REQUEST FOR PROPOSALS:

Ann Theodore Foundation Sarcoidosis Inhibitor of mTOR (SIM) Trial

The Ann Theodore Foundation (ATF) is launching a new funding program to support the study of repurposed mechanistic target of rapamycin (mTOR) inhibitors as treatments for cutaneous sarcoidosis. This program will be executed in partnership with the Milken Institute Science Philanthropy Accelerator for Research and Collaboration (SPARC).

The ATF Sarcoidosis Inhibitor of mTOR (SIM) Trial is now accepting applications for two-year investigator-initiated clinical trials that will test the efficacy of mTOR inhibitors in treating cutaneous sarcoidosis. This trial would be considered an early Phase 2 trial and would provide scientific support for a future Phase 2b/3 or a Phase 3 trial. ATF will fund this trial, and SPARC will operate as program administrators.

Description

The ATF SIM Trial will award one two-year investigator-initiated clinical trial grant led by established, independent investigators at qualifying research-based organizations around the world. The awarded team will be eligible for up to US$250,000 in funding for direct costs per year plus 15 percent in indirect costs, totaling US$287,500 per year for a total of US$575,000 over two years. Applications that define the trial population to appropriately power the trial and demonstrate a history or capacity to fully enroll during the grant period, including clinical trial networks and consortia, will be prioritized.

Background

Sarcoidosis is a disease hallmarked by clusters of immune cells, known as granulomas, that can form in various organs. The lungs are the most frequently affected organ, but many other organs can be impacted. Skin is the second most affected organ in sarcoidosis. Cutaneous sarcoidosis

symptoms include painful rashes, skin lesions, and subcutaneous growths that often form around scars and tattoos.

Although sarcoidosis is often considered a rare disease, its true prevalence may be higher because of underdiagnosis and a lack of awareness among clinicians. As of this program's launch, the only Food and Drug Administration (FDA)-approved pharmacological agents for sarcoidosis treatment are prednisone and repository corticotropin injection. Treatment options for individuals with sarcoidosis are limited. Regulatory approval for other drugs would make insurers more likely to cover patient costs for these treatments and would pave the way for new regulatory approvals.

Potential for mTOR Inhibitor Sarcoidosis Treatment

The FDA has approved mTOR inhibitors for the treatment of atherosclerosis, renal and breast cancers, tuberous sclerosis complex, lymphangioleiomyomatosis, and other conditions. A recent trial testing the safety and efficacy of the mTOR inhibitor sirolimus in treating cutaneous sarcoidosis found that systemic treatment alleviated symptoms in seven of 10 participants. This effect persisted for over one year after treatment concluded for all seven responders (https://pubmed.ncbi.nlm.nih.gov/38267106/). Additionally, a recent review paper indicates that many patients who received sirolimus experienced significant improvement; however, it also notes that no randomized controlled trials have been conducted (https://pubmed.ncbi.nlm.nih.gov/40996589/). ATF seeks to replicate these findings at an appropriate scale to support movement toward regulatory approval for a sarcoidosis treatment.

Scientific Focus

All submitted applications must propose to test the efficacy of an mTOR inhibitor in treating individuals diagnosed with cutaneous sarcoidosis. Recruited participants may have additional sarcoidosis subtype diagnoses. Submitted proposals should outline a trial designed to generate essential data on mTOR inhibitor efficacy and safety in people with cutaneous sarcoidosis (with or without other organ involvement). Trial results should enable the determination of whether the specific intervention merits further development toward the ultimate goal of regulatory approval. To be eligible for funding, the proposed trial must:

- Study the interventional effects of an existing pharmacological mTOR inhibitor, with priority given to previously studied mTOR inhibitors,
- Recruit a representative population of individuals diagnosed with cutaneous sarcoidosis, with or without other organ involvement,
- Be at a mid-stage of clinical testing, ideally Phase 2a or 2b, to explore safety or efficacy with the goal of providing justification for a larger Phase 2b or Phase 3 trial, and
- Include primary endpoints focused on the impact of mTOR inhibitors on cutaneous sarcoidosis.

Examples of research topics that will not be considered for the Request for Proposals (RFP) include the following:

- Preclinical and nonclinical studies
- Observational research on sarcoidosis-specific pathophysiology or epidemiology
- Clinical trials that do not primarily include people diagnosed with cutaneous sarcoidosis
- Clinical trials assessing combinations of interventions. However, participants are permitted to have a history of taking other sarcoidosis therapeutics, except mTOR inhibitors
- Clinical trials evaluating lifestyle interventions such as diet and exercise

Eligibility Criteria

1. Each applicant organization may be:
    a. a nonprofit academic or research organization, including domestic and non-US nonprofit organizations and domestic and non-US public/private academic universities or organizations of higher learning (including colleges, universities, medical schools, and other related academic research organizations)
    b. a certain qualified governmental agency with active biomedical research programs
    c. a for-profit organization, including pharmaceutical companies

    Successful applicants must agree to and adhere to the ATF open science policy (see Grant Terms #10 below). Applications from established consortia or clinical trial networks will be prioritized.
2. All proposed research projects must be led by a principal investigator (PI) who holds a doctorate (e.g., PhD, MD) or a related degree. The PI must be an independent investigator.

Application Requirements

All completed applications must be submitted through a Survey Monkey Apply grant portal, found at https://milken.smapply.io/prog/ann_theodore_foundation_sarcoidosis_inhibitor_of_mtor_sim_trial

Each applicant should keep in mind the portal's requirements when preparing the application. **Applications must be single-spaced and formatted in Calibri 11 pt font with one-inch margins, except where provided templates apply.**

1. **Proposal Submission.** A formal proposal outlining the intended project must be no more than 11 pages in length and organized as follows:
    a. Cover Page. One page, including the following:

i. Project title (a short title identifying the project).

ii. Lay summary (succinct summary intended for a public audience describing the project's aims, goals, any relevant previous accomplishments, and how it will benefit the field).

iii. Name of the applicant organization and PI.

b. Project Summary Page. Two pages, including the following:

i. Technical abstract.

ii. Aims and milestones (summary of what the project aims to accomplish and the major milestones that the PI anticipates the project will complete in the process of meeting the project aims). Aims should include future development plans. Major milestones should include an estimated time frame to completion.

iii. Full roster of project team members.

c. Trial Design and Rationale (outline of the intended research methodology, as well as definition of and justification for key project outcome measures). Six pages maximum, inclusive of references in the applicant's preferred format. The primary, secondary, and tertiary endpoints, as well as the number of participants, must be described and justified in the application.

i. Proposals must include a description and justification of the proposed mTOR inhibitor that will be tested, including any existing regulatory approvals. SIM will require a copy of the investigator brochure and full protocol before initial payments.

ii. Any preliminary studies and previous experience in sarcoidosis relevant to the proposed project must be described.

iii. Proposals must be accompanied by a brief protocol synopsis and timeline milestones. As noted below, Institutional Review Board (IRB) and Ethics Committee (EC) approval or the approval of the local equivalent organization will be required before initial payment is made for any project that SIM, in its sole discretion, selects for funding. If new approvals are required during the course of funding, those approvals should be submitted to SIM as soon as possible. Conditional IRB or EC approvals will not be sufficient to receive initial payments.

iv. Proposals must include a participant recruitment or acquisition plan that will be inclusive of diverse backgrounds as much as possible, including race, age, gender, ethnicity, and geography. Projects that incorporate participants from a variety of geographic regions, organizations, and/or countries, will be prioritized.

- SIM recognizes that diversity will vary based on organization, sponsor, and geography. Diversity will be assessed based on the local population in the sponsor's geographical region.

v. Any intellectual property considerations that the proposed research may entail should be noted.

vi. Proposals must include a discussion of how participants will be selected, how efficacy will be assessed, necessary sample size, and control populations.

vii. Proposals must include a timeline that provides an overview of how the trial will be completed within two years.

viii. Proposals must include a discussion of alternative plans should local or systemic conditions prevent research from proceeding as planned.

d. Data sharing plan specifying the applicant organization's commitment to, and plan for, sharing project results and data (de-identified, where applicable) with other organizations and researchers for noncommercial use to advance the understanding of sarcoidosis and to maximize scientific impact, including designation of the particular data repository to which the applicant intends to upload and share such project results and data, and policies and procedures for ensuring that the applicant organization's PI and all other applicable employees and contractors will comply with and adhere to such plan. One page maximum.

i. The data sharing plan must include a brief description of the electronic data capture (EDC) system that will be used.

ii. SIM expects that all deidentified participant data will be made available for other researchers or clinicians to reference for meta-analyses or other proposed research aims.

iii. The data sharing plan must include a description of how the data will be validated.

iv. Consent information must be shared with SIM upon request.

v. Data sharing standards must be consistent across multiple sites, if applicable.

e. A development plan that outlines the next phase of the development process, provided the trial is successful, commercialization potential, and any current or anticipated intellectual property. One page maximum.

2. **Project Site Location and Diversity Action Plan.** This section must describe the project location(s) and the proposed strategy for ensuring that the trial participants represent diverse backgrounds. Two pages maximum.

a. Project Site Location(s) (a list of each of the clinical trial sites that intend to participate in the proposed trial). One page maximum.

b. A Diversity Action Plan that includes the following, with one page maximum:

i. goals for enrollment in the clinical trial, disaggregated by race, ethnicity, sex, and age group of clinically relevant trial populations,

ii. rationale for such goals, and

iii. an explanation of how the research team intends to meet such goals.

3. **Team Description and Capabilities.** This statement must outline the research group's ability to address the research question, support the research, manage patients, if applicable, and identify any key personnel in addition to the PI. A brief explanation of each team member's expertise and contribution to the project is required. One page maximum.

4. **Budget Submission.** A detailed budget in USD with a narrative summary and justification for each item, including how the PI intends to spend their time on the project. Two pages maximum using the provided template, and one page maximum providing narrative justification of budget items. Projects can be budgeted for two years. Projects can be budgeted for up to US$500,000 (US$250,000 per year) in direct costs and up to 15 percent of the total budget, or up to US$75,000 (US$37,500 per year) in indirect costs if they are two years in length. Note: If more than one organization is involved in the project, one must be proposed as the applicant organization responsible for directing funding to the other organizations as sub-grantees. Acceptable expenditures for direct costs include:

    a. salary for the PI, site coordinators, nurses, research assistants, staff scientists, and other personnel (fringe benefits are also covered).

    b. equipment and software.

    c. laboratory supplies such as reagents and tools.

    d. consultant costs.

    e. patient recruitment.

    f. patient-related costs including travel, stipend, and materials.

    g. project-related travel.

    h. publication costs.

    i. regulatory application fees and costs.

    j. up to an additional 15 percent indirect expenses to support organizational infrastructure. Indirect costs will be proportional to either the US$400,000 budget, and therefore will not exceed US$60,000, or the US$500,000 budget, and therefore will not exceed US$75,000. It is not necessary to provide specifics about the indirect cost expenditures.

Please note that grants will be made in USD, and ATF is not responsible for changes in conversion rates. 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.

5. **Clinical Trial Documentation** within the online form will include:

    a. Data Safety and Monitoring Plan (DSMP). In compliance with federal regulations, all applicants must submit a general description of the DSMP for any proposed trial that places human subjects at more than a minimal risk. A DSMP helps to ensure subject safety, as well as the validity and integrity of the data. Additionally, a DSMP enables the monitoring of trial data to assess whether or not an early

termination is necessary for safety or efficacy reasons. Large, multi-center interventional clinical trials may be required to utilize a Data Safety and Monitoring Board (DSMB). The DSMP must address the following areas:

i. Assessment of Risk: Describe the level of risk the proposed research presents to trial subjects and provide a detailed justification for the level of risk. Discuss who will monitor the trial.

ii. Anticipated Adverse Events and Grading Scale: Describe anticipated adverse events (AEs), including expected frequency and the grading scale to be used. Discuss plans for addressing AEs.

iii. Reporting of AEs: Detail the plan for reporting AEs, including who will be notified in the event an AE should occur.

iv. Safety Monitoring Plan: Describe all tests, evaluations, and exclusion criteria that will be implemented to ensure and monitor the safety of human subjects. Discuss stopping rules for the trial subjects or for the overall trial if necessary.

v. Safety Reviews: Describe the process for monitoring and reviewing subject safety data, including the frequency of such reviews. Include details about who will perform the monitoring (e.g., DSMB Membership Roster) and plans for reporting. Provide the frequency of meetings, the reporting requirements, including AEs and severe AEs (SAEs), and the procedure for interim reporting as necessary. This information will be required prior to ATF releasing funding.

vi. Registrations for Investigator-Initiated Clinical Trials:

- Clinicaltrials.gov (United States): Applicants must register all non-exempt human subjects trials in the Clinicaltrials.gov database to ensure that information is freely available. The registration should be no later than 21 days after the first subject is enrolled. ATF requires copies of registration confirmation when applicable.
- EudraCT Registration (European Union): For interventional clinical trials with medicinal products conducted in the European Union, the organization must provide documentation to ATF confirming registration of the clinical trial, when applicable.

b. a copy of the investigator's brochure for the mTOR inhibitor that will be tested.

c. a copy of the informed consent form that will be distributed to potential trial participants.

d. 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 organization to criminal, civil, or administrative penalties.

e. a list of any relevant conflicts of interest and all financial disclosures.

6. **Additional Documents**
    a. Lead PI's and any Co-PI's biosketch using the National Institutes of Health (NIH) template or equivalent. Five pages or fewer using the NIH template.
        i. Please note that we **will not** require applicants to use the new NIH Common Form biosketch and we ask all applicants to either submit a CV or to continue to use the previous NIH biosketch template.
    b. Institutional letter of commitment stating that the applicant organization will be able to support the research led by the PI.

7. **Tax Status Documentation**
    a. Applicants from nonprofit organizations may be asked to submit the following documentation to verify their organization's tax status at the time of the award:

Non-US applicant organizations may be asked to provide:

- a list of voting board members and officers, as well as the name of the organization's highest-ranking staff member (e.g., Chief Executive Officer).
- additional organization governing documents and other documentation via a secondary questionnaire, following proposal submission. ATF will make this request during proposal review. For more information, visit https://www.ngosource.org/how-an-ed-works.

US-based governmental organizations (excluding academic/research organizations that are public charities) may be asked to 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 IRS confirming the organization's tax status, if applicable.

Formatting and length will be strictly enforced by the review team. Any submissions that exceed the page limit or do not follow the aforementioned requirements should not be considered for review.

Note on Artificial Intelligence (AI) Use: ATF understands that AI tools are being used to support authors. The human authors who choose to use these tools are accountable for anything that AI has developed or edited. Applicants and awardees are expected to abide by best practices in research and publishing ethics and must address any questions pertaining to the accuracy or integrity of any of their work.

As all applications are considered confidential, neither ATF nor SPARC will use AI to analyze any submissions.

Review

The Scientific Advisory Board will review each application. All applications will be reviewed based on:

- scientific and technical merit,
- team capabilities and competencies,
- path to regulatory approval plan, and
- the realism of the cost.

Key Dates and Timeline

1. **Thursday, February 26, 2026**: Informational session on SIM will be held over Zoom at 3 p.m. Eastern Time. Use the following link to register: https://milkeninstitute-org.zoom.us/meeting/register/x2EHV718SOWhJz-fwQeJig.
2. **Monday, April 20, 2026**: Applicants must submit their full proposals via the Survey Monkey Apply grant portal by 11:59 p.m. Eastern Time.
3. **June 2026**: Awardees who are selected for funding are notified.
4. **August 2026**: Projects begin.
5. **Summer 2026:** The Funded Investigators Meeting occurs. Lead PIs of all teams funded by ATF sarcoidosis grant programs are expected to attend.

Grant Terms

Each funded research organization and the lead PI will be required to co-sign and agree in writing to SIM's grant terms within 30 days from receipt of notice of the award and prior to funds being released. SIM's grant terms include the following:

1. Signature confirming that the information provided in the grant proposal is true, complete, and accurate. False or fraudulent statements may subject the funded organization to criminal, civil, or administrative penalties.
2. SIM will require a copy of the full protocol before initial payments.
3. Any substantial changes to the project, including activities, new clinical sites, budget, protocols, or grant period, require written approval from SIM before proceeding with such activities, spending, or committing any remaining funds from the grant.
    a. Any funds not expended or committed for the purposes of the grant must be returned to SIM unless otherwise agreed by ATF in writing.
    b. If an applicant organization proposes to supplement any funds provided by SIM with funds provided by a third party, the organization must first provide notice to SIM 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.

4. The applicant organization must be able to receive awarded funds and allocate them toward the funded sarcoidosis research project.
    a. For-profit organizations must retain funding received from SIM in an account specifically for these funds and provide SIM with accurate expenditure reporting every six months.
5. The lead PIs must submit a lay, nonconfidential scientific abstract intended for a public audience for SIM to display on its website.
6. The lead PIs are expected to attend and participate in annual investigators' meetings to present and discuss their research plan and preliminary results in the research supported by the collaborative grant. The annual investigators' meeting is planned for August 2026.
7. The funded investigators are expected to attend and participate in Quarterly Check-In Meetings. These virtual meetings will bring together currently funded investigators among all ATF grant programs, to provide opportunities to share updates and solicit feedback from their peers. These meetings may also be used as workshops to support the investigators or the sarcoidosis ecosystem.
8. Funded organizations must agree to the following reporting requirements:
    a. Submission of written narrative and financial reports at the conclusion of the granting period, at 24 months, following the award payment.
    b. At 12 months after receiving funding, applicants should also share brief updates describing major project highlights and/or progress based on pre-determined milestones after the initial award payment as well as participate in a brief virtual meeting with other grant recipients to discuss plans, progress, and findings.
9. Full IRB and EC or the local equivalent approval will be required before initial payments are made. Conditional IRB/EC approvals will not be sufficient for initial payments.
10. It is a condition of any funding provided by SIM that the investigator seeks to have the results of the funded project be made available in the format most appropriate for the trial results. If trial results can be published in a peer-reviewed journal, then they must be submitted to an open-access journal or a pre-print journal within 18 months after project completion. Each publication would acknowledge SIM's role in supporting the project in a form approved by SIM. If the investigator does not publish the results within such a time frame, then SIM would have the right to make such results public. Investigators may specifically budget for such publications. If the results are not appropriate to submit to a peer-reviewed journal, the trial results must be submitted to a preprint journal within 18 months after completion of the project. Funded investigators must make SIM aware of any publication supported by SIM funds within 30 days of publication.
11. A lay summary of the project goals and findings must be sent to all recruited participants within three months of project completion.

Data and Intellectual Property

The funded organization will own the rights in all intellectual property developed by or on behalf of that organization under SIM funding, in accordance with such organization's applicable intellectual property policies. SIM will have the right to use and to practice all such intellectual property for internal, noncommercial research purposes, and will 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). Intellectual property will be sublicensable to nonprofit research organizations for noncommercial educational and research purposes only and will only be used in research related to the prevention, diagnosis, treatment, or cure of sarcoidosis and conditions or complications caused by sarcoidosis.

Each funded organization must agree to share project results, data (de-identified where applicable), reagents, and other research tools developed under SIM funding with other ATF-funded investigators for noncommercial use to advance the understanding of sarcoidosis and to maximize scientific impact.

Funding Awarded in SIM's Discretion

Responding to this RFP or submitting a full proposal does not entitle any individual or organization to receive funding from SIM. Funding, if any, would be provided in SIM's sole discretion pursuant to the terms of a written grant agreement executed by SIM and the selected awardee organization and acknowledged by the PI.

Contact Information

For all inquiries about the online process, necessary documentation, research priorities, or scientific requirements, please contact sarcoidosisgrant@milkeninstitute.org.

An automated email confirmation is generated upon submission of the application. If you do not receive confirmation within 24 hours of submitting your application, please check your spam filters and then contact sarcoidosisgrant@milkeninstitute.org.