



Funding Opportunity Concept Plan

ReMIND: Research using Multidisciplinary, Innovative approaches in Neuro Diseases

BACKGROUND

The mission of CIRM is to accelerate world-class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world.

The Research using Multidisciplinary, Innovative approaches in Neuro¹ Diseases (ReMIND) Program is developed in response to Proposition 14's mandate to dedicate at least \$1.5 billion, out of the total of \$5.5 billion, in bond funding to the support of research and development of treatments for diseases and conditions of the brain and central nervous system (CNS).

The vision for the ReMIND Program has been informed by multiple stakeholder discussions over the past 3 years. Major takeaways from these discussions include: There are **major gaps in our understanding of the mechanisms underlying disease processes in the brain** and this has hindered progress in the development of effective therapies for CNS disorders. Understanding the causes and biological mechanisms of complex diseases and conditions of the brain would be aided by **collaborative research across various scientific disciplines and methodologies**, and by **promoting knowledge sharing and expanding shareable resources**.

To date, CIRM has demonstrated a strong commitment to advancing scientific progress to address CNS disorders in the context of regenerative medicine. While a relatively small proportion of prior grants were dedicated to the study of mechanisms underlying normal and disease processes in the brain, CIRM's strategic focus on funding the development of human in-vitro models has been

instrumental in priming the field for significant advancements in disease mechanism research.

To further accelerate the discovery of novel insights into mechanisms of CNS diseases, CIRM is proposing the **ReMIND Program**. The ReMIND Program aims to establish collaborative networks of multidisciplinary research teams through new funding structures that are complementary to current CIRM Discovery stage awards (DISC0 – Foundation, and DISC2 – Quest). Furthermore, existing external-funding opportunities in this space are generally driven by the internal priorities and interests of the administering body and are often limited in scope and focus. By harnessing the expertise of various scientific disciplines, promoting knowledge sharing among researchers and by supporting the adoption of latest innovations in stem-cell and genetic research, CIRM's ReMIND program provides a unique opportunity to California scientists for discovery research into CNS disorders that are unlikely to receive timely or sufficient funding from other sources.

In alignment with recommendations from CIRM Board's Task Force in Neuroscience and Medicine, the ReMIND Program will begin with funding opportunities focused on **neuropsychiatric disorders** and **will be further delineated in the Request for Applications (RFA) documents**.

OBJECTIVE

The overall objective of the ReMIND Program is to support fundamental research to accelerate the discovery of mechanisms underlying neuropsychiatric diseases and disorders. The goal is to identify and validate novel targets and biomarkers, thereby providing new avenues and rigorous foundations for future translational and clinical investigations.

The ReMIND funding opportunities and supporting program activities aim to establish a network of multi-disciplinary research teams that will:

- **Accelerate** foundational scientific understanding of neuropsychiatric disease mechanisms, or development of relevant, transformative tools and technologies,
- **Catalyze** multi-disciplinary innovation, attract new talent and ideas into neuropsychiatric research and seed new partnerships,
- **Drive** open and collaborative science by leveraging CIRM-funded and externally funded infrastructure for data, resource or knowledge sharing.

AWARD INFORMATION

How is the Program Structured?

The ReMIND Program includes **two funding opportunities** with distinct award structures that will be offered through independent Requests for Applications (RFAs).

ReMIND-L

The ReMIND-L RFA will support expansive cross-disciplinary studies led by large (L) collaborative teams applying a range of technologies and approaches. The proposed projects may include multiple subprojects and should clearly articulate how synergies will be leveraged across the breadth of the overall project. Proposed projects should lead to novel biological insights, further current understanding of disease mechanisms, expand research to include the study of diverse human populations, and/or identify and validate novel therapeutic hypotheses, targets or biomarkers. Preliminary data are required.

ReMIND-X

The ReMIND-X RFA will support high-risk, exploratory (X) studies led by small multi-disciplinary teams. The proposed projects will be expected to lead to initial validation or proof of concept of novel models, tools, technologies or hypotheses. Minimal preliminary data required².

What activities will CIRM fund?

The following are illustrative examples of activities that CIRM will fund under the ReMIND Program and should not be considered an exhaustive list.

1. Research designed to advance our fundamental understanding of neuropsychiatric disease mechanisms.
2. Studies aimed at identifying or validating novel biomarkers for neuropsychiatric disorders.
3. Studies aimed at identifying or validating novel targets or therapeutic strategies for neuropsychiatric disorders.
4. Research that advances the use of human stem or progenitor³ cells (collectively, “stem cells”) as tools for discovery research in neuropsychiatric diseases.
5. Genetic research⁴ relevant to neuropsychiatric disorders including studies that identify or characterize genes or loci that contribute to disease risk, progression, severity or to resilience.
6. Research to improve our understanding of neuropsychiatric disorders in the context of diverse human ancestral backgrounds.
7. Advancements in relevant supporting technologies applied to discovery research in neuropsychiatric disorders including functional phenotyping, electrophysiology, imaging and single-cell technologies.

8. Reverse translation studies related to approved or investigational therapies for neuropsychiatric disorders.
9. Studies that record or analyze behaviors and other systems-level outcomes in human subjects.
10. Research applying existing or developing novel computational and/or analytical approaches to enable full use of the datasets generated. CIRM also encourages proposals that complement ongoing research initiatives or leverage existing data sets to amplify the impact of the ReMIND Program.
11. Derivation of new induced pluripotent stem cell lines to address specific project needs, especially those derived from ancestral backgrounds currently under-represented in research studies.

CIRM will also support:

- Other activities intended to promote and uphold principles of Diversity, Equity and Inclusion (DEI) in the conduct of the study.
- Activities associated with sharing data and knowledge from the study.
- Partnering activities with patient-centered organizations.
- Activities to support outreach or communication of research plan or outcomes with the wider public.

CIRM encourages proposals that incorporate multiple approaches including the research listed activities described above, however,

- Proposals must include studies that employ stem cells or genetic research⁴ as part of the central approach or hypothesis to be tested by the multi-disciplinary team. Applicants should provide justification for studies that do not directly involve stem cells/genetic research⁴ and describe how they complement or promote the utility and/or validity of stem cell and/or genetic research⁴ in the study of neuropsychiatric disorders.
- Activities should focus on human derived data, cells, models and tissues but may include studies using nonhuman cells or nonhuman model systems **only** if findings are experimentally validated in human cells or tissue during the course of the award.

CIRM funds **cannot** be used to support the following activities under this opportunity:

- Therapeutic or other commercial development activities including lead optimization, manufacturing, pre-clinical toxicology and pharmacology studies and other activities targeted by CIRM's TRAN and CLIN programs.

What is the award amount and duration?

The ReMIND Program will consist of 2 separate RFAs with the following amounts and durations:

ReMIND-L

CIRM will fund direct project costs of up to \$8.0 million per award for up to four years duration. If the project period is less than four years with a proposed budget for any given one-year period above \$2,500,000, strong justification must be provided.

ReMIND-L Supplemental Funding (optional)

Additional funding of up to \$0.5 million per award per year may be requested IF an equivalent (or larger) amount of matching funds is provided and the research activities supported by this supplemental budget are described and well justified. Matching funds may be contributed by either CA or non-CA organizations.

ReMIND-X

CIRM will fund direct project costs of up to \$1.0 million per award for up to two years duration. If the project period is less than two years with a proposed budget above \$700,000 for any given one-year period, strong justification must be provided.

How will funds be awarded?

Awards will be made in the form of a grant. Funds will be disbursed pursuant to a CIRM Notice of Award. The first payment will be issued upon initiation of an award and subsequent payments will be disbursed on a regular interval at CIRM's option. Continued funding is contingent upon timely progress, as outlined in the project and data milestones and timeline established under the Notice of Award.

ELIGIBILITY

What types of projects are eligible for funding?

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

(1) The application must

- a) Define a key knowledge gap or research bottleneck in our understanding of neuropsychiatric diseases AND propose research or develop tools and technologies to address that knowledge gap or research bottleneck in neuropsychiatric diseases.
- b) Include studies that employ stem cells or genetic research⁴ as part of the central approach or hypothesis to be tested by the multi-disciplinary team. Applicants should provide justification for studies that do not directly involve stem cells/genetic research⁴ and describe how they complement or promote the utility

and/or validity of stem cell and/or genetic research⁴ in the study of neuropsychiatric disorders.

c) Justify any proposed use of non-human models and include research to validate any discoveries made in those nonhuman model systems with comparable studies using relevant tissues or models based on human cells.

(2) The applicant team must

a) Include one Principal Investigator and

ReMIND-L: No fewer than four (4) co-Investigators.

ReMIND-X: No fewer than one (1) co-Investigator.

b) Must include one member (Principal Investigator, co-Investigator or Key Personnel) with relevant clinical expertise (ReMIND-L only).

c) Must include one member (Principal Investigator, co-Investigator or Key Personnel) with relevant computation/bioinformatics expertise (ReMIND-L only).

(3) ReMIND-L applications must include an experienced Data Project Manager on the team

To ensure effective data management and compliance with CIRM's Data Sharing guidelines (see Data Sharing section below), ReMIND-L applicant teams must include at least one dedicated Data Project Manager (minimum 15% effort). This individual must have demonstrated experience in data handling and is responsible for overall project data management, interfacing with CIRM's planned Data Coordinating and Management Center (see DCMC section below), reporting progress on data management and sharing as well as maintaining the integrity of data during the course of the project.

(4) Must be ready to initiate work on the funded project within 120 days of approval

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 120 days of approval and authorization for funding by the Application Review Subcommittee of the Independent Citizens' Oversight Committee.

(5) Co-funding is not required

However, optional ReMIND-L supplemental funding requests (see section above) must be accompanied by demonstration of matching amount equivalent to the additional funds requested.

(6) Application must be accurate and complete

All required components of the application must be completed and may not contain false or inaccurate information.

(7) Applicant must be in “good standing”

To be eligible to apply for CIRM funding, an applicant must certify that it is in good standing, as follows:

- The applicant’s Chief Executive Officer, Chief Financial Officer, and Principal Investigator must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation; and
- The applicant must have accounting systems in place that are capable of tracking CIRM funds; and
- All investigators and other key personnel must not be currently under investigation for research misconduct by the applicant institution or a funding agency and must not be currently debarred by HHS Office of Research Integrity.

Who can apply?

Only California-based organizations are eligible to apply for this opportunity.

A California Organization is a for-profit or non-profit organization that employs and pays more than 50% of its employees in California and that directs and controls the award activities from California.

For a California Organization, Allowable Project Costs include:

- Costs for research activities conducted wholly in California; and
- Costs for research activities conducted outside of California, provided that the California Organization exercises direction and control over the activities.

Unallowable Costs

Unallowable Project Costs include the costs of activities performed by a separate out-of-state organization that retains intellectual property or independent publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM funded project. Unallowable costs also include project costs incurred before the date the ICOC approves the application for funding, which can be as early as 90 days post application submission.

Who can serve as the Principal Investigator (PI)?

Teams must nominate one PI who will manage the overall collaboration and will serve as the main administrative contact for CIRM and any grant partners.

To be eligible, the PI must satisfy the following requirements:

- Must be an employee of the applicant organization or be accountable for the conduct of the proposed project to the applicant organization through a formal contract.
- Must commit at least the minimum percent effort specified for each RFA as follows:
 - ReMIND-L: at least 15%,
 - ReMIND-X: at least 5%.
- Any effort for which salary from CIRM is claimed must be expended in California.
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI.
- Must not currently be listed as PI on another application pending review or approval under the same RFA (ReMIND-L or ReMIND-X).
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

Who can serve as a co-Investigator?

To be eligible, co-Investigators must satisfy the following requirements:

- Must be an employee of a California-based organization or be accountable for the conduct of the proposed project to their California-based organization through a formal contract.
- Must commit at least the minimum percent effort specified for each RFA as follows:
 - ReMIND-L: at least 10%,
 - ReMIND-X: at least 5%.
- Any effort for which salary from CIRM is claimed must be expended in California.
- Must be authorized by their organization to conduct the research and assume the responsibilities of the co-Investigator.
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

ADDITIONAL REQUIREMENTS

Diversity, Equity and Inclusion in CIRM-Funded Projects

Applicants must address how the proposed project upholds the principles of diversity, equity and inclusion (DEI). All applicants to the ReMIND Program will be required to provide a statement in their proposal describing how their overall study plan and design has considered the influence of race, ethnicity, sex, gender and age diversity. Examples include use of models and tools that account for population diversity, increased focus on diseases that pose an outsized burden on underserved populations or additional efforts to validate and extend findings to diverse populations (e.g., propose studies using iPSC lines derived from multiple genders and from diverse ancestries). Applicants should also address how the research team has or will incorporate diverse and inclusive perspectives and experience in the implementation of the research project, including, for example, developing partnerships with patient organizations, acquiring training in cultural competence and/or DEI, utilizing institutional resources for DEI, and allocating funds and/or personnel to address DEI. The Grants Working Group (GWG) and CIRM's governing board will evaluate these statements as a review criterion in making funding recommendations. Priority will be given to projects with the highest quality plans in this regard.

ReMIND Program Conferences

To facilitate knowledge sharing and the formation of collaborative networks, CIRM will fund and co-lead the organization of ReMIND program conferences. CIRM will work with ReMIND program grantees to obtain input on the scientific program agenda, potential invited speakers, and mechanisms to enhance participation by predoctoral and post-doctoral trainees from grantee labs. Awarded teams are required to participate in this conference and are highly encouraged to share unpublished data. Selected awardees and trainees funded through other CIRM Discovery and Education grants may also be invited to participate to facilitate broader scientific exchanges across CIRM's network of grantees.

Discovery Advisory Panels (ReMIND-L only)

Upon approval of an award, CIRM will work with awardees to appoint a Discovery Advisory Panel (DAP) to partner with the awardee. The DAP will be composed of at least one CIRM Science Officer, at least one external advisor, and at least one patient/community engagement consultant. The DAP will provide guidance and advice to awardees to maximize successful outcomes. Multiple DAP meetings may take place over the course of the award period as needed. DAPs may assist CIRM science officers in reviewing the annual progress reported by the awardees, help awardees identify and leverage resources and may enlist the help of CIRM's external subject matter experts when needed.

Data Sharing

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating treatments to patients. A general overview of a plan for sharing data produced in the proposed project (Data Sharing Overview) must be included in the application and is subject to evaluation by the GWG. Applicants must allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project. CIRM requires awardees to develop and execute a Data Sharing and Management Plan (DSMP) that includes management and preservation of raw data, processed data and metadata and making applicable data and metadata available to the broader scientific community. To ensure data processing steps can be replicated and data can be reused by other researchers, CIRM requires sharing of data in accordance with [FAIR](#) data principles (Findability, Accessibility, Interoperability and Reusability) through established repositories where possible. The data repositories selected, and summary of the data shared must be reported to CIRM during and after the project period. To promote FAIR data sharing and open science, CIRM may publicly share information about CIRM-funded data, including what types of data were generated and where data are deposited.

Data Coordination and Management Center

Subject to board approval, CIRM has preliminary plans to fund the creation of a Data Coordination and Management Center (DCMC) through a separate funding opportunity. At such time, CIRM will require ReMIND awardees to comply with data sharing processes developed by the DCMC, and work with the DCMC to deposit applicable data and metadata generated as part of their ReMIND award, in DCMC-identified data repositories and according to DCMC processes. This coordination will be directed by CIRM staff and managed by the Science Officer in consultation with the awardee team and the data project manager in a timely manner. CIRM will require that awardees finalize processes for data sharing with the DCMC in a reasonable timeframe after the DCMC has established data sharing protocols. CIRM will require that an investigator from each awarded team participate in a DCMC Advisory Committee to advise on joint DCMC-ReMIND activities and issue consensus recommendations pertaining to data management and sharing between network members and with the DCMC. CIRM will require awarded teams to adhere to the recommendations of the DCMC Advisory Committee.

Consideration of Past CIRM Award Information

The GWG may consider information from a previously funded and related CIRM award as part of its review. CIRM will provide the GWG with objective information regarding a related award that CIRM, in its sole discretion, deems relevant, including

but not limited to achievement of specific milestones, data and outcomes for a related CIRM award or awards.

A “related CIRM award” includes: (1) an award for which the applicant PI served as the PI, a co-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) an award that includes overlapping team members.

Positive Selection (ReMIND-X only)

In the event that the number of applications received is significantly more than the number that can be reviewed by the GWG panel, the GWG members will conduct the review in two stages. In the first stage, GWG members (including scientific members and patient advocate and nurse members of the Governing Board) will conduct a pre-review of applications (called “Positive Selection”) to identify applications that the panel believes are most responsive to the funding opportunity and hold the most potential for impact. Applications that are not selected are examined by CIRM Scientific Programs and Education team and CIRM President to determine whether any additional applications merit a full GWG review. The remaining non-selected applications are deemed to be denied. Positively selected applications will advance to the second stage of review.

Procedure for Recommending Grant Applications

For the ReMIND-L program, CIRM will employ a scoring mechanism for the GWG that allows the possibility of resubmission IF fewer than the targeted number (6) of ReMIND-L applications are awarded by the ARS after the initial review and IF the ARS votes to consider revised applications.

SCHEDULE AND DEADLINES

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| Applications Due | ReMIND-L: Expected by June 2024 ReMIND-X: Expected by end 2025 |
| Grants Working Group (GWG) Review | Approximately 90 days post submission |
| ICOC Review and Approval | Approximately 120 days post submission |
| Award Start | Must start within 120 days of award approval (i.e., approximately 240 days post submission) |

REQUESTED FUNDING ALLOCATION

The indirect cost rate will be set at 20% for non-profit applicant organizations. CIRM will not fund indirect costs for for-profit applicant organizations.

REQUESTED DELEGATION OF BOARD AUTHORITY

To streamline the processes for high volume application review and to enable timely calls to highly specific opportunities or challenges, CIRM requests the Governing Board delegate to the President or his/her designee the authority to examine those applications that are not selected for a full review and to make the final determination whether to submit such applications to the GWG for a full review or to deny funding.

¹ For the scope of this solicitation, CIRM considers Neuro to include neurodevelopmental, neurodegenerative, neuromuscular, CNS injury/stroke/trauma and neuropsychiatric disorders.

² While no prior publications or formal preliminary evidence is required, applicants will be encouraged to speak to the plausibility and feasibility of the proposed research.

³ Under Proposition 14, progenitor cells are “multipotent or precursor cells that are partially differentiated but retain the ability to divide and give rise to differentiated cells.” Progenitor cells may include directly reprogrammed cells if they meet the criteria in the above definition.

⁴ For the scope of this solicitation, CIRM considers genetic research to mean research that alters genomic sequences of cells (edit, remove or add DNA sequences) or introduces or directly manipulates nucleic acids (such as coding and non-coding RNAs, antisense oligonucleotides) in cells.