DISC4 Concept Overview

March 27, 2025

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

DISC4 I Outline

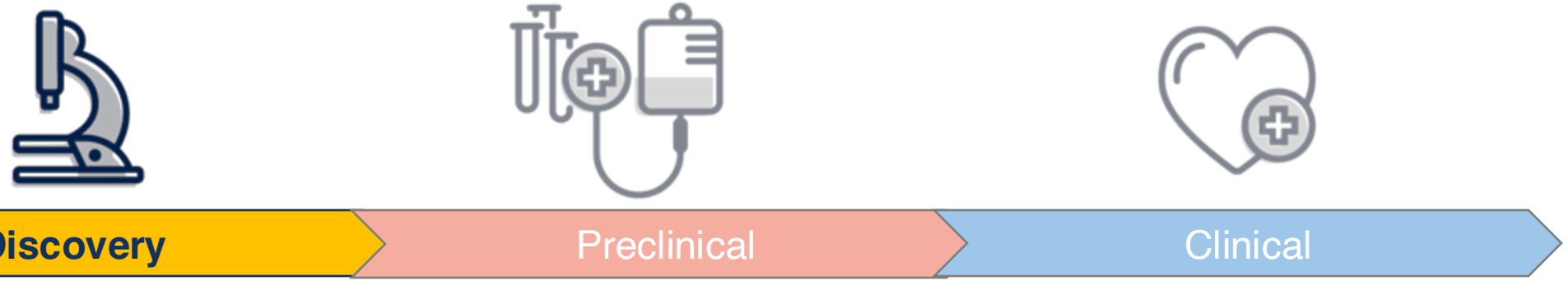
1. Background (SAF alignment)
2. Objective
3. Scope
4. Structure
5. Timeline
6. Request for Motion

Goal 1 I 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 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

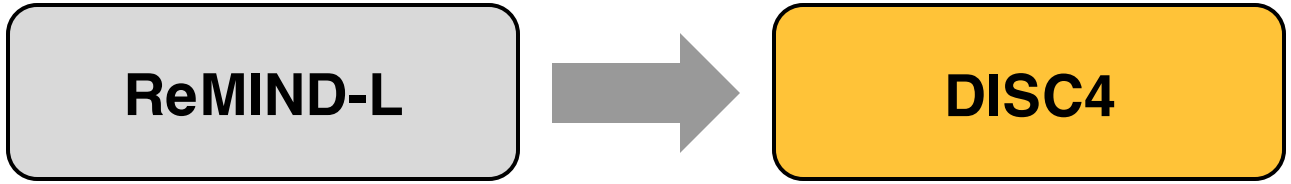
DISC4 | Scope & Expected Outcomes

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



Specific Focus

Broad Scope / NTF Preferences

High-Level Program Objectives

Expand Scope

Systems biology approach that cut across research silos

Facilitate Progression

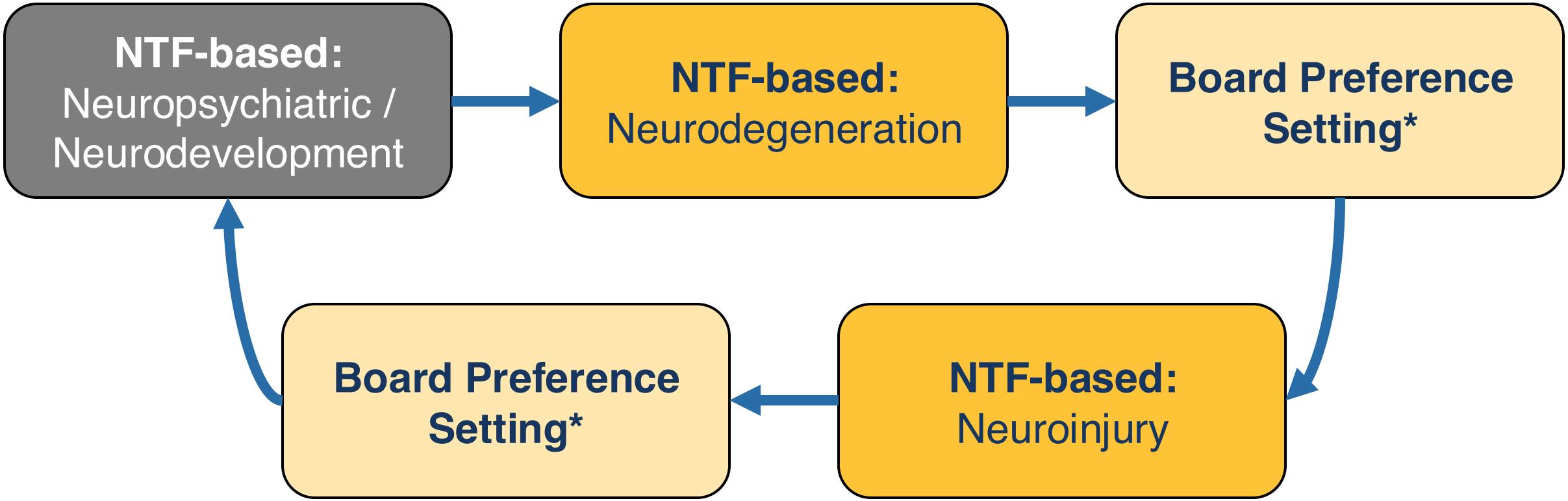
Position teams for readiness for target validation by end of award

DISC4 | Areas of Funding

1. **DISC4 is open to eligible applications without restrictions in topic/disease**
2. **Preference setting will occur within the program yearly in order to:**
   - Address NTF opportunities
   - Increase potential for synergy across teams
   - Increase potential to leverage external partnerships
   - Respond to an evolving research landscape and portfolio changes

DISC4 I Alternating Neuro Cycles

Enabling NTF Prioritization while allowing other diseases to use this structure



*All cycles will be open to all-comers with alternating preferences determined by either NTF or by the Board each June based on portfolio analyses

DISC4 I Award Structure

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

DISC4 I Award Budget

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

DISC4 I 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 I Team Eligibility

	Eligibility Requirements
Applicant	California non-profit or for-profit research institutions
Core Team	• 1 CA-based Principal Investigator, as main point of contact with CIRM staff • 4 or more CA based co-Investigators • **Muti-Institutional (>1 member of Core team must be from different institution)**
Expertise Requirements	• Minimum 1 KP with relevant clinical expertise • Minimum 1 KP with relevant computational expertise • **Minimum 1 KP with relevant industry/translational expertise** • Minimum 1 Data Project Manager
Investigator Effort	• PI - 15% min • Co-I – 10% min

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

DISC4 | Application & 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 I Pre-submission Process Workflow

1 Pre-submission

Applicant completes a short pre-submission form in GMS (estimate ~ 50-100 per cycle)

2 CIRM Reviews

CIRM rank orders pre-submissions based on preferences and related objective criteria

3 Full Application

CIRM invites select applicants (~30 teams) to submit full application

DISC4 I Pre-Submission Rubric

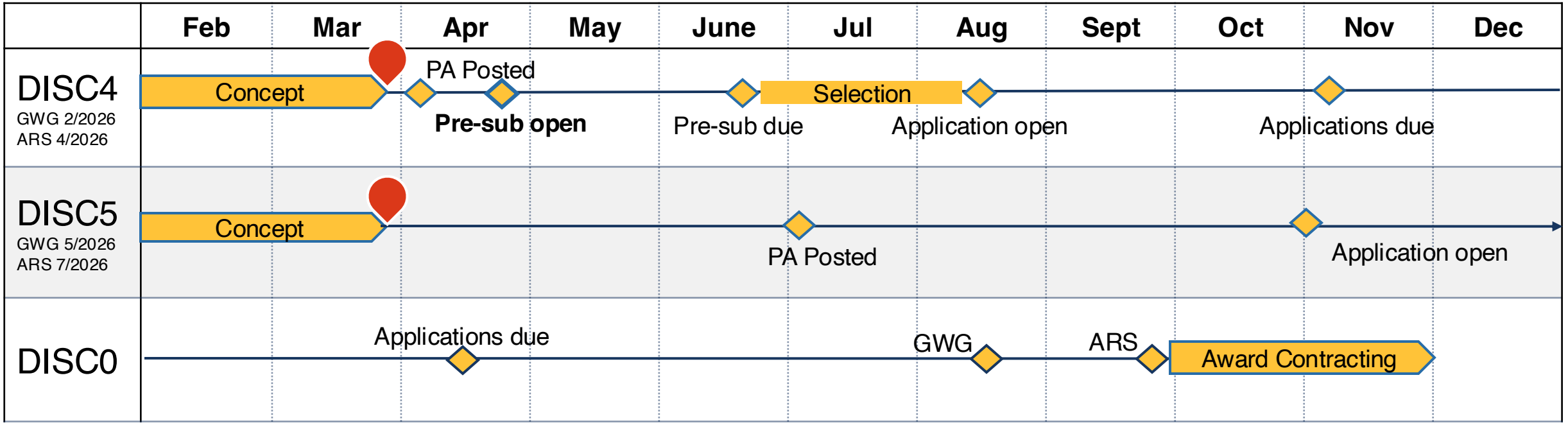
Criteria		Key Considerations
1	**Preference topics (by FY)**	• Neurodegenerative Diseases (FY 25/26)
2	**Relevance to human disease biology**	• Relevant to prevalent diseases or diseases of high unmet need • Includes significant target validation or early translational plan
3	**Cross-disciplinary and systems biology**	• Includes major clinical or computational workflows • Applies cross-disease or cross-organ systems biology approach
4	**Stem cell or genetic research innovations**	• Includes Strong/Innovative stem cell-based approaches • Includes Strong/Innovative genetic research in approaches

DISC4 I Other Attributes or Improvements

Data Sharing

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

DISC Program Timeline



Request for Motion

CIRM requests the ICOC approve the proposed DISC4 Concept Plan