Regenerative Medicine Minnesota (RMM) Award Program

APPLICATIONS DUE 3/11/2024

OBJECTIVE:

Regenerative medicine aims to alter the current practice of medicine by treating the root causes of disease and disorders through augmenting, repairing, replacing or regenerating organs, tissues, cells, genes, and metabolic processes in the body (Alliance for Regenerative Medicine). Regenerative medicine-based innovations include gene therapies, cell therapies, tissue-engineered products, diagnostics, medical devices, combination products and tools to enable regenerative medicine discovery and development. See Appendix I for examples of regenerative medicine based innovations.

The objectives of RMM awards are to support discovery, development, translation and commercialization of regenerative medicine-based innovations in the state of Minnesota to improve human health in Minnesota and beyond.

To accomplish this goal, RMM offers awards in 4 separate funding tracks:

1. **Discovery:** Supports exploratory research and discovery of novel regenerative medicine therapeutic approaches or regenerative medicine-based innovations and tools (see Appendix for definitions)
2. **Translation:** Supports completion of activities necessary for advancement of regenerative medicine-based innovations towards clinical study or broad end use
3. **Clinical Trial:** Supports completion of activities through any stage clinical trial for regenerative medicine-based interventions
4. **Infrastructure:** Supports Minnesota organization's capabilities to develop and commercialize regenerative medicine-based innovations

See Project Eligibility for more information, including the types of projects eligible for each funding track.

AWARD INFORMATION:

Award amounts and duration vary based on the type of award:

- **Discovery:** <$200K, <2 years
- **Translation:** <$400K, <2 years
- **Clinical Trial:** <$500K, <4 years
- **Infrastructure:** <$200K, <2 years

Award amount limits include both direct and indirect costs. Funds will only be provided for work critical to advance a project. Only request the amount that is needed. See Eligible Expenses section for more details.

See Award Administration section for more details on award issuance and conditions.

ELIGIBILITY:

Organization:

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 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.

Principal Investigator (PI) /Applicant:

- The PI must be an employee of the applicant organization and authorized by the applicant organization to conduct the research and assume the responsibilities of the PI.
- Applications can only have 1 PI.
- PI, key personnel and any business leadership of small businesses must be in good standing (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.
- PIs can only:
  - Hold 1 RMM award at a time as a PI or in any other role to a RMM awarded project.
  - Submit 1 application to a given funding track (Discovery, Translation, Clinical Trial or Infrastructure) per funding cycle.
  - Submit an application to more than one funding track if the proposed work is unique with non-overlapping aims.

Projects:

Each funding track supports different types of projects:

Discovery	● Basic research into stem cell mechanisms or genetics ● Investigating stem cells as tools for drug discovery, development, disease modeling, or enabling regenerative medicine research and innovation ● Research tools related to diversity, equity and inclusion ● Modeling of cells/tissues (omics) ● Auxiliary research (biomarker discovery, gene editing, imaging tools, mechanism of disease)
Translation	● Activities that will lead to selection and/or translation of a novel candidate therapeutic, diagnostic, medical device, combination product, or tool for use in developing new drugs, devices, disease models, or products for use in research and preclinical work (e.g. reprogrammed cells, organoids, tissues, animal models, or new cell lines) ● Feasibility and Proof-of-concept studies ● Developing a Target Product Profile ● IND and IDE-enabling studies

	● Preparation for and conduct of stage appropriate regulatory meetings ● Activities necessary for advancement to clinical study or end use
Clinical Trial	● All activities necessary for the planning, conduct, and completion of a clinical trial with a single therapeutic candidate or medical device ● Product development and manufacturing for the proposed clinical trial ● Correlative studies or comparability studies associated with a clinical trial ● Activities intended to promote and uphold principles of diversity, equity, and inclusion in the conduct of the study
Infrastructure	● Development of infrastructure (including personnel, equipment, supplies, and/or services) to design, develop, manufacture, test, gain regulatory approval, and market regenerative products ● Purchase of non-expendable equipment or instrumentation to improve infrastructure for the development of regenerative medicine products ● Implementing Quality Management System & GMP standards

Note that clinical trial projects must have regulatory approval (e.g. active IND or IDE) for the proposed candidate and indication and take place in Minnesota.

See Appendix II for more examples of types of projects supported for each funding track.

Expenses:

Direct and indirect expenses are allowed. Indirect costs should be included in the budget at the established NIH-negotiated rate or, in the absence of a federally-negotiated rate, at 10 %. (see: https://oamp.od.nih.gov/division-of-financial-advisory-services/indirect-cost-branch/indirect-cost-submission/indirect-cost-definition-and-example).

Funds should remain and the work shall 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. Partnerships with other institutions based within Minnesota 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.

APPLICATION PROCESS AND CONTENTS:

Applications must be completed and submitted online through the InfoReady system at:

https://umnodat.infoready4.com/#freeformCompetitionDetail/1928288

Any prospective PI must create a login in the InfoReady system to access application materials and apply. University of Minnesota PIs and any applicants who already have an InfoReady account can log in using their UMN login credentials or existing InfoReady login.

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 for alignment with the RFA and specific funding track. Provide a summary of the project, gap or unmet need being addressed, product in development, overview of project plan and impact.
4. **Resubmission Statement:** If this application is a resubmission from previous RMM review cycles, provide a brief statement on how this application addresses the previous reviewers' critiques.
5. **Description of Future Product (if applicable for Translational, Clinical Trial and Infrastructure projects):** Describe the product in development, how it addresses an unmet need, potential value to end users, patients, providers, caregivers, and proposed indication/application for first use.
6. **Statement of Significance and Impact:** Description of how the project could: 1.) address a critical knowledge gap in the field of regenerative medicine or a critical bottleneck to the discovery, development, or use of regenerative medicine-based innovations**;** 2.) advance or increase likelihood of successful development or use of regenerative medicine-based innovations to address an unmet need**;** and/or 3.) increase diversity of application of regenerative medicine-based innovations
7. **Objective and Specific Aims/Milestones:** A concise description of the project objective and project aims/milestones.
8. **Rationale/Previous Supporting Work:** Description of the scientific rationale for the proposed research or how published and preliminary research findings support the project. Include IND- or IDE enabling studies and clinical study results (if applicable **for Clinical Trial projects**).
9. **Project Plan:** A concise but detailed description of the methods and techniques to be employed to achieve aims, and criteria for success, potential pitfalls/risks, alternative approaches and risk mitigation strategies. Include FDA correspondence, manufacturing plan, clinical trial protocol synopsis and operational plan (if applicable **for** C**linical Trial projects**). Include commercial development plan with timeline and milestones to be met to get the product to market (if applicable for I**nfrastructure projects**).
10. **Next Steps:** After the proposed project is complete, describe the next steps to continue development, translation to broad end use and/or commercialization or for sustaining infrastructure.
11. **Data Sharing and Management Plan:** A description of the proposed plan to share and manage data generated from the project.
12. **Timeline:** Activities-based timeline and cost for achieving project aims, including any potential delays that could impact the ability to complete the project on time and strategies to mitigate them. **For Clinical Trial projects-** 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.

13. **Team and Entity:** A description of the PI and team's roles, expertise, and experience. **For Infrastructure projects**, briefly describe the Entity, including operational history (goals, founders, and key participants), business structure, revenue history for the past three years (if any for the past 3 years, government funding and/or private investment) and how the proposed effort/equipment will fit into existing operations (if applicable).
14. **Resources and Environment:** A brief description of the resources available to the project and environment.
15. **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.
16. **Intellectual Property:** A brief summary of any intellectual property related to the proposed project, including protection status and ownership/assignment (if applicable).
17. **References**
18. **Budget Information:**
    - **Direct** costs requested
    - **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 %.)
    - Length of award
    - Estimates (if applicable for infrastructure grants)
19. **CV/Biosketches for Key Personnel**

REVIEW INFORMATION

Review Criteria:

Significance and impact

- Does the project define, address and have the potential to impact a key knowledge gap in the field, unmet need, or a critical bottleneck to the discovery, development, or use/application of regenerative medicine-based innovations?
- Is the approach or innovation likely to provide an improvement over current practice by providers, users, patients or caregivers for the intended patient population or application?
- Does the project address chronic disorders that impact patients and health care costs in Minnesota?

Rationale

- Is the proposed project based on sound scientific rationale?
- Are preliminary data compelling and supportive of the proposed project?
- Do the data and plan support the proposed project, continued development, translation and/or commercialization of a technically and/or commercially feasible regenerative medicine-based product?

Project Plan

- Is the project appropriately planned and designed to meet the objective of the funding track and achieve meaningful outcomes to support further development of the innovation?

- Are potential pitfalls identified and alternative approaches presented?
- Is the proposed plan well-constructed with appropriate milestones, timelines, manufacturing, clinical operation plans? (if applicable for clinical trial projects)
- Is it clear how the infrastructure will contribute to the commercial development and is it possible to implement? (if applicable for infrastructure projects)

Feasibility

- Are the proposed aims/milestones/objectives and expected project outcome logical and likely to be achieved within the proposed timeline?
- Is the proposed team appropriately qualified and staffed and have access to all the necessary resources (e.g. facilities, equipment, manufacturing, etc.) to conduct the proposed activities?
- Is the budget appropriate for the research proposed?
- Does the team have a viable contingency plan to manage risks and delay?

Review Process

Pre-submission Consultation: Prospective applicants are encouraged to contact RMM with questions or to discuss their project's eligibility before applying.

Eligibility Review: RMM program will assess whether the proposed project meets eligibility requirements and intent of the program and specific funding track. Projects that meet eligibility requirements will advance to further review and funding consideration. Projects that do not meet eligibility requirements will be removed from further review and funding consideration.

In-depth Review: RMM Board members and scientific reviewers will evaluate each application according to the review criteria described above that are relevant to each funding track.

Funding decision: 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 by the RMM Review Committee. Although the evaluations of the scientific reviewers are a key factor, the additional consideration of programmatic fit 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, including, but not limited to achievement of specific milestones, data, and outcomes for a related RMM award or awards.

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 and the associated budget prior to issuance of a NOGA/Subaward Contract, including, when applicable, establishing project milestones, success criteria, and timelines at its sole discretion after consultation with the PI and based on information provided in the application.

Payments and Reporting

Payments are made on a cost-reimbursement basis. For University of Minnesota awards, this is done automatically up to the award amount. For non-University of Minnesota 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. Grantees will have ongoing communication with the RMM Program throughout the duration of the award.

Award Conditions

The PI and 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 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. RMM will consider a No-Cost Extension (NCE) request, submitted at least 30 days before the project end date. Such a request should clearly justify how such an extension will advance the project towards its expected outcome, but Grantees should not assume RMM will approve a NCE request.

RFA TIMELINE:

Applications Due	March 11, 2024, at 5 pm
Application Review	March through June 2024
Awards Announced	July 2024
Earliest Start Date	September 1, 2024

PROGRAM CONTACT INFORMATION
regenmedmn@gmail.com

Appendix I

Examples of Regenerative Medicine-based Innovations

Regenerative medicine-based innovations include: Stem or genetic cell therapeutics as well as devices, diagnostics and tools that are based on, critical for development or use of, or address critical bottlenecks to the discovery and development of stem cell or genetic therapies.

Therapeutics:

- Cell therapy where human stem or progenitor cells either compose the therapy or are used to manufacture the cell therapy
- Genetic therapy that targets a human somatic cell for its therapeutic effect and is intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs
- A combination product including a cell or genetic therapy component
- Small molecule or biologic that acts on or is dependent on endogenous human stem cells, modifies a stem cell therapy, or where a human stem cell is necessary to manufacture the therapy (e.g., extracellular vesicles)

Devices, Diagnostics, Tools:

- Human stem or progenitor cells either are a necessary component of the device, diagnostic or tool, or are used to manufacture the device, diagnostic or tool
- Diagnostics (including medical imaging agents) based on stem cells, or critical for stem cell-based or genetic therapy development or use
- Medical devices (non-diagnostic) for a stem cell-based therapy or critical for stem cell-based or genetic therapy development or use
- Addresses a critical bottleneck to translation, clinical development or use of human stem cell or genetic therapies and where testing with human stem or relevant genetic therapy-targeted cells confirms the utility of the device, diagnostic or tool for genetic or stem cell-based therapy development
- Where the therapeutic mechanism of action of the device requires the recruitment or incorporation of an endogenous human stem cell
- Novel tools that addresses a critical bottleneck to the discovery or development of stem cell-based or genetic therapy
- Novel stem cell based tools such as reprogrammed cells, organoids, tissues and animal models for use in the development of new drugs and devices
- New cells (e.g., neurons from iPSCs, organoids, and humanized mouse and pig models) to be developed as products for use in research and preclinical work

Appendix II

Examples of Types of Projects Supported Through Each Funding Track

Discovery

RMM funds will support activities under this track including, but not limited to:

- Basic research into stem cell mechanisms as they relate to human biology
- Investigating stem cells or their derivatives as tools for discovering and enabling therapeutic or other innovations, e.g., for studying or modeling disease
- Basic genetic research relevant to human biology and as it pertains to stem cells or regenerative medicine
- Research and tools related to diversity, equity, and inclusion in science, i.e., extending or validating the applicability of regenerative medicine discoveries to underserved populations (e.g., use of human induced pluripotent stem cell lines or omics analysis from diverse groups of individuals, target diseases or disease subtypes more are frequently experienced by underserved groups)
- Basic research and development of tools to address bottlenecks in the development of stem cell-based and gene therapies, such as cell/tissue targeting, immunogenicity and toxicity, in vivo gene therapy delivery, engineering human pluripotent stem cells to evade the immune system
- Studies to better understand human cells and tissues to be modeled in vitro or targeted with regenerative medicine approaches (e.g., omics and other profiling, human cell/tissue atlases), a human stem cell/regenerative medicine component (wet lab and/or data-related) must be included in the project
- Auxiliary research activities that support regenerative medicine science (e.g., biomarker discovery, genome and epigenome editing tools, imaging tools, mechanism of disease to enable rational design of stem cell- or gene therapy-based treatments, data science and computational approaches), a human stem cell/regenerative medicine component (wet lab and/or data-related) must be included in the project

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

- Projects that propose solely or mainly to derive new pluripotent stem cell lines without a larger novel objective
- Any project involving the use of embryonic stem cells

Translation:

RMM funds will support activities under this track including, but not limited to:

Activities that will lead to selection of a novel candidate therapeutic, diagnostic, medical device, or tool ready for translation to enable broad use and ultimately, improve patient care including:

- Studies to further characterize candidate biomarkers for development into a diagnostic test
- Developing and implementing assays to identify/test/characterize candidate (or prototype) therapeutic, device, diagnostic test, tool/technology
- Feasibility and initial reproducibility assessment

- Proof of concept studies with candidate; for non-stem cell-based candidates (e.g., certain devices, diagnostic tests, tools), proof of concept testing with human stem, progenitor, directly reprogrammed cells, or relevant human somatic cells targeted by a genetic therapy
- Developing Target Product Profile (Product Concept Document) for candidate therapeutic, device, diagnostic test or tool
- Preparation for and conduct of stage appropriate regulatory meetings (e.g., for stem cell-based cell therapeutic candidates – an INTERACT meeting)
- Translational activities necessary for advancement to clinical study or end use for a stem cell-based therapy, device, diagnostic or tool
- All activities to conduct and complete IND-enabling activities necessary for the filing of a single IND or IDE with the FDA to initiate a clinical trial with a single therapeutic candidate
- Product development activities appropriate to support the IND/IDE filing and the resulting clinical trial
- Manufacturing of the therapeutic candidate to support IND/IDE-enabling studies or to support the intended clinical trial(s)

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

- RMM funding is intended to support research or advance stem-cell based therapies that require human stem/progenitor cells or directly reprogrammed cells. Projects without a strong rationale for the unique necessity of these cells to achieve the project deliverable will not be considered for funding.
- Projects focused primarily on biomarker discovery are eligible for funding through the RMM Discovery track and, therefore, do not qualify for RMM Translational track.

Clinical Trial

RMM funds will support activities under this track 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 track:

- 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)

Infrastructure

RMM funds will support activities under this track including, but not limited to:

- Development of infrastructure, including personnel, equipment, supplies, and/or services required to establish the design, development, testing (including clinical), and manufacturing of a product(s) or provision of a service(s).
- Purchase of non-expendable advanced scientific equipment or instrumentation that contributes to an improved infrastructure for developing commercializable regenerative medicine-based therapeutics, diagnostics, medical devices, or tools.
- Implementing Quality Management System and GMP standards.

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

- Development of infrastructure or purchase of equipment to support research activities not directly related to commercialization of a regenerative medicine-based therapeutic, diagnostic, medical device, or tool.
- Development of infrastructure or purchase of equipment to be used outside of Minnesota.