DISCOVERY

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DISC4: ReMIND-L Awards

Research using Multidisciplinary, Innovative approaches in Neuro Diseases

REQUEST FOR APPLICATIONS

11.01.23

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DISC4: ReMIND-L Awards:
A Discovery Stage Research Funding Opportunity Under the ReMIND Program

Objective

The mission of the California Institute for Regenerative Medicine (CIRM) is to accelerate world-class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world.

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

The initial vision for ReMIND emerged through discussions and workshops conducted by CIRM staff with a diverse group of scientific experts from 2019 to 2023. These discussions highlighted the fact that major gaps remain in our understanding of mechanisms underlying CNS diseases hindering progress in the development of effective therapies for CNS disorders. Discussants further emphasized that 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.

Since its inception, CIRM has demonstrated a strong commitment to advancing scientific progress to address CNS disorders in the context of regenerative medicine. To further accelerate the discovery of novel insights into mechanisms of CNS diseases, CIRM proposed the ReMIND Program**.** This program envisions collaborative networks of multidisciplinary research teams supported through new funding structures, that are complementary to current CIRM Discovery stage awards (DISC0 – Foundation and DISC2 – Quest). The program will complement existing federal and private funding opportunities, which may be limited in scope and focus, to support innovative early research in California that is unlikely to receive timely or sufficient funding from other sources.

CIRM's scientific staff has worked closely with the Neuroscience and Medicine Task Force of CIRM's governing board in 2023 to refine the scope of the ReMIND program. These discussions highlighted the following considerations:

- There remains a large unmet need for effective treatment of neuropsychiatric disorders in the US and California.
- Fundamental neuropsychiatric disease research has been under-represented in the CIRM portfolio in the past.

- Key advances in the use of genetic research[1] and human stem and progenitor[2] cells (collectively, “stem cells”) for the study of neuropsychiatric disorders have emerged and are poised to accelerate.
- Recent studies have started to reveal the genetic architecture of these disorders, but mechanistic understanding remains poor.

Informed by these considerations, funding opportunities of the ReMIND Program will focus on **Neuropsychiatric Disorders** due to the unusual opportunity for high impact at this time. The ReMIND Program will provide new avenues and rigorous foundations for future translational and clinical investigations by establishing and funding a network of multidisciplinary 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.

CIRM’s governing board voted on September 28, 2023 to approve the ReMIND Program concept, which includes plans for two funding opportunities **ReMIND-L and ReMIND-X** with distinct award structures that will be offered through independent Requests for Applications (RFAs).

This RFA details the ReMIND-L award.

The ReMIND-X award RFA will be announced in 2024.

Contact

For information and assistance with this program announcement please send email correspondence to program officer ctan@cirm.ca.gov or discovery@cirm.ca.gov with the subject “ReMIND”

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[1] For the scope of this solicitation, CIRM considers genetic research to mean research that alters genomic sequences of cells (edits, removes, or adds DNA sequences) or introduces or directly manipulates nucleic acids (such as coding and non-coding RNAs, antisense oligonucleotides) in cells.

[2] 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.

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Award Information

What is the expected outcome of the ReMIND-L awards?

The ReMIND-L Awards will support expansive, cross-disciplinary and integrated studies, led by large collaborative teams applying a range of technologies and approaches. Outcomes of proposed projects may include:

- Uncovering novel mechanistic insights into the pathobiology of neuropsychiatric disorders or further current understanding of disease mechanisms,
- Addressing major bottlenecks in the study of neuropsychiatric disorders,
- Extending understanding of neuropsychiatric disease mechanisms to diverse human populations,
- Identifying and/or validating novel therapeutic hypotheses, targets or biomarkers for the treatment of neuropsychiatric disorders.

The ReMIND-L Awards will support the study of neuropsychiatric disorders including schizophrenia, bipolar disorder, major depressive disorder, post-traumatic stress disorder, attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, anxiety disorders, mood disorders, idiopathic developmental intellectual disability, autism spectrum disorders, and substance use disorders.

The primary emphasis of the ReMIND-L Awards is on advancing understanding of neuropsychiatric disease mechanisms. Applications that seek to examine neuropsychiatric disease mechanisms in the context of other CNS disorders may be eligible as long as primary focus is on elucidating neuropsychiatric disease mechanisms. Applicants should contact CIRM staff to discuss eligibility of proposed research.

What is the award amount and duration?

The CIRM Governing Board has allocated $88.2 million for funding of the ReMIND-L awards. CIRM will fund direct project costs of up to $8,000,000 per award. Direct project costs must be adequately justified and are subject to adjustment prior to the issuance of an award based on assessments by the Grants Working group (GWG), the CIRM team, or by the Application Review Subcommittee of CIRM's Governing Board. The proposed project period must not exceed 4 years.

If the project period is less than four years with an annual proposed budget above $3,000,000, a strong justification will be required, and the GWG will be instructed to consider that budget rationale in their scoring.

Additional funding of up to $0.5 million per award per year ($2 million in total) may be requested IF an equivalent (or larger) amount of matching funds is provided and the research activities or expenses supported by matching funds are described and well justified (See Matching Funds).

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. Except for the first payment issued upon initiation of an award, continued funding is contingent upon timely progress, as outlined in the activity-based project milestones and data milestones established under the Notice of Award.

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What activities will CIRM fund?

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

- ✓ Research designed to advance our fundamental understanding of neuropsychiatric disease mechanisms, including:
  - Studies that investigate cellular and molecular mechanisms e.g., synaptic plasticity, neuroinflammation and epigenetic regulation.
  - Studies that bridge multiple levels of analysis and inquiry, from genes, cell-types, tissue organization to circuit dynamics and behavior.
  - Studies that consider mental health disorders in the context of human neurobehavioral domains (e.g., NIMH Research Domain Criteria Initiative Framework) rather than within current diagnostic categories.
  - Studies to understand how non-CNS systems and other biological processes influence the development of neuropsychiatric disorders (e.g., neuro-immune interactions, gut-brain axis, sleep).
  - Studies to identify or understand how environmental factors impact disease risk or outcome.
- ✓ Research that advances the use of human stem or progenitor[2] cells (collectively, "stem cells") as tools for discovery, including:
  - Studies to develop new in vitro models of neuropsychiatric disorders or normal human brain development and function.
  - Research to improve the reproducibility or predictive validity of existing models.
- ✓ Genetic research relevant to neuropsychiatric disorders, including studies that identify or characterize genes or loci that contribute to disease risk, progression, severity or resilience.
- ✓ Studies aimed at identifying or validating novel targets or therapeutic strategies for neuropsychiatric disorders.
- ✓ Studies aimed at identifying or validating novel biomarkers, including:
  - Diagnostic, predictive, and prognostic biomarkers for neuropsychiatric disorders as well as biomarkers to aid in the development of targeted therapies and personalized medicines.
  - Investigating factors that contribute to the heterogeneity of neuropsychiatric disorders and identifying disease subtypes or developing stratification methods to improve diagnosis and treatment outcomes.
- ✓ Research to improve our understanding of neuropsychiatric disorders in the context of diverse human ancestral backgrounds.
- ✓ 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.

- ✓ Advancements in relevant supporting technologies, including behavioral phenotyping, electrophysiology, imaging and single-cell technologies.
- ✓ Reverse translation studies related to approved or investigational therapies for neuropsychiatric diseases.
- ✓ Studies that record or analyze behaviors and other systems-level outcomes in human subjects including studies employing fMRI or EEG technologies.
- ✓ Research applying existing or developing novel computational or analytical approaches to enable full use of datasets generated. CIRM also encourages proposals that complement ongoing research initiatives or leverage existing data sets to amplify the impact of the ReMIND Program.

CIRM funds **will also** support -

- ✓ 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 plans or outcomes with the wider public.
- ✓ Travel and accommodation expenditures associated with attendance of ReMIND program conferences.

CIRM encourages proposals that incorporate a variety of research approaches and methods, including those listed above, to maximize scientific synthesis and discovery, however:

- Proposals must include studies that employ stem cell or genetic research as part of the central approach or hypothesis to be tested by the multidisciplinary team. Applicants should provide justification for studies that do not directly involve stem cell/genetic research and describe how they complement or promote the utility and/or validity of stem cell/genetic research in the study of neuropsychiatric disorders.
- Projects 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 resources **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 activities targeted by CIRM's TRAN and CLIN programs. (see www.cirm.ca.gov)
- ✘ Activities already budgeted or paid for under a prior, existing or future CIRM award.

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Potential applicants are strongly encouraged to discuss their research concept and approach with the program contact while developing their applications to ensure that applications align with the priorities and goals of this award mechanism.

Eligibility

What types of projects are eligible for funding?

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

(1) The applicant must:

a. Define key knowledge gap(s) or research bottleneck(s) in the study of neuropsychiatric disorders AND propose research studies to address them.

b. Include studies that employ stem cells or genetic research[1] as part of the central approach or hypothesis to be tested by the multi-disciplinary team. Applicants should provide justification for project components that do not directly involve stem cells/genetic research[1] and describe how they complement or promote the utility and/or validity of stem cell and/or genetic research[1] in the study of neuropsychiatric disorders.

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

(2) The applicant team must:

a. Include one (1) Principal Investigator (PI) and no fewer than four (4) co-Investigators. There are no limits on the number of Key Personnel.

b. Include one member (Principal Investigator, co-Investigator or Key Personnel) with relevant clinical expertise in neuropsychiatric disorders.

c. Include one member (Principal Investigator, co-Investigator or Key Personnel) with relevant computational biology or bioinformatic expertise.

(3) Applications must include an experienced Data Project Manager.

To ensure effective data management and compliance with CIRM's Data Sharing guidelines (see Data Sharing section below), 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 (if approved by CIRM's governing board, 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) The applicant 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 CIRM's governing board, the Independent Citizens' Oversight Committee ("ICOC").

(5) For-profit organizations must demonstrate solvency.

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For-profit organizations must provide documentation that shows 180 days cash on hand from date of application submission and the financial ability to meet the co-funding and contingency requirements for the term of the project. The determination of solvency will be made at CIRM's sole discretion.

(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:

a. 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

b. The applicant must have accounting systems in place that are capable of tracking CIRM funds; and

c. The Principal Investigator, co-Investigators and other Key Personnel named in the application 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 organizations are eligible to apply for this opportunity.

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

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.

CIRM funds will be disbursed to the Applicant Organization which will be responsible for subsequent disbursement of funds (subawards/subcontracts) to co-Investigators and Key Personnel. An institution or organization may submit more than one application under this opportunity.

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.
- ✘ Project costs incurred before the date the ICOC approves the application for funding, which can be as early as 90 days post application submission.

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Who can serve as the Principal Investigator (PI)?

Teams must nominate one PI on the application who will manage the collaboration and 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 15 percent effort to working on this project. 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 this funding opportunity.
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.
- Must not currently be listed as co-Investigator on more than one other application pending review or approval under this funding opportunity.

Who can serve as the co-Investigators?

To be eligible, the co-Investigators on the application 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 10 percent effort to working on the project. 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.
- Must not currently be listed as co-Investigator on more than one other application pending review or approval under this funding opportunity.

Application Review Information

What is the process for evaluating an application?

Pre-submission Consultation

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Prospective applicants are encouraged to contact CIRM Scientific Programs and Education team before applying to discuss their project's eligibility. To start a consultation, please email program officer Dr. Chan Lek Tan ctan@cirm.ca.gov.

Eligibility Review

CIRM will assess whether the proposed project meets eligibility requirements sought under this program. If CIRM determines, in its sole discretion, that an application does not meet the eligibility requirements of the program or that the submitted application is incomplete or contains false or inaccurate information, CIRM will notify the applicant of its decision and, if CIRM deems it appropriate, allow an opportunity to remedy. If CIRM deems it inappropriate, or if the applicant does not remedy the error in a timely manner, CIRM will terminate all further action on the application. CIRM may exercise its authority to make eligibility determinations at any time before an award is executed.

Scientific Review

The scientific merit of each application will be assessed by the GWG, which is composed of fifteen subject matter experts from outside California, seven patient advocate or nurse members of the ICOC (called "GWG Board Members"), and the Chair of the ICOC. The list of scientific members who may participate in the GWG review can be found at http://www.cirm.ca.gov/WorkingGroup_GrantsReview. The composition of the ICOC can be viewed on the CIRM website http://www.cirm.ca.gov/GoverningBoard.

The fifteen participating scientific reviewers of the GWG will evaluate the applications and score them according to scientific and technical merit, applying the review criteria described below. The GWG will score each application and make one of the following specific recommendations to the ICOC's Application Review Subcommittee (ARS):

"1" - the application has exceptional merit and warrants funding.

"2" - the application needs improvement and does not warrant funding, but may be resubmitted to address areas for improvement if the ARS does not approve the application for funding following the GWG's review; or

"3" – the application is sufficiently flawed and does not warrant funding or the possibility of resubmission.

The CIRM team will tally the number of scientific reviewers who assigned a score of 1, 2 and 3, respectively, and will present that information for each application to the entire GWG. If a majority of scientific reviewers score the application a 1, 2 or 3, then that score shall constitute the recommendation of the GWG. If no majority exists for a score of 1, 2, or 3, then the application shall automatically be assigned a score of 2.

The ARS will make final funding decisions giving consideration to the GWG recommendations and additional CIRM team recommendations. If fewer than the targeted number (6) of applications are approved for funding after the first round of review, and subject to ARS approval, CIRM will provide for a second round of review. Applications with a score of "2" that were not approved for funding in the first round will be invited to revise and resubmit their applications. Revised applications will be evaluated by the full GWG to make new recommendations to the ARS.

Consideration of Past CIRM Award Information (If Applicable)

The GWG will consider information from previously funded and related CIRM awards 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.

Confidentiality

CIRM's confidentiality and conflict screening rules apply to everyone who will have access to applications or who will attend any review meeting in which confidential information is discussed, including but not limited to CIRM team members, reviewers and members of the ICOC. (Per Gov. Code §6254.5(e), non-public records may be disclosed to government agencies under confidentiality agreements).

How will the scientific merit of an application be evaluated?

Scientific GWG and GWG Board Members will evaluate applications and the scientific members will score them based on the following key questions:

1. Does the project hold the necessary significance and potential for impact?

- How will the successful completion of the project address key knowledge gaps or research bottlenecks in the study of neuropsychiatric disorders?
- If successful, how will the project have a broad impact on our understanding or treatment of neuropsychiatric disorders?
- What are the project outcomes (data, resources, cell lines) that will enable the research community to formulate and test novel hypotheses?

2. Is the proposal innovative?

- Does the proposal bring in new technologies to the study of neuropsychiatric disorders?
- Does the proposal cut across technical silos and engage different disciplines to address questions in the study of neuropsychiatric disorders?
- Are the applicants testing new conceptual frameworks or hypotheses regarding neuropsychiatric disease mechanisms?

3. Is the rationale sound?

- Are the overall project and subprojects based on sound scientific rationale?
- Are the preliminary data compelling and supportive of the proposed activities?
- Is the project relevant to human biology and disease?
- When and if utilizing non-human models, how is it justified?

4. Is the project well planned and designed?

- How are the overall project and subprojects planned and designed to accomplish the specific aims?
- Are potential pitfalls identified and alternative approaches presented?
- How do the components/subprojects of the overall effort offer scientific synergies?

5. Is the project feasible?

- Is the proposed team qualified and appropriately staffed to achieve the proposed outcomes?
- Does the team have appropriate plans to manage the collaboration?
- Does the team have access to all the necessary resources to conduct the proposed activities?
- Is the budget appropriate for the research proposed?

6. Does the project uphold principles of Diversity, Equity and Inclusion (DEI)?

- Does the project plan and design adequately address and account for the influence of race, ethnicity, sex, gender and age diversity?
- Would the project outcomes extend or validate the applicability of discoveries to populations or diverse ancestries or underserved populations, including underserved racial/ethnic communities?
- Has the applicant described prior efforts or proposed plans for outreach, partnership or educational activities to inform the development of DEI within the research project?

Schedule and Deadlines

Applications Due	March 5, 2024
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

Visit CIRM's Funding Opportunities for Discovery Stage Research page to find the most updated version of this RFA and the application submission deadline(s).

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Application Components and Submission

How does one apply?

Applications must be completed and submitted online using the CIRM Grants Management Portal at http://grants.cirm.ca.gov. The PI must create a login in the system to access application materials and apply. Applications are available in the system only to the PI. Each PI may submit only one (1) ReMIND-L Award application.

What components does an application include?

CIRM's online application is designed to collect information for CIRM staff to assess eligibility, for Grants Working Group reviewers to evaluate the project and for CIRM to rapidly initiate an award if the project is approved for funding.

In the online portal, applicants must fill out an eligibility form, indicate key personnel involved in the project, describe how the proposal addresses the objective of the funding opportunity, provide an overview of proposed activities and prepare and justify an appropriate budget.

The application uploads page provides templates and guidelines for writing the Proposal, Budget, Budget Justification, Biosketches, Project Timelines and other key components of the application. Applicants must use the provided templates.

What are the contents of the Proposal?

The Proposal comprises the bulk of detailed information on the project and is central to evaluation by the Grants Working Group. It includes these sections:

1. **Statement of Significance and Impact:** Description of how the proposed research, if successful, will address a critical basic knowledge gap or research bottleneck in the study of neuropsychiatric diseases. Applicants may highlight the impact of the approach and collaboration proposed, as well as public resources and datasets that would become available to the research community as a result of this work.
2. **Statement of Innovation:** Description of how the proposed research engages unique and/or innovative approaches. Description of synergies or advantages achieved by the multi-disciplinary proposed approaches.
3. **Statement of Diversity, Equity and Inclusion:** Statement describing how the project will help fulfill the unmet medical needs of the diverse California patient population. See full description below.
4. **Overall Objective and Specific Aims:** A concise description of the overall project goals and objectives, including short description of any subprojects and list of specific aims.
5. **Project Milestones:** Project milestones are activity-based milestones which are objective and demonstrable events that allow CIRM to track progression and should be based on specific aims listed above. A detailed description of all project milestones should be included.
6. **Project Organization:** Overview of the organizational structure of the project including subprojects, significant subcontracts, collaborations, partnerships and assigned leads for each. This section should include a detailed description of how the collaborative effort will be managed.
7. **Rationale:** Description of the scientific rationale for the proposed research and all relevant preliminary data.

8. **Research Plan:** A concise but adequately detailed description of methods and techniques to be employed to achieve aims, potential pitfalls and alternative approaches. All project components should be detailed here, including significant subcontracts and collaborations.
9. **Data Sharing Overview:** A description of how raw data, processed data and metadata produced from the project will be made available to the research community consistent with FAIR (Findability, Accessibility, Interoperability and Reusability) data sharing principles.
10. **Principal Investigator and Team:** A description of the PI, co-Investigators and most relevant Key Personnel, highlighting the team's expertise and experience relevant to the execution of the proposed study. Team members that fulfil the requirements for relevant clinical expertise and relevant bioinformatic or computational expertise must be highlighted here.
11. **Resources and Environment:** A brief description of the resources available to the project and environment,
12. **References**

How does one address Diversity, Equity and Inclusion (DEI)?

Applicants must address how the proposed project upholds the principles of DEI. In the DEI section of the ReMIND-L proposal, applicants should describe how the overall study plan and design has considered the influence of race, ethnicity, sex, gender and age diversity. For example, the plan could incorporate the use of models and tools that account for population diversity (e.g. HLA types, gender, genomics data, cell models **– see Appendix: Other Resources**). Applicants should explain how the project outcomes might extend or validate the applicability of discoveries to underserved populations, including underserved racial/ethnic communities. Applicants should also describe the research team's prior efforts or proposed plans for outreach, partnership, or educational activities to inform the development of DEI within the research project, including, for example, developing partnerships with patient-centered organizations, acquiring training in cultural competence and/or DEI, utilizing institutional resources for DEI, and allocating funds and/or personnel to address DEI.

The 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.

What are CIRM's requirements for Data Sharing?

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating the discovery, validation and development of treatments for patients. CIRM requires awardees to manage and preserve raw data, processed data, and metadata, and make applicable data and metadata available to the broader scientific community. CIRM also requires applicants to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project.

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), using established repositories where possible. The data repositories selected and other information about deposited data must be reported to CIRM during and after the project period. To promote FAIR data sharing and open science, CIRM may publicly share

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information about CIRM-funded data, including what types of data were generated and where data are deposited.

At the Application Stage – Data Sharing Overview

A general overview of a plan for sharing data produced in the proposed project (**Data Sharing Overview**) must be completed as part of the proposal (see proposal template) 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. For guidelines, please refer to the Data Sharing Budget Justification Guidelines.

Pre-funding administrative review for awarded projects – Data Sharing and Management Plan (DSMP)

For omics and/or flow cytometry data, a completed DSMP, using templates provided, must be submitted to CIRM as Just in Time (JIT) material during pre-funding administrative review (PFAR). CIRM will review DSMPs and work with awardees to optimize the DSMP, including negotiation of milestones and budget. Awardees must agree with CIRM on a DSMP and associated milestones and budget prior to CIRM issuing a Notice of Award. Guidelines and templates to complete the DSMP for Omics / Flow Cytometry Data can be found here. The DSMP consists of 2 documents:

- Part A - DSMP for Omics and Flow Cytometry Data - Data Catalog
- Part B - DSMP for Omics and Flow Cytometry Data – Questionnaire

The templates for these 2 documents must be used when preparing the DSMP for Omics and Flow Cytometry Data as JIT documents during PFAR. For **data from other types of experiments** (e.g., imaging, electrophysiology, etc.), CIRM may work with the awardee to establish data sharing milestones prior to CIRM issuing a Notice of Award.

Active award stage

Grantees will report on their data sharing and management activities during regularly scheduled progress reporting and will work with CIRM staff to adjust the DSMP and other data-related milestones as necessary.

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 align data sharing processes and protocols with recommendations developed by the DCMC (see below).

Who are Key Personnel?

In the application, we ask you to list by name and affiliation all pertinent Key Personnel and their specific roles on the project. Key Personnel are defined as (1) the Principal Investigator and co-Investigators; or (2) any other person, including an independent consultant or an employee of a Subcontractor or Partner, who is expected to contribute to the scientific development or execution of the project in a substantive, measurable way *and* who is expected to: (a) receive or has been promised income, or anything else of value, of $10,000 or more per year for his or her contribution to the project or (b) contribute one percent (1%) or more effort to the proposed project. “Key Personnel” does not include a person who is expected to be involved in the proposed project but who does not satisfy conditions (1) or (2).

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Individuals who do not meet the definition of Key Personnel may be supported with CIRM funds but should **not** be identified by name in the application. Such unnamed personnel may be referenced indirectly by their role on the project (e.g., technician). The budget includes a line item for requesting support for unnamed personnel.

What should one know before preparing the budget?

Budgets must be justified in detail, including all subcontracts and consulting fees, including, if applicable, any additional costs that would be funded from another source. Allowable Project Costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy for Discovery, Translation and Education Projects. Generally, project costs for personnel, supplies, travel, equipment, data sharing/management and subcontracts may be claimed. Limits for specific cost categories must be observed.

CIRM makes no prior stipulations on how funds are distributed among the Principal Investigator and co-Investigators in the team. However, specific budget allocations for each member of the team (PI and co-Investigators) should be delineated in the budget worksheet and should reflect relative contributions and project needs. This aspect of the budget will be subject to evaluation by the Grants Working Group. If matching funds are provided and supplemental funding is requested, the budgets should detail allocations for these funds as well.

What are Matching Funds?

CIRM will fund direct project costs of up to $8,000,000 per award. Additional funding of up to $0.5 million per award per year ($2 million in total) may be requested IF an equivalent (or larger) amount of matching funds is provided and the research activities or expenses supported by matching funds are described and well justified.

Matching funds may take the form of cash funds or in-kind contributions. Expense categories may include salary for full-time personnel, research supplies and resources uniquely dedicated to this project, facilities with existing recharge rates and third-party subcontracts. Expenses covered by matching funds must be described in the research proposal and detailed in the application budget. The matching funds or in-kind contributions may come from any non-CIRM funding source (institutional or third party) arranged by the applicant and may be contributed by either CA or non-CA sources.

Documentation demonstrating the commitment of funds/in-kind contributions to cover the necessary matching funds must be provided during pre-funding administrative review (e.g., copy of executed term sheet showing amount of contribution, conditions and source). CIRM retains the right to adjust final award funding and research plan (including milestones) during pre-funding administrative review of matching fund commitments. Applicants should contact CIRM staff to discuss additional guidance on this requirement.

What are Direct Facilities Costs?

Direct Facilities Costs are the general operating costs of the grantee's facilities attributable to housing all elements of the CIRM-funded project or activity. Facilities costs for non-profit applicant organizations are limited to the current applicable, federally negotiated rates for the organization as defined by the Office of Management and Budget (OMB) Circular A-21 or A-122. Facilities costs for for-profit Awardees or any non-profit Awardees without a federally negotiated Facilities & Administrative Rate agreement are limited to 35% of direct project costs and must be consistent with facilities rates applied to similar research awards at the organization. Facilities rates are applied to direct project costs exclusive of the costs of equipment,

tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant and service agreement in excess of $25,000. The facilities cost rates approved and in place at the time of the application are to be applied to the entire award project period.

What are indirect costs and how much can an applicant claim?

Indirect Costs are administrative costs of the awardee incurred for common or joint objectives, which cannot be readily and specifically identified with a particular project. For-profit organizations cannot claim indirect costs. For non-profit organizations, indirect costs will be limited to 20% of allowable direct research funding costs awarded by CIRM (i.e., project costs and facilities costs), exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant and service agreement in excess of $25,000. The indirect cost rate budgeted at the time of application is to be applied to the entire award project period.

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Award Administration

Issuance of Award

A CIRM award is issued via a Notice of Award (NOA), which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM. CIRM reserves the right to modify or establish funded project activities and the associated budget prior to issuance of the Notice of Grant Award, including, when applicable, optimizing data sharing and management plans (DSMP), establishing activity-based project milestones and timelines at its sole discretion during pre-funding administrative review (PFAR) after consultation with the applicant team and based on information provided in the application and DSMP. Project milestones are activity-based milestones that is indicative of completion of key research activities proposed in the application. CIRM may also review key contracts/agreements that are critical to the success of the project for compliance with CIRM's policies and regulations.

Milestones and Payment

Upon execution of the NOA, CIRM will issue an initial payment; subsequent disbursements will be made as outline in the NOA. Continued CIRM funding is contingent upon timely and successful scientific progress against milestones as outlined in the project milestones, DSMP milestones, and timelines established under the NOA. Where project and/or DSMP milestones are not timely met, CIRM reserves the right to either redirect resources to maximize the project outcome or, at its sole discretion, to suspend payment and/or terminate the project. Twenty-five percent (25%) of the final year budget will be withheld pending completion of all remaining milestones and reporting requirements.

Reporting

Grantees will be required to provide periodic written progress and financial reports to CIRM. CIRM will partner with the grantee to foster the success of the project. Grantees will have ongoing communication with the CIRM Science Officer throughout the duration of the award, typically meeting by teleconference and periodically in person. Upon approval of an award, CIRM will consult with Data Advisors towards optimizing the Data Sharing and Management Plan and implement DSMP milestones as part of the NOA.

No-Cost Extensions

Timely progress on funded projects is of critical importance to CIRM. Therefore, CIRM will consider a one-time, No-Cost Extension (NCE) request of no more than 12 months, submitted at least 30 days before the project end date. Grantees should properly justify how such an extension will advance the project towards its expected outcome, and should not assume CIRM will approve a NCE request.

Discovery Advisory Panels

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. CIRM staff will convene at least one DAP meeting with awardees per year, but additional DAP meetings may be convened over the course of the award period if requested by the awardee or deemed necessary by CIRM Science Officer. DAP members 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 external subject matter experts when needed.

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 grantees to obtain input on the scientific program agenda, speakers and mechanisms to enhance participation by trainees. Awarded teams are required to participate in this conference and highly encouraged to share unpublished data. Grantees and trainees funded through other CIRM awards may be invited at CIRM staff discretion, to facilitate scientific exchanges across CIRM's network of grantees. Dates and frequency of ReMIND Program conferences will be determined by CIRM staff and communicated to ReMIND investigators at least 3 months in advance of the conference start date. Applicants are required to account for costs associated for investigators, staff and trainees to attend ReMIND conferences in their budget.

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 and protocols 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. CIRM will require that awardees finalize processes for data sharing with the DCMC no later than 180 days after the DCMC has established data sharing protocols. CIRM may require that investigators from each of the awarded teams participate in DCMC Advisory Committee meetings CIRM will require awarded teams to adhere to the recommendations of the DCMC Advisory Committee.

Donor Consent and Data Use Limitations

Proposals that include plans for prospective collection of human biosamples (including for derivation of novel hiPSC lines) or plan work with existing human biosamples/cell lines should ensure that resources and data generated from these samples can be broadly shared across the scientific community. All applicants must consider:

- Obtaining comprehensive donor informed consent for planned prospective collections. Applicants should reach out to CIRM staff to learn more.
- Prioritizing the use of existing cell lines/biosamples that are consented for broad utility and data-sharing or re-consenting original donors of samples that were not suitably consented.

During pre-funding administrative review, CIRM Science Officers will work with awardees to review any **Data Use Limitations** associated with prospective or existing human biosamples or human stem cell lines to ensure that hiPSCs generated through this award mechanism can be broadly shared and data can be made broadly available.

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CIRM Regulations

Grant awards made through this PA will be subject to all applicable CIRM regulations. These regulations can be found at https://www.cirm.ca.gov/our-funding/cirm-stem-cell-grant-regulations/

Contacts and Resources

For more information about this and CIRM's other Discovery stage programs, please visit our Current Funding Opportunities page to access program announcements, webinar materials and FAQs. For scientific questions that are not addressed in the above resources, send email correspondence to program officer Dr. Chan Lek Tan ctan@cirm.ca.gov or discovery@cirm.ca.gov with the subject ReMIND.

For questions related to application review, send email correspondence to review@cirm.ca.gov.

For questions related to budgets or allowable project costs, please consult the Grants Management FAQ on CIRM's website under "For Researchers > Grants > Managing your Grant."

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Definitions

"**California organization**" means: An entity, regardless of profit status, that has >50% of its employees located in, and paid in, the state of California, and conducts the award activities from the California location.

"**For-profit organization**" means: a sole-proprietorship, partnership, limited liability company, corporation, or other legal entity that is organized or operated for the profit or financial benefit of its shareholders or other owners. Such organizations also are referred to as "commercial organizations".

"**Non-profit organization**" means: (1) a governmental entity of the state of California; or (2) a legal entity that is tax exempt under Internal Revenue Code section 501(c)(3) and California Revenue and Taxation Code section 23701d.

"**Subcontractor**" means an organization (other than the applicant organization) that is expected to: (a) contribute to the scientific development or execution of the project in a substantive, measurable way *and* (b) receive $25,000 or more through the proposed project. "Subcontractor" does not include suppliers of widely available goods.

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Appendix

Other Resources

CIRM iPSC Repository

As a resource to the regenerative medicine community, CIRM has funded the creation of an Induced Pluripotent Stem Cell Repository, a large, genetically diverse collection of stem cells produced from thousands of individuals representing various diseases of interest and healthy controls. The 2600+ lines were uniformly derived, have undergone rigorous quality control and include demographic and clinical data. The CIRM Repository is managed by Fujifilm Cellular Dynamics, Inc., who have made the lines available for purchase at https://www.fujifilmcdi.com/cirm-ipsc-products/. SNP data for 2166 CIRM lines and whole genome sequence data for 299 of the CIRM iPSC donors is available at dbGaP. A list of CIRM lines with WGS data can be found here.

Applicants who are interested in using iPSCs to investigate mechanisms of disease, develop novel tools, discover therapeutic targets or increase diversity in their experimental design are encouraged to explore the CIRM iPSC Repository and request additional information from CIRM Science Officers at discovery@cirm.ca.gov using the subject line “ReMIND-L application - iPSC Repository.”

Please note, cells in the CIRM iPSC Repository are for research use only and are not eligible nor consented for clinical use.