



## ALS Breakthrough Research Fund

# REQUEST FOR PROPOSALS

Tambourine is launching the ALS Breakthrough Research Fund. This new fund will support basic and discovery-focused research in amyotrophic lateral sclerosis (ALS). The ALS Breakthrough Research Fund is operated in partnership with the Milken Institute Center for Strategic Philanthropy and is now accepting two-year research proposals with the potential to drive significant breakthroughs for improving ALS diagnosis, treatment, management, prevention, and cures.

## Background

Tambourine will award up to 10 two-year research grants led by doctorate-level investigators at qualifying research-based institutions around the world. Projects will be eligible for up to US\$300,000 in funding per year (including up to 15 percent indirect costs) for a total of US\$600,000 over two years. Funded investigators will be eligible to apply for a third year of support that will commence after the conclusion of the original two-year term.

ALS is a progressive, fatal, neurodegenerative disease that affects an estimated 350,000 individuals around the world at any given time. Despite common patterns of symptoms, ALS is a highly heterogeneous disease. The mechanisms that govern disease onset and progression in most people are either unknown or poorly understood.

ALS doesn't have a cure yet, but increased attention and investment from public and private funders over the last two decades have generated critical progress and momentum. In 2021, Tambourine partnered with the Milken Institute Center for Strategic Philanthropy to review the ALS scientific and funding landscapes and identify [opportunities for strategic philanthropic investments](#). This analysis revealed that an incomplete understanding of the disease's fundamental biology and mechanisms remains a central, underfunded scientific barrier. This grant program builds directly on those findings.

## The Opportunity

### *Scientific Scope*

The ALS Breakthrough Research Fund aims to accelerate innovative basic and discovery-focused ALS research by supporting rigorous, cutting-edge scientific proposals that display great creativity and potential for impact. Tambourine particularly encourages proposals that reflect exciting, foundational scientific directions and high-risk, high-reward ideas that may not otherwise find support through existing grant programs.

Applicants are encouraged, but not required, to address at least one of the following priorities in their research proposals:

- **ALS Mechanisms:** Applying novel methods, cutting-edge technologies, and/or innovative and paradigm-shifting approaches to the discovery-driven interrogation of disease mechanisms in ALS. Examples include:
  - identification of new biological pathways or mechanisms,
  - discovery science for brain-machine interfaces or assistive technologies,
  - pursuit of digital biomarkers, and/or
  - adoption of other novel methods to understand disease mechanisms in ALS.
- **Sporadic ALS:** Resolving the causes and/or drivers of sporadic ALS, such as by focusing on underlying molecular mechanisms and pathways that may be common to multiple types of ALS. Examples include:
  - neuroinflammation,
  - contribution of non-neuronal and/or glial cells to ALS pathology,
  - pathological protein aggregation, and/or
  - other mechanisms and pathways that may drive sporadic ALS.
- **Non-inherited Contributions:** Investigating non-inherited contributors to ALS, including epigenetics, environmental factors, gene x environment interactions, and/or gene x other factor interactions (e.g., profession, lifestyle, trauma), such as by:
  - testing novel approaches or technological solutions that can overcome current limitations to studying multiple and multistep contributors,
  - developing and validating experimental and preclinical models of ALS, and/or
  - proposing other creative approaches to understanding non-inherited contributions.

## *A Call for Novel Approaches to Study ALS*

The ALS Breakthrough Research Fund hopes to attract expertise and talent from scientists across disciplines to resolve the field's most pressing scientific priorities. Tambourine encourages not only applications from ALS researchers but also from:

- scientists focused on adjacent diseases, such as Parkinson's, Alzheimer's, multiple sclerosis, dementias, etc.;
- scientists working in other relevant disciplines, such as data science, environmental science, computational science, physiology, biostatistics, epidemiology, etc.; and
- scientists planning to leverage common infrastructure and shared resources developed by the ALS community (including biorepositories and tissue banks, patient registries, stem cell lines, multidimensional datasets, and animal models) to perform basic and discovery-focused research.

Applicants without ALS experience are not required to co-apply with an ALS expert; however, they will be expected to demonstrate a fundamental understanding of ALS disease biology to be considered for funding.

## **Important Dates**

- **May 24, 2023:** RFP released
- **June 21, 2023:** Letters of Intent (LOIs) due
- **September 1, 2023:** Proposals due
- **October–November 2023:** Scientific and strategic evaluation
- Awardees notified as early as **December 2023**

## Eligibility

1. Each applicant organization must be a nonprofit academic or research institution, including domestic and non-US nonprofit organizations and domestic and non-US public/private academic universities or institutions of higher learning (including colleges, universities, medical schools, and other related academic research institutions); certain qualified governmental agencies with active biomedical research programs may also apply.
2. All proposed research projects must be led by one designated principal investigator (PI) who holds a PhD, MD, or related research doctorate degree. PIs must be independent investigators.
  - a. New and/or early-stage investigators are encouraged to apply. New investigators are those who have not yet received substantial independent federal funding for their independent research programs, while early-stage investigators are new investigators who are within 10 years of completing their terminal research degree, medical residency, or equivalent.
  - b. Multidisciplinary investigator collaborations are encouraged to apply. Collaborators should be identified as co-investigators and provide the materials described in the sections below.
3. Institutions may submit multiple proposals, but a unique PI must lead each.

## Application Requirements

All completed LOIs and proposals shall be submitted through the Milken Institute's online grant portal at [https://milken.smapply.io/prog/ALS\\_Breakthrough\\_Research\\_Fund](https://milken.smapply.io/prog/ALS_Breakthrough_Research_Fund). Below is a list of required components for an application to be considered complete.

Applications shall be single-spaced and formatted in Arial 11-point font with one-inch margins, except where provided templates apply. The Milken Institute shall strictly enforce formatting and length. Any submissions that exceed the page limit or do not follow the requirements above shall not be considered for review.

### *Letter of Intent (maximum one page)*

All applicants must first submit an LOI, which Tambourine's scientific review team will review to ensure applicant eligibility and determine whether the proposed research fits within the funding program's scope. Applicants who meet these criteria will be invited to submit a full proposal. If Tambourine determines that a project falls outside the scope of this funding program, applicants will receive constructive feedback on their LOI and are encouraged to apply to future calls for funding.

All proposals must be focused on basic and discovery-focused ALS research. Clinical research studies or studies that are only tangentially related to ALS will not be considered.

The LOI is a one-page letter that includes the following information:

- Project title
- PI name and applicant institution
- Project aims
- The scientific priority area—described above, within the Scientific Scope—or another important gap within basic ALS research that the project will address
- A succinct description of how the proposed research would be innovative and impactful

The LOI also requires, via a separate form within the application portal, the applicant organization's legal name; PI name, degree, position, and contact information; and the organization's tax ID (for US) or registered charity number.

- LOIs are due **June 21, 2023**.
- LOIs should be submitted through the Milken Institute's online grant portal, which can be accessed via this link: [https://milken.smapply.io/prog/ALS\\_Breakthrough\\_Research\\_Fund](https://milken.smapply.io/prog/ALS_Breakthrough_Research_Fund).
- Should Tambourine, in its sole discretion, find that a project described in an LOI falls within the scope of the program, the applicant will be invited via email to submit a full proposal within approximately two (2) weeks of the LOI submission deadline.

### *Scientific Proposal (maximum six pages)*

Applicants must include a formal proposal outlining the intended project. Proposals are due **September 1, 2023**.

Proposals shall be no more than six pages in length and must include the following materials, organized in the following order:

- **Cover Page and Project Summary.** One page maximum, including the following information:
  - Project title
  - Lay summary (one to two paragraphs): a succinct summary of the project intended for a nonexpert audience describing the project's aims and goals, including rationale regarding its creative and/or innovative approach and benefit to the ALS field
  - Specific aims
  - Name, degrees, positions, and institutions of principal and any co-investigators, if applicable
- **Scientific Approach.** Five pages maximum, inclusive of references in the applicant's preferred format, including the following sections.
  - **Project Goal and Significance:** a statement of what the project plans to accomplish and why the proposed research is important with a high potential for impact on the ALS field.
  - **Background:** a description of the scientific rationale and foundational knowledge that underlie the proposed research.
    - Preliminary data are not required.
  - **Innovation:** a description of how the proposed research represents a novel, creative, and innovative approach.
    - Applications should convey why this specific idea or proposed line of research has not received sufficient support in the past, if applicable.
  - **Methods:** a description of the research methods the PI intends to use in pursuit of the project.
  - **Timeline:** a statement of how the PI plans to accomplish the project goal and scientific aims within a two-year grant term.

### *Protocol Synopsis (maximum one page)*

Proposals must include a brief protocol synopsis. As noted below, Institutional Review Board (IRB) or the local equivalent (for human studies) or Institutional Animal Care and Use Committee (IACUC) or the local equivalent (for animal studies) approval will be required before initial payment is made for any project that Tambourine selects for funding. If new approvals are required during the grant term, those approvals should be submitted to the Milken Institute as soon as possible. Studies utilizing human tissue, samples, or animal models should specify an acquisition plan and include any fees associated with accessing or using these resources in their proposed budgets.

## *Research Team (maximum one page)*

Applicants must outline the research group's ability to address the proposed scientific question and support the research. This statement should identify key personnel in addition to the PI and co-investigator(s), if applicable.

## *Data Sharing Plan (maximum one page)*

Applicants must describe their commitment to, and plan for, openly sharing project results and other collateral, such as data (de-identified, where applicable), reagents, protocols, and other research tools developed under Tambourine funding with other institutions and researchers for noncommercial use to advance the fundamental understanding of ALS and maximize scientific impact.

- Applicants should identify the specific repository to which they intend to upload and share project protocols, datasets, and study results.
- Applicants are strongly encouraged to upload study results to preprint servers.
- Applicants are strongly encouraged to publish any manuscripts resulting from funded research in an open-access venue and are permitted to include article processing charges for open-access publications in their proposed budget.
- Applicants should describe policies and procedures for ensuring that key personnel and other applicable employees and contractors will comply with and adhere to the data sharing plan.

## *Detailed Budget (use provided template)*

Applicants must provide a detailed budget using the template provided. The detailed budget in USD should be accompanied by a narrative summary and budget justification, including how the PI and any co-investigators, if applicable, intend to spend their time on the project. Projects can be budgeted for two years and up to US\$600,000 (US\$300,000 per year) inclusive of up to 15 percent indirect costs. If more than one institution will be involved in the project, one shall be proposed as the applicant organization and the other included as a sub-grantee, and the maximum allowable indirect rate across all institutions will remain 15 percent of the total award budget. Acceptable expenditures for direct costs include:

- salary for the PI, co-investigators (if applicable), graduate students, postdocs, staff scientists, and other personnel;
- fringe benefits for the PI, co-investigators (if applicable), graduate students, postdocs, staff scientists, and other personnel;
- equipment, supplies, and software;
- computing costs and data storage;
- any fees required to access or use human tissue, samples, datasets, or animal models;
- project-related travel, such as to conferences to share research results or between institutions to facilitate a collaborative project;
- publication costs, including article processing charges for open-access publications; and
- up to 15 percent in indirect expenses to support institutional infrastructure. It is not necessary to provide specific details regarding indirect cost expenditure.

Grants selected for funding will be made payable to the applicant organization. Under no circumstances will funding be paid to, or earmarked for, any individual. International applicants should note that grants will be made in USD, and Tambourine is not responsible for changes in conversion rates. Payments will be made annually.

## PI Biosketches (maximum five pages per PI)

A biosketch of the PI and co-investigators (if applicable), utilizing the [National Institutes of Health \(NIH\) template](#), is required and shall not exceed five pages per PI. If the PI or co-investigators do not have a biosketch in an NIH template, a CV is sufficient.

## Institutional Letter of Commitment

Each application must include an institutional letter of commitment stating that the applicant institution will be able to support the research led by the PI and administer the grant according to a written grant agreement to be entered into between the selected organization and Tambourine. The letter should be signed by an authorized organizational representative (e.g., department chair or dean of sponsored research). Collaborative applications from multiple institutions can either submit separate letters of commitment from each institution or have one letter signed by all relevant authorized institutional representatives from each institution. There is no required template for this letter.

- Additional documentation within the online form will include a completed electronic signature confirming that the grant proposal contains information that is true, complete, and accurate and that false or fraudulent statements may subject the institution to criminal, civil, or administrative penalties.
- Upon request, an applicant institution may be required to submit additional information to document its nonprofit status.
- **Non-US-based governmental organizations** must also provide:
  - A list of voting board members and officers, as well as the name of the organization's highest-ranking member (e.g., CEO).
  - Additional organization governing documents and other documentation via a secondary questionnaire, following your proposal submission. Tambourine will make this request during the proposal review. For more information, please visit <https://www.ngosource.org/how-an-ed-works>.
- **US-based governmental organizations** (excluding academic/research institutions that are public charities) must provide:
  - A full copy of the enabling statute that authorized the organization's creation.
  - A copy of the organization's governing documents (such as articles of organization or constitution and bylaws), if applicable.
  - Any correspondence from the Internal Revenue Service confirming the organization's tax status, if applicable.

## Selection Process

### Selection Criteria

Applications displaying strength and creativity across the following domains will more likely be selected for funding by Tambourine.

- **Scientific and technical merit:** the quality of the scientific rationale and the use of resources, equipment, and experimental designs to rigorously evaluate the central scientific question or test the stated hypothesis/hypotheses. Experimental design is highly rigorous, and the study is appropriately statistically powered to produce meaningful findings even in the absence of supportive or positive results.
- **Significance and potential impact:** the success of this proposed research would be significant in furthering our fundamental understanding of ALS, demonstrate potential to lead to breakthrough discoveries for the disease, and achieve near-term scientific impact.

- **Innovation:** a proposal's ability to bring new ideas, knowledge, methods, approaches, or perspectives to the ALS field and generate new avenues to understand, diagnose, treat, manage, prevent, or cure ALS.
- **Team capabilities and competencies:** the research group's ability to address the research question and support the research.
- **Cost realism:** a realistic budget that adequately supports personnel, equipment, overhead, open-access publishing costs, and other needs to carry out the project successfully.

## Review Process

Funding decisions will be made after a multistep review process comprising the following:

- **Eligibility and scientific scope review:** As described above, LOIs will first be reviewed by Tambourine's scientific review team to ensure applicant eligibility and determine whether the proposal fits within the funding program's scope.
- **Peer review:** Applications will be peer reviewed by an external panel of expert reviewers utilizing the selection criteria described above. Applications will be ranked according to peer review, and a select number of highly prioritized applications will move forward to the next round of evaluation.
- **Scientific leadership review:** Tambourine's scientific leadership—including the Scientific Advisory Board—will evaluate the highly prioritized peer-reviewed applications and overlay program strategy to achieve an overall grant portfolio that meets the fund's goals.
- **Tambourine determination:** The scientific leadership of the ALS Breakthrough Research Fund will provide a final prioritized list of funding recommendations to Tambourine for consideration. Tambourine will make final funding decisions, and applications will be funded subject to a written agreement, as further discussed below.

## Progress Reporting and Evaluation

Funded investigators will be expected to share biannual updates on project highlights, progress, and challenges.

- At six months after receiving funding, each PI will engage in a brief discussion with Tambourine's scientific leadership focused on any additional support needed to initiate the project as planned.
- At 12 and 18 months after receiving funding, each PI will provide short, written updates describing major project progress based on milestones identified when the proposal was submitted and any challenges they have faced along the way.
  - Depending on the substance of these updates, PIs may be asked to engage in brief conversations with Tambourine's scientific leadership.
- At 18 months after receiving funding, funded investigators may be eligible for an additional year of follow-on support based on satisfactory progress against milestones, specific project needs, and overall program alignment. These funding decisions will be made at the sole discretion of Tambourine.
- At the end of the grant term (24 months after receiving funding for projects that do not continue for an additional year or 36 months for projects that continue for an additional year), PIs will submit a full, written narrative and financial report for the overall project.
- Funded investigators may be invited to participate in annual funded investigators' meetings to present and discuss their research plan and preliminary and/or unpublished results of research supported by Tambourine. Expenses associated with the meeting will be funded separately by Tambourine.

## Grant Terms

Each funded research institution and PI will be required to cosign and agree in writing to Tambourine's grant terms within 30 days from receipt of notice of the award and prior to funds being released. Tambourine's grant terms include, but are not limited to, the following items.

Any substantial changes to the project, including activities, budget, protocols, or grant period, require written approval from Tambourine before proceeding with such activities or spending or committing any remaining funds from the grant.

### *Use of Funds*

- The applicant organization must be able to receive awarded funds and allocate them toward the funded ALS research project.
- IRB or the local equivalent (for human studies) or IACUC or the local equivalent (for animal studies) approval will be required before initial payments are made.
- If an applicant organization proposes to supplement any funds provided by Tambourine with funds provided by a third party, the organization must first provide notice to Tambourine and must ensure that the funding terms that attach to any such third-party funds do not preclude sharing of data or publication of project results as contemplated in this RFP.
- Teams may request no-cost extensions within the first 18 months of the award period.

### *Intellectual Property and Sharing Data and Results*

Each funded organization shall own the rights to all intellectual property developed by or on behalf of that organization under Tambourine funding, in accordance with such organization's applicable intellectual property policies. Tambourine shall have the right to use and practice all such intellectual property for internal, noncommercial research purposes. Tambourine would also have the right to publicly disclose research results in press releases, announcements, and otherwise (subject to the funded organization's advance approval if any such public disclosure will occur prior to publication of the applicable results).

Each funded organization must agree to share project results and other collateral, such as data (de-identified, where applicable), reagents, protocols, and other research tools developed under Tambourine funding with other researchers for noncommercial use to advance the understanding of ALS and to maximize scientific and patient impact.

It is a condition of any funding provided by Tambourine that the investigator seeks to publicly release the results of the funded project, such as on a preprint server, within 12 months after completion of the project. Furthermore, funded investigators are strongly encouraged to publish the results of the funded project open access in a peer-reviewed journal within 18 months after the completion of the project. Each publication would acknowledge Tambourine's role in supporting the project. If the investigator does not publish the results within such a timeframe, Tambourine shall have the right to make such results public. Specific financial support for such publications are allowable expenses in the project budget. Funded investigators must inform Tambourine of any publication supported by Tambourine funds within thirty 30 days of publication.

## Funding Awarded at Tambourine's Discretion

Responding to this RFP, submitting an LOI, and/or submitting a full proposal do not entitle any individual or institution to receive funding from Tambourine. Funding, if any, would be provided at Tambourine's sole discretion pursuant to the terms of a written grant agreement executed by Tambourine and the selected awardee institution and acknowledged by the PI.



## Contact Information

For all inquiries about the online process, necessary documentation, research priorities, or scientific requirements, please contact [alsgrants@milkeninstitute.org](mailto:alsgrants@milkeninstitute.org).

An automated email confirmation is generated upon submission of the application. If you do not receive a confirmation within 24 hours of submitting your application, please check spam filters and then contact [alsgrants@milkeninstitute.org](mailto:alsgrants@milkeninstitute.org).