CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the ICOC
From: Rosa Canet-Avilés, Chief Science Officer
Re: Revision to DISC4 Concept Plan
Date: March 27, 2025

Please be advised that the DISC4 Eligibility Requirements 6 & 7 were revised to correct errors referencing concurrent DISC5 applications on pg. 6.

DISC4 Awards: Funding Opportunity for Discovery Stage Research

Summary

OVERVIEW	
Objective	Support comprehensive discovery research across a diverse range of diseases and bottlenecks that will accelerate the development of potential therapeutics and biomarkers in regenerative medicine.
Scope	Expansive, cross-disciplinary and integrated studies led by large collaborative teams applying a range of technologies and approaches to address knowledge gaps or bottlenecks in our understanding of human diseases.
Program Recurrence	Once per year

AWARD DETAILS	
Investigators	1 Principal Investigator (PI) + 4 or more Co-Investigators (Co-I)
Maximum Award Amount	Up to $13,000,000 total costs
Maximum Award Duration	Up to 4 years
Matching Fund Contributions	Maximum total project costs may be increased (up to additional $1,000,000 per award to maximum of $14,000,000) **if** an equivalent (or larger) amount of eligible matching fund contributions is provided.

ELIGIBILITY REQUIREMENTS	
Applicant Organization	Only non-profit and for-profit organizations that meet CIRM's definition of a California Organization are eligible to apply.
Applicant PI and Co-I	Must be California-based. PI must commit at least 15% effort. Co-Is must commit at least 10% each. At least 1 Co-I must be based at a different institution than the PI.
Critical Role(s) and Expertise	Applicant team must include 1) a Data Project Manager; 2) a team member with clinical expertise; 3) a team member with industry/translational expertise 4) a team member with computational or bioinformatics expertise.
Co-funding	Not required

SCHEDULES AND DEADLINES	
Pre-submission Due Date	Once per year
Application Due Date	Approximately 60 days post pre-submission deadline
GWG Review	Approximately 120 days post submission deadline
Award Approval	Approximately 180 days post submission deadline
Start Date	Must be ready to start award activities within 120 days of award approval

CONTACT AND ADDITIONAL RESOURCES

https://www.cirm.ca.gov/researchers/funding-opportunities-discovery-stage-research/

For additional information on the program or applications, contact discovery@cirm.ca.gov. For questions related to the review and approval of applications, contact review@cirm.ca.gov.

Additional requirements and definitions may be found in **CIRM Funding Opportunities: Common Requirements and Definitions,** and are incorporated herein by reference.

Background

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. In September of 2024, CIRM's Governing Board, the Independent Citizens' Oversight Committee (ICOC), approved a Strategic Allocation Framework (SAF) to guide and optimize the value of CIRM's current and future investments. One key outcome of this exercise was defining an ambitious goal for CIRM, through its discovery stage opportunities, to catalyze the identification and validation of at least 4 novel targets and biomarkers and ensure their integration into preclinical or clinical research for diseases in California.

The most important impediment to the development of effective treatments is the lack of well-validated or actionable therapeutic targets due to an incomplete understanding of disease biology. Due to the complexities of disease processes, sustained investments in foundational, cross-disciplinary research are necessary to identify high-quality targets for therapeutic or biomarker development. In 2024, the ICOC approved a recommendation to support comprehensive discovery research through at least 2 new complementary award structures (DISC4 and DISC5) that promote innovative, collaborative research at varying levels of scale and maturity. These awards will fund a network of multidisciplinary research teams that will be further supported by CIRM to facilitate knowledge sharing and to leverage other CIRM-funded resources to ensure readiness for further translational efforts.

CIRM's Discovery Program seeks to build on rapid advances in stem-cell biology and genetic research including:

1. Advances in stem cell biology and stem cell derived models in basic and translational research, particular in facilitating the study of human tissues, cells and genes.
2. Advances in the understanding of the genetic underpinning of diseases and biological processes including insights from human genetic studies and functional genomic tools to map genes to cellular functions and disease processes.
3. Advances in a broad range of research technologies (single-cell omics, imaging, machine-learning etc.) that greatly enhance the study and use human stem cells in research and medicine.

The DISC4 program aims to integrate these advances with CIRM's pioneering support for stem cell science to accelerate foundational insights in disease biology across a wide range of disease areas. The program will also incentivize the integration of diverse sources of evidence (clinical specimens, *in-vivo* models, stem-cell models, computational modeling) to strengthen the validity and reproducibility of novel targets and biomarkers uncovered.

DISC4 awards build on the multi-disciplinary framework piloted through CIRM's 2024 DISC4 ReMIND-L awards which have a specific focus on neuropsychiatric disorders. The DISC4 program will support a broad set of disease areas while adding new program elements to facilitate readiness for target validation and preclinical translation by the end of the award.

Existing federal funding opportunities for discovery research are primarily driven by the internal priorities and interests of the administering body and may be unpredictable or limited in scope or focus. Since its inception, CIRM has created funding opportunities for basic research that are unique in scope and design, provide reliable and predictable funding, support data and knowledge sharing, and accelerate translation of research insights into therapies and diagnostics. Through the following unique opportunity, CIRM continues its support for basic discovery research that are unlikely to receive timely or sufficient funding from federal or other sources.

Objective

The overarching objective of CIRM's Discovery Program is to support comprehensive, discovery research across a diverse range of diseases and bottlenecks that will accelerate the development of potential therapeutics and biomarkers in regenerative medicine.

This vision is achieved through unique funding opportunities supporting research at different scales and levels of maturity, with an emphasis on multidisciplinary innovation, knowledge sharing and leveraging synergies across CIRM-funded programs, to catalyze the discovery of targets and biomarkers and support their entry into preclinical development.

Scope and Structure

The DISC4 Awards will support expansive, cross-disciplinary and integrated studies led by large collaborative teams applying a range of technologies and approaches to achieve one or more of the following outcomes:

- Discovering novel mechanistic insights or advance our understanding of the pathobiology of human diseases,
- Extending understanding of disease mechanisms to diverse human populations, and/or
- Identification and validation of novel therapeutic strategies, targets, and/or biomarker(s).

To maximize the impact of these project outcomes, CIRM requires that applicant teams appropriately manage and share data generated in the course of a DISC4 award.

Program funding areas

The DISC4 program awards are open to all applications that fulfil eligibility requirements detailed below, without restrictions in research topics or disease indications.

However, to align with CIRM's Proposition 14 mandate, optimize synergy across teams, leverage external partnerships, and remain responsive to an evolving research landscape, funding preferences will be set on an annual basis. These preferences will be guided by recommendations from CIRM's Task Force on Neuroscience and Medicine (NTF), portfolio analyses, and other strategic considerations in a cyclical manner. Each year, CIRM staff will present funding preference recommendations to the ICOC, which retains sole authority for approval. Once approved, these preferences will be implemented through the DISC4 pre-submission process (described below) and during programmatic considerations by the Application Review Subcommittee of the ICOC, ensuring a structured yet flexible approach that balances inclusivity with strategic focus.

Program activities

Applicants may request funds to cover costs for research activities conducted wholly in California and may also request costs for activities conducted outside of California, provided that the California Organization exercises direction and control over the activities.

CIRM **will fund** the following activities under this opportunity:

REQUIRED ACTIVITIES	
✓	Activities associated with managing, preserving, and sharing data and knowledge from the study

ALLOWABLE ACTIVITIES	
✓	Any activities contributing to expansive, cross-disciplinary and integrated research that meets the DISC4 objective to address knowledge gaps or bottlenecks in our understanding of human

	disease, where human stem cells or genetic research is part of the central approach or hypothesis, and that falls into one or more of the below categories: • Discovering novel mechanistic insights or advance our understanding of the pathobiology of human diseases • Extending understanding of disease mechanisms to diverse human populations • Identification and validation of novel therapeutic strategies, targets, and/or biomarker(s)
✓	Partnering activities with patient-centered organizations or other project-relevant community groups.
✓	Activities to support outreach or communication of research plans or outcomes with the wider public.
✓	Travel and accommodation expenditures associated with attendance of CIRM organized meetings and conferences.
✓	Engagement activities with trainees supported through CIRM's EDUC or INFR programs.

CIRM **will not fund** the following activities under this opportunity:

UNALLOWABLE ACTIVITIES	
✘	Therapeutic or other commercial development activities including lead optimization, manufacturing, pre-clinical toxicology and pharmacology studies and other activities targeted by CIRM's PDEV and CLIN programs.
✘	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 120 days post application submission
✘	Activities already budgeted or paid for under a prior, existing or pending CIRM award, or which are already supported by another funder

Award amount and duration

The maximum amount of funding that may be requested for a DISC4 Award is $13,000,000 per award, inclusive of direct and indirect project costs. The maximum award duration is four (4) years.

Maximum total project costs may be increased up to an additional $1,000,000 per award (maximum $14,000,000 per award) IF an equivalent (or larger) amount of eligible matching fund contributions is provided (see Matching Fund Contributions below).

The proposed budget may not exceed $5.0 million in a single budget year.

The amount requested must be adequately justified. The requested amount is subject to adjustments 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 the ICOC. 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.

Matching fund contributions

Eligible matching fund contributions must take the form of either:

(i) Unique resources that will be leveraged by the project team e.g. cell-lines, biosamples, research/computational resources, etc.; or

(ii) Independently funded activities undertaken during the award period to generate data or resources that will be leveraged by the project team during the award period.

Matching fund contributions may be contributed by either CA or non-CA organizations, including non-profit and for-profit organizations.

Pre-submission process

To ensure that proposals most well-aligned with the funding area preferences, scope, and objective of the program receive an in-depth scientific review by the GWG panel, CIRM will implement a pre-submission process for the DISC4 awards.

Pre-submissions will be evaluated by CIRM staff to assess alignment with program objectives and scope, incorporating funding preferences set annually by the ICOC. These funding preferences will be determined in a cyclical manner, informed by recommendations from the NTF and portfolio analyses identifying critical gaps. This approach allows for a dynamic prioritization strategy that addresses NTF opportunities, adjusts to emerging research needs, and meets evolving scientific advancements.

Pre-submissions will NOT be evaluated for scientific merit or feasibility but will serve as a mechanism to ensure that applications invited for full review align with CIRM's strategic goals.

Provisional timetable

The DISC4 funding opportunity will recur annually. The timeline of each funding cycle is as follows:

PROVISIONAL TIMETABLE	
Pre-submission Open	Once per year
Pre-submissions Due	Approximately 60 days after pre-submissions open
Applications Open for Invited Projects	Approximately 60 days after pre-submissions due
Applications Due	Approximately 90 days after applications open
Grants Working Group (GWG) Review	Approximately 120 days after applications due
Application Review Subcommittee (ARS) Award Approval	Approximately 60 days after Grants Working Group Review
Award Start	120 days after award approval

Eligibility

All the following requirements must be fully satisfied for an application to be accepted and considered for funding by CIRM. Requirements marked with a * incorporate by reference the requirements and definitions described in **CIRM Funding Opportunities: Common Requirements and Definitions**.

ELIGIBILITY REQUIREMENTS	
1	The proposal must address knowledge gap(s) or research bottleneck(s) in the study of human diseases
2	The proposal must include studies that employ human stem cells or genetic research as part of the central approach or hypothesis
3	A strong justification must be provided for any proposed use of non-human models
4	The core team (Principal Investigator (PI) and Co-Investigators) must be multi-institutional and include at least five (5) investigators based in California
5	The project team must include members with specific relevant expertise including a) an experienced data project manager; b) a team member with clinical expertise; 3) a team member with industry/translational expertise 4) a team member with computational or bioinformatics expertise

6	An individual may not serve as PI on >1 DISC~~4~~5 application per funding cycle
7	An individual may not serve as PI or Co-I on >2 DISC~~4~~5 applications per funding cycle
8	The PI and/or any Co-I must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity
9	The PI and Co-Investigators must commit at least 15% effort or 10% effort respectively
10	The applicant must be ready to initiate work on the funded project within 120 days of award approval
11	The application must be accurate and complete
12	The applicant organization must meet CIRM's definition of a California Organization*
13	For-profit organizations must demonstrate solvency*
14	The applicant must be in "good standing"*