive of indirect costs for the implementing institution as well as any subcontracts. For-profit organizations may not include any indirect costs.

- **Direct costs allowed**:
  - Allowable costs include:
  - Purchase and care of laboratory animals
  - Small pieces of laboratory equipment and laboratory supplies
  - Purchases over $10,000 require prior approval, even if included in the project proposal budget
  - Computer software if used strictly for data collection (requires prior approval)
  - Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including laboratory technicians and administrative support directly related to the funded grant); there is no salary cap.
  - Costs associated with Contract Research Organizations (CROs)
  - Costs associated with the management and sharing of research data
  - Support for travel to scientific and professional meetings and additional support for travel expenses necessary to carry out research planned – this may include site visits. A total of $12,500 over a three year period may be requested for travel purposes and is not to exceed $7,000 in any given year. If you request the full $12,500 towards just two years of travel and are requesting a three year award you will not be able to request travel funds for one of those years.
  - Remuneration for human volunteers should follow the recommendations proposed by the National Alzheimer's Coordinating Center (NACC) located here: https://files.alz.washington.edu/documentation/remuneration-guidelines.pdf
  - Travel expenses for projects involving human volunteers are allowable expenses not included in the travel above. This can be captured under other expenses (itemized) in the budget.
- **Direct costs *not* allowed**:
  - Computer hardware or standard software (e.g. Microsoft Office, mouse monitor, computer parts, AppleCare)
  - Laboratory equipment such as freezers, ultracentrifuges, RT-PCR machine, microscopy/imaging equipment
  - Service contract fees of equipment
  - Construction or renovation costs
  - Tuition
  - Rent for laboratory/office space
  - Visa costs and fees
  - Expenses such as Data Network Recharges and Computing and communication device support services. However, data sharing and/or data storage for imaging, sequencing and other study data is allowed.
  - General liability insurances, such as GAEL

- Wire and currency exchange fees; it is important to note that the Association does not adjust total funded amount in relation to fluctuations in exchange rates. All grants are paid in U.S. dollars.
- Institutional overheads associated with staff time
- The Alzheimer's Association Medical and Scientific Advisory Group (MSAG), the International Research Grant Program (IRGP) Council members and current employees of the Alzheimer's Association are allowed to be key personnel or collaborators on projects, however they are NOT ALLOWED to receive any salary or compensation. A complete list of MSAG and IRGP Council members can be found on our website alz.org/grants.

The Alzheimer's Association reserves the right to decline any charge that is an institutional fee and/or service charge.

Application Review Criteria and Process:
All applications are subject to a multiple stage peer-review process carried out with an online system. This multi-stage process is central to the Alzheimer's Association's award decisions and is designed to ensure both scientific rigor and fairness in the review of all submitted applications.

In the first stage, applications are reviewed and rated by peer scientists with expertise in the proposed area of research. Applicants may include recommended reviewers and have the option to exclude specific reviewers from evaluating their application if a conflict of interest exists. Conflicts of interest include (but are not limited to):

- The applicant trained with/ by the reviewer.
- The reviewer published with the Applicant in the last four ~~(4)~~ years. This excludes workshop or large consortia (i.e. ADNI, IGAP, etc.)
- The reviewer has been a co-investigator on a grant application or award with the applicant in the last four years.
- The reviewer has a conceptual difference of opinion with the applicant that will prevent a fair review.
- The reviewer will receive financial benefit from the applicant receiving an award.

In stage one of review, each application will be evaluated with the following criteria:

- **Scientific Rationale and Impact:** Whether the scientific hypothesis is clearly articulated, with compelling rationale connecting the proposed molecular target or therapeutic strategy to Alzheimer's disease or related dementias. Strength of evidence or justification indicating how success could substantially influence the field or clinical practice.
- **Entry Specific Criteria:**
  - IND-Specific Entry Criteria: The extent to which the identified clinical candidate is clear with comprehensive preliminary data, including efficacy, preliminary ADME and toxicity profiles, and readiness for regulatory interactions and IND submission.
  - Lead Optimization-Specific Entry Criteria: Qualified hit or lead series with experimentally confirmed activity in disease-relevant assays, supported by an established assay cascade suitable for SAR-driven optimization, plus initial developability and selectivity signals sufficient to justify advancement into a milestone-driven lead optimization program.
- **Innovation and Differentiation:** Whether the approach sufficiently demonstrates substantial novelty or a meaningful improvement over existing therapies in development or marketed treatments for Alzheimer's disease and related dementias. The clarity of description of what differentiates their therapeutic approach from existing therapies or competitors.
- **Feasibility and Risk Management: Whether the i**dentification of potential risks in the proposed approach and a clear plan to address or mitigate these risks is sufficient. The extent to which timelines and deliverables, supported by clearly outlined project's milestones, are feasible and

achievable.

- **Resource Availability and Institutional Support : Whether the resources,** resources, including laboratory facilities, equipment, and experienced personnel, are adequate and appropriate to complete the proposed studies within the stated timelines. If identification of any collaborators, consultants, or CROs and a rationale for their involvement are clear and appropriately justified.
- **Potential for Clinical Translation and Commercialization: Whether the proposal demonstrates** clinical relevance, translational feasibility, and market potential. The extent to which the preliminary IP position and strategy to secure intellectual property supports commercial development and does not present barriers.

The second stage includes further review and discussion of the scores and comments resulting from the initial review process to normalize across reviews and programs. The second review is carried out by a selected panel of the International Research Grant Program (IRGP) Council members and invited review committee members to ensure fairness and balance in the initial review procedures and to make funding recommendations to the Association.

Final recommendations from the IRGP Council are shared with the Medical and Scientific Advisory Group (MSAG) and with the Alzheimer's Association for final approval. Members of the IRGP Council and MSAG are internationally recognized experts with distinguished careers in Alzheimer's and related dementia.

Financial Responsibility:

Funding is awarded to the institution and/or organization, not to the individual principal investigator. The principal investigator or a first-degree relative cannot be listed as the signing official or financial officer, or have checks sent to their attention if awarded.

Appeals of Scientific Peer Review:

To maintain a fair and rigorous review system, the Alzheimer's Association has a process for appeal of funding decisions. Appeals will not be considered for the letter of intent stage. Regarding applications, an appeal is intended to address extraordinary circumstances.

Appropriate reasons for initiating an appeal might include:

- Evidence that a reviewer has an undeclared conflict of interest.
- An egregious error or misunderstanding in the review process.
- Active malfeasance or demonstrable lack of due diligence.

The appeal process is not intended to provide a mechanism for routine protest of failure to receive a grant. It is anticipated that funding through the Alzheimer's Associations grant programs will be extremely competitive and is limited by availability of funds.

If an applicant believes an extraordinary circumstance has contributed to failure to receive funding, the principal investigator may send a two-page, double-spaced formal letter of appeal (Word document) to grantsappeals@alz.org. Any supporting documents included must be submitted as a PDF. Appeals must be submitted within two weeks from the date your application outcome notification is sent. Notification of action on the appeal will be made via email, usually within 90 days of the appeal deadline.

Reporting Requirements, if Funded:

For funded awards through this program, there will be required scientific and financial reporting. Interim Scientific & Financial Reports must be submitted at the end of each reporting period as long as the grant remains active. Final Scientific & Financial Reports must be filed within 90 days of the grant's end date. All reports must be submitted electronically via proposalCENTRAL. The Financial Report must be approved and signed by someone with financial authority in the Office of Research and Sponsored

Programs or Grants & Contracts.

Office at the recipient's institution. Unobligated funds remaining at the end of the award must be returned to the Alzheimer's Association.

Note: The continuation of the grant over the awarded duration is contingent upon the timely receipt of all required reports.

In addition, while animal welfare and human volunteer ethical assurances are not required at the time of application, investigators have until their chosen start date (within 6 months or less of award notification) to submit these approved documents. The Alzheimer's Association encourages investigators to initiate their certification applications on a schedule that recognizes that rDNA certification, IRB/IACUC approval at many institutions can take more than 90 days. The Association accepts only certifications that apply specifically to the funded project and must include the name of the awardee.

Electronic copies of publications, presentations and abstracts that report research supported by funds from the Alzheimer's Association must be submitted electronically at the time of publication. These copies will become part of the official file of the grant and will be provided to the Communications Division of the Alzheimer's Association to assist in the efforts to further inform the public about the International Research Grant Program of the Association. Any intellectual property disclosures resulting from the award must be submitted electronically at the time of publication. The Alzheimer's Association may request any of the research outputs listed here from any awardee up to 7 years following the end of the award.

U.S. Sanctions:

Alzheimer's Association grants are generally open to scientists and researchers across the globe; however, as a U.S.-based charity, the Alzheimer's Association is subject to, and complies with, U.S. law. As a result, the Alzheimer's Association cannot award, and will not award, grants in violation of applicable U.S. statutes and regulations. This means, among other things, that the Alzheimer's Association cannot, and will not, fund any individual or entity (i) that is subject to U.S. comprehensive or targeted sanctions or if awarding funding would result in a violation of such sanctions, (ii) that is on the U.S. List of Specially Designated Nationals or entities owned or controlled by such persons, or (iii) when doing so is otherwise prohibited by U.S. laws related to combating terrorism.

Nondiscrimination and Harassment Statement:

The Alzheimer's Association is committed to providing an environment free from harassment and discrimination. The Alzheimer's Association strictly prohibits harassment and discrimination based on race; creed; color; religion; sex; sexual orientation; national origin; ancestry; age; Veteran status; citizenship status; marital status; physical or mental disabilities; pregnancy, gender identity or expression (including transgender status); genetic information; and any other characteristic protected by federal, state, or local law.

Contact Information:

For any inquiries or additional information, please contact a member of the Alzheimer's Association Grants staff at grantsapp@alz.org.

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