Grants Working Group Recommendations

DISC4 Awards

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Gil Sambrano, PhD

Vice President, Portfolio Development & Review

ICOC/ARS Meeting

March 26, 2026

Our Mission

Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

Strategic Impact Goals

Accelerating Discovery & Translation

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

Goal 2: Accelerate the development and utilization of 5-8 technologies that have the potential to improve safety, efficacy, and/or quality of cell and gene therapies

Cell & Gene Therapy Approvals

Goal 3: Advance 4-7 rare disease projects to Biologics License Application (BLA)

Goal 4: Propel 15-20 therapies targeting diseases affecting Californians to late-stage trials

Accessibility & Affordability of Therapies

Goal 5: Ensure that every BLA-ready program has a strategy for access and affordability

Diverse Workforce Development

Goal 6: Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine

Strategic Impact Goals

Accelerating Discovery & Translation	Cell & Gene Therapy Approvals	Accessibility & Affordability of Therapies	Diverse Workforce Development
Goal 1: Catalyze the identification and validation of at least four novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California	**Goal 3:** Advance 4-7 rare disease projects to Biologics License Application (BLA)	**Goal 5:** Ensure that every BLA-ready program has a strategy for access and affordability	**Goal 6:** Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine
Goal 2: Accelerate the development and utilization of 5-8 technologies that have the potential to improve safety, efficacy, and/or quality of cell and gene therapies	**Goal 4:** Propel 15-20		

Discovery recommendations

- 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

DISC4 Awards

DISC4 awards support 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.

A DISC4 award should achieve one or more of the following outcomes:

- Discover novel mechanistic insights or advance understanding of human disease pathobiology;
- Extend understanding of disease mechanisms across affected human populations; and/or
- Identify and validate novel therapeutic strategies, targets, or biomarkers.

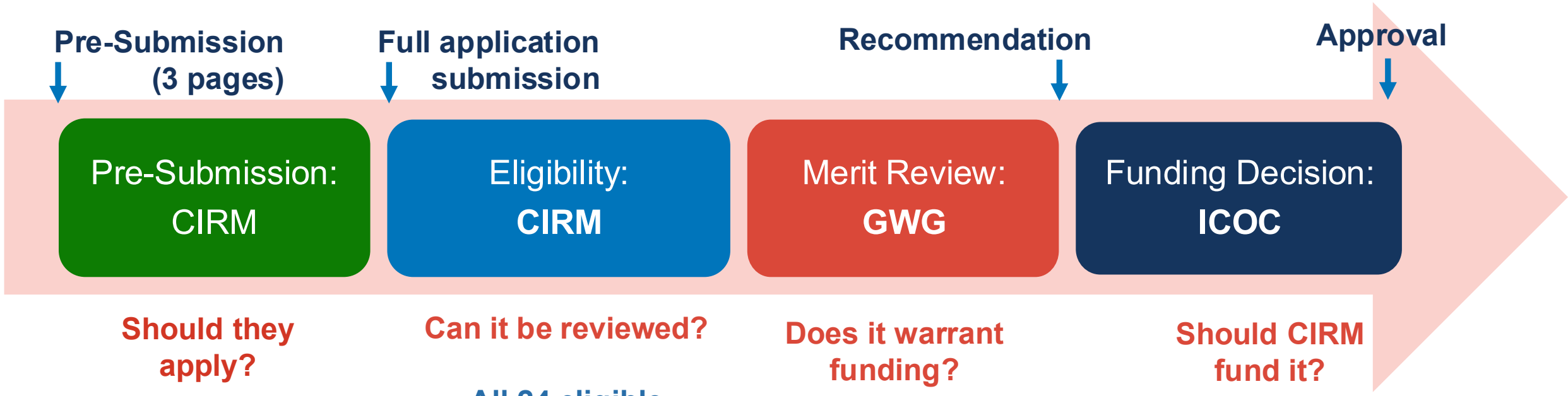
DISC4 awards have an annual, board-approved preference topic. This year, the preference topic is **Neurological Diseases** (including conditions and disorders of the brain, spinal cord, and peripheral nervous system)

DISC4 Program Structure

Program Overview

Max duration and budget (total cost)	Four (4) years $13M, additional $1M with matching funds
Applicant team	Single Principal Investigator (PI) Minimum 4 Co-Investigators (Co-Is)
DISC4 26.1 allocation	$84M total, or roughly up to 6 awards
Full applications invited by staff	24 of 138 pre-submissions/LOIs

DISC4 Application and Review Process



DISC4 GWG Panel Composition and Roles

Who participates and how they contribute

Scientific GWG Members

- Scientific evaluation based on broad subject area or methods expertise
- Enter final scores for **every** application

GWG Board Members

- Patient perspective on significance and potential impact, oversight on process
- Do not enter scores

Visiting Specialists

- Scientific evaluation based on specialized expertise
- Provide recommended scores in the discussion

Scientific Scoring System

Using the 1 to 100 scale

Median score of 85-100: *Exceptional merit and warrants funding, if funds are available.*

Median score of 1-84: *Not recommended for funding.*

Scoring is holistic and based upon all facets of the expert review.

GWG are encouraged to make full use of the scoring range to signal their enthusiasm for each project.

DISC4 Scientific Review Criteria

What reviewers considered when scoring

1. Significance and potential for impact
2. Innovation relative to the current state of research
3. Scientific rationale
4. Project plan and design
5. Applicant's consideration of impact across affected populations

GWG Recommendations

Recommendation	Number of Apps	Total Applicant Request	Funds Available
Recommended for funding Score of 85-100	**8**	$108,531,482	**$84,000,000**
Not recommended for funding Score of 1-84	16		

For each award, the final award amount shall not exceed the amount approved by the ICOC Application Review Subcommittee and may be reduced contingent on CIRM's assessment of allowable costs and activities.

Minority Reports

- Under Prop 14, any application that is not recommended for funding by the GWG, but which had 35% or more members score to fund the application must include a minority report.

- The minority report is included in the review summary and provides a brief synopsis of the opinion of reviewers that scored the application 85 or above.

No DISC4 applications qualified for a minority report this cycle.

CIRM Team Recommendations

App Num	Total Budget Request	GWG SCORE	Hi	Lo	Y	N	CIRM Recommendation
DISC4-19200	$13,578,858	90	95	80	12	3	Fund
DISC4-19271	$12,995,613	90	90	75	11	2	Fund
DISC4-19334	$13,957,175	90	90	75	9	5	Fund
DISC4-19371	$13,999,999	89	92	85	14	0	Fund
DISC4-19291	$13,000,000	87	90	85	12	0	Fund
DISC4-19391	$12,999,837	85	87	80	11	3	Fund
DISC4-19196	$14,000,000	85	86	70	8	6	Do Not Fund
DISC4-19226	$14,000,000	85	88	50	8	6	Do Not Fund
	$80,531,482						

CIRM Team Recommendations

The CIRM Team recommends funding the **top ranking six (6) applications** with a **score of 85 or above** and with at least a two-thirds majority recommendation to fund by the GWG.

Of the three applications scoring 85, CIRM team is recommending two of the three applications NOT be funded at this time (DISC4-19196 and DISC4-19226) due to insufficient budget.

Rationale for supporting DISC4-19391:

- All three applications scoring 85 strongly aligned with DISC4 program objectives and included numerous strengths.
- DISC4-19391 has greater consensus on merit, (11:3 vs 8:6) and a lower perceived risk profile.

CIRM Team Recommendations: DISC4-19196

CIRM **does not** recommend that the ARS fund application DISC4-19196. DISC4-19196 tied for the 6th highest median score and ranked 7th in mean GWG scores with a slight majority recommending to fund.

Rationale:

- This application is focused on neurodegenerative diseases, particularly amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), and aims to understand how RNA localization relates to disease state.
- Reviewers noted an excellent team, innovative approaches, and the potentially high impact of the datasets to be produced.
- A significant risk was noted: while RNA mis-localization is a common observation in ALS, reviewers highlighted uncertainty whether this plays a causal role in ALS and cited the lack of direct preliminary evidence in this context.
- DISC4-19196 had lesser GWG consensus (8:6) for recommendation compared to the sixth ranked application that is also on focused on ALS.

CIRM Team Recommendations: DISC4-19226

CIRM **does not** recommend that the ARS fund application DISC4-19226. DISC4-19226 tied for the 6th highest median score and ranked 8th in mean scores with a slight majority voting to fund.

Rationale:

- This application is focused on understanding cytokine responses in the brain and microglial mechanisms in the context of Alzheimer's disease.
- Reviewers noted an excellent team, innovative approaches, and the potential creation of high value datasets.
- For some reviewers, their enthusiasm was offset by significant concerns around the lack of power calculations, the selection of some analytical methods, and a lack of clarity on how information and data from the disparate aims will be integrated.
- DISC4-19226 had lesser GWG consensus (8:6) for recommendation compared to higher ranked applications.