Regenerative Medicine Minnesota
Clinical Trial Award Program

APPLICATIONS DUE 3/10/2023

Objective of Clinical Trial Awards

The objective of the Regenerative Medicine Minnesota (RMM) Clinical Trial Award program is to support the completion of a clinical trial for a regenerative medicine-based therapy (stem cell-based or genetic therapy) that addresses an unmet need. Projects funded through this program should be:

- First-in-human clinical trials with the therapeutic candidate (or feasibility studies if the product is a medical device) in a specific disease indication and using a given route of administration
- Succeeding clinical trial studies conducted after the first-in-human trial
- Clinical trials that aim to expand patient access to a regenerative medicine-based therapy

Award Information

What is the award amount and duration?

RMM will fund total (direct and indirect) project costs of up to $500,000. Larger budgets may be allowable with adequate justification and approval of RMM. The proposed project period must not exceed 48 months from the award start date. Project costs must be adequately justified and are subject to adjustment prior to the issuance of an award.

How will the funds be awarded?

An RMM award is a formal contract that defines the terms and conditions of an award and documents the commitment of the funds from RMM. Projects will be monitored by RMM for progress and adherence to the project milestones, timeline and budget. If at any time RMM determines that a project is not complying with the terms of the program, or is unable to advance the project, a project may be closed and the unused funds returned to RMM.

Costs resulting from a delay or failure to meet milestones will be the sole responsibility of the recipient. Successful applicants will have thoughtfully accounted for foreseeable project risks and developed contingency plans that do not involve additional funding from RMM.

What activities will RMM support?

RMM has special interest in broadening the portfolio of research that can help relieve chronic, genetic, and/or rare disorders that impact patients and health care costs in Minnesota.

RMM funds <u>will</u> support activities under this opportunity including, but not limited to:

- All activities necessary for the conduct and completion of a clinical trial with a single therapeutic candidate or medical device
- Correlative studies associated with the current proposed trial such as elucidating mechanism of action, biomarker identification, patient selection
- Manufacturing of product to supply the proposed clinical trial, including a follow on clinical trial, where appropriately justified
- Commercial development activities including pharmacoeconomic analysis

- Product development activities to support the clinical trial or clinical development
- Comparability studies
- Activities intended to promote and uphold principles of Diversity, Equity, Inclusion, and Accessibility (DEIA) in the conduct of the study
- Activities associated with sharing data and knowledge from the study

RMM resources cannot be used to support the following activities under this opportunity:

- Preclinical IND-enabling activities as these studies would be eligible for funding through the RMM Translational Research Award program.
- Clinical studies that do not meet the NIH definition of a clinical trial (https://grants.nih.gov/ct-decision/index.htm)

Eligibility

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) Must be ready to initiate work on the funded project within 90 days of approval

(2) Must propose a single clinical trial using a regenerative medicine-based therapy (stem cell-based or genetic therapy)

a. A cell therapy where human stem cells or progenitor cells (collectively, "stem cells") either compose the therapy or are used to manufacture the cell therapy. Minimally manipulated bone marrow, minimally manipulated cord blood or unmodified hematopoietic stem cells (HSCs), are eligible only if being developed as a novel method of addressing a rare or unmet need.

b. A genetic therapy approach (i) that targets a human somatic cell for its therapeutic effect AND (ii) is intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs.

c. A small molecule or biologic that acts on or is dependent on endogenous human stem cells for its therapeutic effect, that is dependent on targeting human cancer stem cells for its therapeutic effect, that modifies a stem cell therapy, OR where a human stem cell is necessary to manufacture the therapy (e.g., extracellular vesicles).

d. Under IDE, phase 1 or feasibility trials of a medical device (including a diagnostic device) as follows:

i. A medical device where human stem cells are a necessary component of the device or are used to manufacture the device.

ii. A device intended for clinical use with a genetic therapy or human stem cells where the genetic therapy or stem cell contributes to the therapeutic mechanism of action of the combination product.

iii. A device intended to address a critical bottleneck to clinical development or use of a genetic therapy or stem cell treatment AND where testing with a genetic therapy or human stem or progenitor cell confirms the clinical safety and efficacy of the device.

iv. A device where the therapeutic mechanism of action requires the recruitment or incorporation of an endogenous stem cell.

(3) Must have regulatory approval to proceed with proposed trial.

a. All applicants must have an active IND or IDE for experimental therapies for the proposed candidate in the proposed indication before applying.

b. Studies of repurposing approved drugs for regenerative medicine purposes might not require an IND. Applicants must provide adequate justification if an IND is not needed.

c. The applicant must provide communication from FDA indicating it is safe to proceed with the proposed clinical protocol if proposing a new trial under an open IND/IDE.

d. Phase 2 trial applicants must have Phase 1 safety data obtained with the proposed treatment in an appropriate indication unless agreement to proceed with the Phase 2 protocol is otherwise indicated by the FDA.

e. Phase 3 trial applicants must have Phase 2 data for the proposed indication(s) and have completed the End-of-Phase 2 meeting or equivalent.

(4) Must include a project manager with experience managing clinical development programs.

(5) RMM applicant must be the IND/IDE sponsor.

(6) The clinical trial must take place in the state of Minnesota.

(7) For all projects developing a product candidate that includes allogeneic (donor-derived) cells:

a. The cell source (tissue or cell line) proposed for use must have been consented by the donor for intended use and for clinical development and commercial sale.

b. The cells must meet the Good Tissue Practices (GTP) requirements for donor eligibility (21 CFR 1271 (subpart C)), or there is a plan in place to address the GTP requirements.

(8) Co-funding is not required

If the project does, however, require funding over and above that which RMM provides, documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission.

(9) Partnerships with other institutions are allowed

Collaborations may include research subcontracts or consulting agreements with laboratories, universities, medical centers, industry partners, etc. in the state of Minnesota. If planning to use a portion of requested funds to support a project at another institution, such as the University of Minnesota or Mayo Clinic, then the application must include that institution's indirect cost rate. The submitted budget should reflect this and include separate indirect costs for the primary organization and any other institution with a different indirect rate. Other institution budgets should be shown separately.

(10) Application must be accurate and complete

Who can apply for RMM funding?

(1) Only Minnesota-based academic institutions and small-businesses performing scientific and/or medical research in the state of Minnesota are eligible for this opportunity. Small businesses (the "Entity") must be based, owned (≥50%), and operating in the state of Minnesota. For this definition, a small business must have at least 2 and no more than 100 affiliated full- or part-time

employees. Entities must be registered with the state of Minnesota's Secretary of State Office (http://www.sos.state.mn.us/business-liens) prior to the application being submitted.

(2) The PI and applicant organization are responsible for being in compliance with federal, state, and institutional research regulations at all times during the funding period, including having active approvals from all regulatory agencies (e.g., Institutional Review Board). A copy of the approval document(s) must be available upon request.

(3) Applicant must be in "good standing"

The PI, key personnel named in the application and any business leadership of small businesses must not have been convicted of, or are under investigation for, crimes involving fraud/misappropriation or research misconduct. The performance of applicants previously supported through the RMM program will be taken into account in funding decisions.

Who can serve as the Principal Investigator (PI)?

RMM encourages early stage investigators from diverse backgrounds to apply. To be eligible, the PI must:

- Be an employee of the applicant organization.
- Be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI.
- Applications can have **only one** PI.
- PIs can only hold one RMM award at a time.
- Not currently have another application pending review or approval under this funding opportunity.
- Not currently have another application that is substantially similar or has overlapping activities pending review or approval under any RMM opportunity.

Schedule and Deadlines

Applications Due	March 10, 2023 at 5 pm
Application Review	March through May 2023
Awards Announced	Late May 2023
Earliest Start Date	July 1, 2023

Application Components and Submission

How does one apply?

Applications must be completed and submitted online at https://umnodat.inforeadv4.com/#competitionDetail/1893436

Any prospective PI must create a login in the system to access application materials and apply. A PI may submit only one RMM application in a given review cycle.

The main components of the application include the following key sections:

1. **Principal Investigator Information** (Responsible Party; there can only be one principal investigator)
2. **Institution Information** (responsible for receiving and disbursing grant funds)

3. **Application Preview Page/Abstract:** This section will be utilized by reviewers to prescreen applications and select a subset to move forward to the next stage of the review process.
   a. Project Summary
   b. Disease Indication
   c. Vision for Progression
4. **Resubmission Statement:** If this application is a resubmission from previous RMM review cycles, the applicant will provide a brief statement on how this application addresses the previous reviewers' critiques.
5. **Target Clinical Indication:** Proposed indication for first use in a clinical setting, including a description of the target patient population for first clinical use.
6. **Value Proposition:** Description of the unmet need and the product's potential value to patients, healthcare providers, and caregivers.
7. **Scientific Rationale:** Explanation of how published and preliminary research support use of the proposed product as a therapy or medical device for the target indication.
8. **IND- or IDE-Enabling Studies:** Summary of IND- or IDE-enabling study results
9. **Clinical Studies:** Summary of completed or ongoing clinical studies with the proposed or a related product.
10. **Timeline:** Detailed timeline for all proposed activities. RMM expects projects under this program to advance rapidly through clinical development. The proposal must aim to enroll and dose all patients in the trial and to complete the initial analysis of the trial's primary endpoint(s) within the maximum 48-month timespan. Patient follow-up activities within the 48 month award period are allowed. Further follow up beyond 48 months consistent with FDA regulations is expected.
11. **Project Plan:** Description of all proposed activities detailing how the objectives of this funding opportunity will be met.
12. **FDA Correspondence:** Summary of regulatory requests and proposed action plans.
13. **Manufacturing Plan:** Synopsis describing key aspects of the manufacturing plan for the proposed trial.
14. **Trial Protocol Synopsis:** Synopsis describing key aspects of the planned clinical trial protocol.
15. **Clinical Operational Plan:** Synopsis describing key aspects of the planned clinical operations for the proposed trial.
16. **Plans for Risk Mitigation & Financial Contingency:** Potential risks, mitigation strategies, associated costs, and non-RMM resources of contingency funding.
17. **Team Organization:** Qualifications of the proposed team and plans for team collaboration.
18. **Resources and Environment:** Resources available to benefit the project.
19. **Commercial Development:** Plans for effective and inclusive commercial development of the product.
20. **New Jobs:** An estimate of the number of new jobs that will be created with this funding (if awarded) and plan for sustaining these jobs after the award has ended.
21. **Intellectual Property:** A brief summary of any intellectual property related to the proposed project, including protection status and ownership/assignment.

22. References

23. Budget Information: Completed budget form (template provided in online application portal).

a. **Direct** costs requested
b. **Indirect** costs requested (see: https://oamp.od.nih.gov/dfas/indirect-cost-branch/indirect-cost-submission/indirect-cost-definition-and-example. These should be included in the budget at the established NIH-negotiated rate or, in the absence of a federally-negotiated rate, at 10 %.)
c. **Total combined** costs requested (must be ≤ $500,000 total)
d. Start date requested (between July 1, 2023 and July 30, 2023)
e. Length of grant (up to 48 months)

24. Biosketches/CVs for Key Personnel

Application Review Information

What criteria are used to evaluate the applications?

1) *Does the project hold the necessary significance and potential for impact?*
    a. Does the proposed treatment address an unmet medical need?
    b. Is the approach likely to provide an improvement over the standard of care for the intended patient population?
    c. Does the proposed treatment offer a sufficient value proposition such as the value created by the treatment supports its adoption by patients and/or health care providers?
    d. To what extent does the proposed treatment address chronic disorders that impact patients and health care costs in Minnesota?
2) *Is the rationale sound?*
    a. Is the proposed project based on sound scientific and/or clinical rationale?
    b. Is the project plan supported by the body of available data?
    c. Do the data support the continued development of the treatment?
3) *Is the project well planned and designed?*
    a. Is the project appropriately planned and designed to meet the objective of this funding opportunity and achieve meaningful outcomes to support further development of the therapeutic candidate?
    b. Is the proposed manufacturing plan appropriately designed and budgeted for both time and cost?
    c. Is the timeline appropriate to complete the essential work without unnecessarily extending it for non-essential activities?
4) *Is the project feasible?*
    a. Are the intended objectives likely to be achieved within the proposed timeline?
    b. Is the proposed team appropriately qualified and staffed?
    c. Does the team have access to all the necessary resources, appropriate facilities and expertise to conduct the proposed activities, including manufacturing?
    d. Does the team have a viable contingency plan to manage risks and delay?

What is the process for evaluating an application?

Pre-submission Consultation

RMM is committed to helping develop promising stem cell-based technologies by partnering with researchers. Therefore, prospective applicants are encouraged to contact RMM with questions or to discuss their project's eligibility before applying.

Eligibility Review

RMM will assess whether the proposed project meets eligibility requirements sought under this program. If RMM determines that an application does not meet the eligibility requirements of the program, RMM will notify the applicant of its decision and, if RMM deems it is appropriate, allow an opportunity to remedy. If RMM deems it inappropriate, or if the applicant does not remedy the error in a timely manner, RMM will remove the application from further review and funding consideration.

Scientific Review

The scientific merit of each application will be assessed by RMM Board members and scientific reviewers from outside Minnesota. Applications will be evaluated according to scientific and technical merit, applying the review criteria described above. The review will be conducted in three stages. In the first stage, RMM program leadership and Board members will conduct a pre-review of applications to identify applications that the Board believes are most responsive to the funding opportunity and hold the most potential for impact. Since the selection process is focused on quickly identifying promising proposals rather than identifying deficiencies in applications, no reviewer comments are collected at this stage.

Selected applications advance to the second stage of review, which involves assignment to specific scientific reviewers outside of Minnesota. Applications are scored according to the review criteria and review comments are collected and discussed by the Application Review Committee, which is made up of the RMM Board and RMM program leadership.

In the final stage of the review, all applications will undergo a review by the Application Review Committee in which applications of high scientific and technical merit will be carefully scrutinized to allocate the funds available to support the award mechanism as wisely as possible. Applications that have the highest potential to help achieve the vision and goals of the RMM program (programmatic relevance, portfolio balance, adherence to the intent of the mechanism) will be selected for funding. Although the evaluations of the scientific reviewers are a key factor, the additional consideration of programmatic intent and portfolio balances means that applications are not funded using an established "pay line" based solely on a numeric scoring system.

Consideration of Past RMM Award Information (If Applicable)

RMM may consider information from a previously funded and related RMM award as part of its review. This includes but is not limited to achievement of specific milestones, data, and outcomes for a related RMM award or awards. A “related RMM award” includes: (1) an award for which the applicant PI served as the PI, a co-investigator, or otherwise substantially participated in the conduct of the award; (2) an award involving the same research project or product; or (3) and award that includes overlapping team members.

Confidentiality and Data Privacy

RMM’s confidentiality and conflict screening policies apply to everyone who will have access to applications or who will participate in any review meeting in which confidential information is discussed. Through administration of the RMM program, the University is committed to protecting the information submitted in your proposal as allowed under state data privacy laws and University policy. Minnesota's Government Data Practices Act contains specific provisions on public grant data and protected trade secret information. In the application, you will be asked to identify specific sections that you believe qualify as your trade secret information (https://mn.gov/admin/data-practices/data/types/tradesecrets/).

Award Administration

Issuance of Award

An RMM award is issued through the Sponsored Projects Office at the University of Minnesota, via a Notice of Grant Award (NOGA) and/or Subaward Contract document, which is a formal contract that defines the terms and conditions of an award and documents the commitment of the funds from RMM. RMM reserves the right to modify or establish funded project activities, milestones (both technical and financial), success criteria, timelines, and budgets prior to issuance of the NOGA/Subaward Contract. RMM reserves the right to review whether an applicant has satisfied the eligibility criteria set forth in this program announcement and, if RMM determines that an applicant has failed to satisfy one or more criteria, to refrain from issuing a NOGA/Subaward Contract.

Payments and Reporting

Payments are made on a cost-reimbursement basis. For University awards, this is done automatically up to the award amount. For non-University awardees, invoices must be submitted per the contract document. Projects will be monitored by RMM for progress and adherence to the project milestones, timeline and budget. If at any time RMM determines that a project is not complying with the terms of the program, or is unable to advance the project, a project may be closed and the unused funds returned to RMM.

Grantees will be required to provide periodic written progress and financial reports to RMM. RMM will partner with the grantee to foster the success of the project through access to both internal experts and the ability to enlist the help of external subject matter experts when needed. Grantees will have ongoing communication with the RMM Program Manager throughout the duration of the award.

Award Conditions

The PI is responsible for being in compliance with federal, state, and institutional research regulations at all times during the funding period, including having active approvals from all regulatory agencies (e.g., Institutional Animal Care and Use Committee). A copy of the approval document(s) must be available upon request.

If the PI of the grant leaves the institution, a request for change in PI may be submitted for consideration. If no request is submitted or the request is denied, unused funds will revert to RMM.

If the PI of the grant is unable to use the funds for the research as proposed in application, funds will revert to RMM.

In keeping with the spirit of the awards, the funds should remain and the work be performed in Minnesota. Exceptions may be made for materials or services not available within the state, and such exceptions should be noted in the budget.

Intellectual Property

Inventions arising from RMM-funded projects are required to be reported to RMM. As with federal funding, RMM permits businesses and nonprofits (including universities) to retain ownership of the inventions, while also giving the Minnesota state government the license to practice the subject invention. In turn, the organizations are expected to file for patent protection and to ensure commercialization for the benefit of public health.

No-Cost Extensions

Timeline progress on funded projects is of critical importance to RMM. Therefore, RMM will consider a No-Cost Extension (NCE) request, submitted at least 30 days before the project end date. Such a request should properly justify how such an extension will advance the project towards its expected outcome, but Grantees should not assume RMM will approve a NCE request.

Contacts

For questions not answered in the RFP, email RegenMedMN@gmail.com.