

# DISC4 Concept Overview

February 2025



# DISC4 | Outline

1. Background (SAF alignment)
2. Objective
3. Scope
4. Structure
  1. Award Budget
  2. Eligibility
  3. Other Changes
5. Timeline
6. Request for Approval

# Goal 1 | Recommendations

**Goal 1 - Catalyze** the identification and validation of at least 4 novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California

## Support comprehensive discovery research through DISC4 & DISC5 funding structures

- Encourage collaborative, multidisciplinary innovation in stem cell and genetic research across diverse disciplines & disease indications with early engagement of industry to address reproducibility & scalability issues



Discovery



Preclinical



Clinical

# Discovery Programs

**Common Objective of CIRM’s Discovery programs** is to support comprehensive discovery research across a diverse range of diseases and bottlenecks, to accelerate the development of potential therapeutics and biomarkers in regenerative medicine.

**Two complementary awards** support research at different scales and maturity

DISC4	DISC5
Large multidisciplinary, collaborative teams focused on disease biology insights to facilitate target/biomarker identification	Small collaborative teams focused on exploratory research to advance the understanding and application of stem cells and address bottlenecks in cell and gene therapy



# Discovery Programs

**Common Objective of CIRM's Discovery programs** is to support comprehensive discovery research across a diverse range of diseases and bottlenecks, to accelerate the development of potential therapeutics and biomarkers in regenerative medicine.

**Program Infrastructures** to facilitate data and knowledge sharing within and beyond CIRM's network of grantees

- Program & Grantee Meetings
- Data Sharing Infrastructure
- External Partnerships
- Leveraging other CIRM funded resources



# DISC4 | Objective

## Objective

Support comprehensive discovery research across a diverse range of diseases and bottlenecks to accelerate the development of potential therapeutics and biomarkers in regenerative medicine

## Approach

Expansive, cross-disciplinary and integrated studies led by large collaborative teams

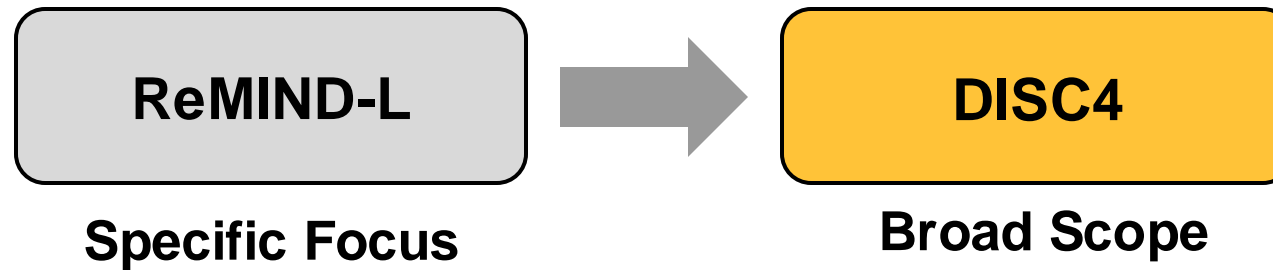
# DISC4 | Scope & Expected Outcomes

DISC4 awards 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
- Identification and validation of novel therapeutic strategies, targets, and/or biomarker(s)

# DISC4 Extends and Enhances Pilot ReMIND-L Program

**Approach:** Build on ReMIND-L multidisciplinary program structure to expand and refine DISC4 scope and facilitate readiness for target validation



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## High-Level Program Objectives

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### Expand Scope

Systems biology approach that cut across research silos

### Facilitate Progression

Position teams for readiness for target validation by end of award



# DISC4 | Award Structure

	DISC4
<b>Structure</b>	Large collaborative teams
<b>Recurrence</b>	Annual
<b>Focus</b>	<b>Broad, cycle-specific</b>
<b>Max Duration</b>	4 years
<b>Applicant</b>	California non-profit or for-profit research institutions
<b>Core Team</b>	At least 5 California-based investigators (1 PI + 4 Co-I)
<b>Max Award</b>	<b>\$13M (Total Cost Capped)</b> (\$14M with matching funds)
<b>Awards/Year</b>	6
<b>Program cost/Year</b>	\$84,000,000 (6 X \$14M)
<b>Total Funds Requested</b>	\$84,000,000

# DISC4 | Award Budget

	ReMIND-L 2024	DISC4
<b>Cost Cap</b>	<b>Direct Cost Cap</b>	<b>Total Cost Cap</b>
<b>Overhead</b>	<b>Average 60%</b> 40% - 84% (range) <i>Past DISC grants</i>	<b>Apply 62.5% estimate</b> <b>Based on historical average</b>
<b>Max Award</b>	\$8.0M (no matching) \$10.0M (with matching) <i>Direct costs</i>	<b>\$13.0M (no matching) = \$8.0M + 62.5%</b> <b>\$14.0M (with matching) = \$13M + \$1M</b> <i>Total costs</i>
<b># of Award</b>	Target 6 awards per cycle (7 awards funded)	Target 6 awards per cycle

# DISC4 | Project Eligibility

To be eligible a project must:

1. Address a key knowledge gap or research bottleneck in the study of human diseases
2. Include studies that employ human stem cells and/or genetic\* research as part of the central approach or hypothesis
3. Provide strong justification for any proposed use of non-human models

\* Research that alters genomic sequences of cells (edit, remove or add DNA sequences); or introduces or directly manipulates nucleic acids (e.g., coding and non-coding RNAs, antisense oligonucleotides) in human cells

# DISC4 | Team Eligibility

	Eligibility Requirements
<b>Applicant</b>	California non-profit or for-profit research institutions
<b>Core Team</b>	<ul style="list-style-type: none"><li>• 1 CA-based Principal Investigator, as main point of contact with CIRM staff</li><li>• 4 or more CA based co-Investigators</li><li>• <b>Muti-Institutional (&gt;1 member of Core team must be from different institution)</b></li></ul>
<b>Expertise Requirements</b>	<ul style="list-style-type: none"><li>• Minimum 1 KP with relevant clinical expertise</li><li>• Minimum 1 KP with relevant computational expertise</li><li>• <b>Minimum 1 KP with relevant industry/translational expertise</b></li><li>• Minimum 1 Data Project Manager</li></ul>
<b>Investigator Effort</b>	<ul style="list-style-type: none"><li>• PI - 15% min</li><li>• Co-I – 10% min</li></ul>

**Bold:** Changes from ReMIND to incentivize multi-disciplinary projects and readiness of translation

# DISC4 | Areas of Funding

**DISC4 is open to eligible applications without restrictions in topic/disease**

**Preference setting will occur within the program yearly in order to:**

- Increase potential for synergy across teams
- Increase potential to leverage external partnerships
- Respond to an evolving research landscape and portfolio changes

# DISC4 | Preference Setting – For Board Decision (Today)

Preference Topics	Portfolio Representation	Relevance to Diseases of High Burden	Stem Cell Modeling Opportunities
<ul style="list-style-type: none"> <li>Metabolic physiology (endocrine, hormonal regulation)</li> <li>Influence of diet or microbiome on health</li> <li>Biology of the gastrointestinal tract, liver, kidney, pancreas, or endocrine organs</li> </ul>	✘	✔	-
<ul style="list-style-type: none"> <li>Neurodegeneration</li> <li>Neuronal regulation (neuro-immune, neuro-tumor, gut-brain interactions)</li> <li>Biology of the brain or spinal cord</li> </ul>	✔	✔	✔
<ul style="list-style-type: none"> <li>Immune regulation and responses (cancer immunology, neuroimmune)</li> <li>Biology of the immune system</li> <li>Biology of the hematopoietic system</li> </ul>	✔    ✔	-	✔
<ul style="list-style-type: none"> <li>Fibrosis, chronic inflammation or senescence</li> <li>Biology of the heart, vasculature, vascular-tissue interactions, or pulmonary system</li> <li>Biology of the reproduction or fertility</li> </ul>	-	✔    ✔	-
<ul style="list-style-type: none"> <li>Biology of pain (transduction, circuits)</li> <li>Biomechanical properties of tissues or bioengineering bottlenecks</li> <li>Biology of the sensory systems, skin, skeletal muscle, bone, or connective tissue</li> </ul>	-	-	-

✘ Low   
 - Medium, Emerging, Varied   
 ✔ High   
 ✔    ✔ Very High

# DISC4 | Application and Review

## DISC4 will incorporate a pre-submission process to:

- Optimize alignment with program scope, objectives, and preference topics
- Reduce burden for applicants and facilitate new collaborations
- Allow review preplanning for improved GWG review

## DISC4 will make other changes to the GWG scoring system to:

- Align across CIRM programs
- Improve granularity and visibility for score driving decisions

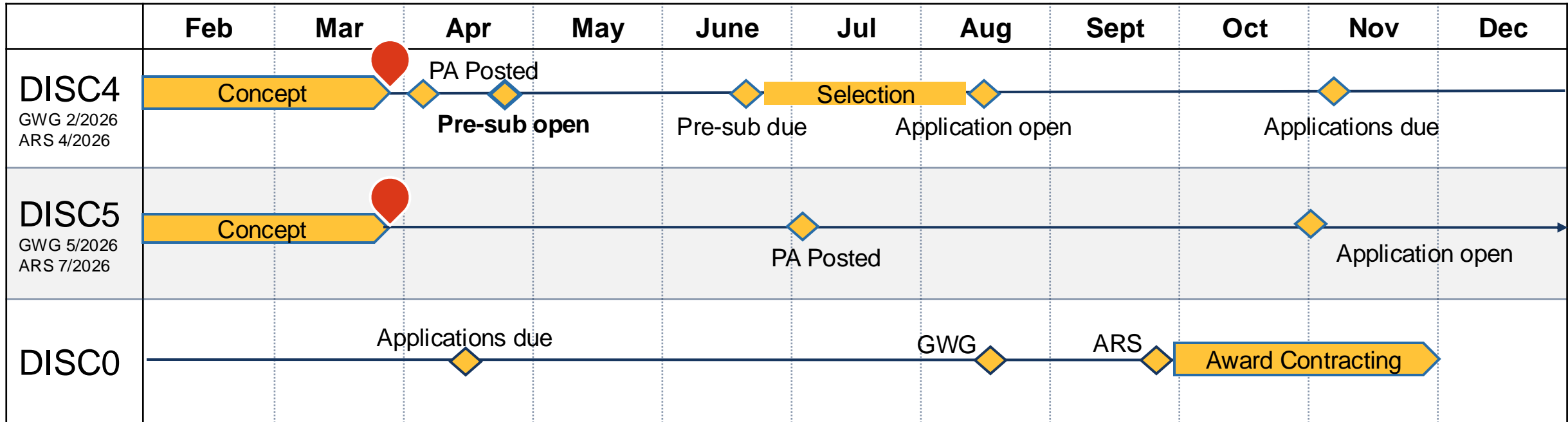
# DISC4 | Other Attributes or Improvements

## Data Sharing

- Require Data Sharing and Management Plan
- Require coordination with CIRM's data initiatives



# DISC Program Timeline



# Formal Request for Funding

CIRM requests the ICOC approve the proposed DISC4 Program Concept, with an initial allocation of **\$84M** in the first annual funding cycle