CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the Application Review Subcommittee
From: CIRM Leadership
Re: CIRM Team Recommendations: DISC4
Date: March 26, 2026

Introduction:

The role of CIRM staff during the Application Review Subcommittee (ARS) meetings is to assist the ARS in making well-informed funding decisions by providing programmatic context alongside the outcomes of the Grants Working Group (GWG) recommendations. The ARS receives the GWG funding recommendations, which include the final scores, assessment against the review criteria, and summary of specific strengths and weaknesses identified during peer review.

Consistent with the CIRM funding recommendation framework presented to the Science Subcommittee (November 2025), ARS may also consider additional factors when making final funding decisions, including:

1. Available program budget and budget utilization
2. Programmatic and portfolio considerations
3. Recommendations from CIRM program leadership
4. Public comment

This memo summarizes the CIRM program leadership recommendations for applications to DISC4 which the ARS will consider on March 26, 2026. In developing these recommendations, CIRM evaluated all applications with a GWG median score of 80 or above, taking into account GWG scores and reviewer comments, the available DISC4 program budget, portfolio considerations, alignment with program objectives, and other relevant information available to CIRM following the GWG review.

Summary of Program Budget Considerations:

Available Program Budget (Annual)	$84M
Budget Utilization – GWG Recommended	$108M
Budget Utilization – CIRM Recommended	$80.5 M
Remaining Program Budget	$-24M (GWG Recommended) / $3.5M (CIRM Recommended)

Summary of CIRM Team Recommendations:

Application	Median GWG Score	Scores to fund	Scores not to fund	GWG Recommendation	CIRM Recommendation
DISC4-19200	90	12	3	Fund	Fund
DISC4-19271	90	11	2	Fund	Fund
DISC4-19334	90	9	5	Fund	Fund
DISC4-19371	89	14	0	Fund	Fund
DISC4-19291	87	12	0	Fund	Fund
DISC4-19391	85	11	3	Fund	Fund
DISC4-19196	85	8	6	Fund	Do Not Fund*
DISC4-19226	85	8	6	Fund	Do Not Fund*
DISC4-19444	80	3	10	Do Not Fund	Do Not Fund
DISC4-19319	80	0	14	Do Not Fund	Do Not Fund
DISC4-19227	80	2	11	Do Not Fund	Do Not Fund
DISC4-19452	80	2	13	Do Not Fund	Do Not Fund

Highlighted applications discussed in the memo. *Team recommendations differ from GWG recommendations

This memo presents the CIRM team recommendations for the highlighted applications tied with a median GWG score of 85: DISC4-19391, DISC4-19196, and DISC4-19226.

CIRM Overall Team Recommendation:

Due to insufficient budget, CIRM is recommending 6 of the GWG-recommended applications for funding.

Of the three applications scoring 85, CIRM team is recommending two of the three applications NOT be funded at this time (DISC4-19198 and DISC4-19226).

All three applications scoring 85 strongly aligned with DISC4 program objectives and included numerous strengths, e.g. outstanding teams, application of diverse, cutting-edge methodologies, and innovative efforts to address significant knowledge gaps. As all were deemed equally impactful in this regard, the decision to support DISC4-19391 lies in its greater consensus on merit, (11:3 vs 8:6) and its lower perceived risk profile.

The remaining proposals, which scored 80 and below, did not have sufficient distinctions that would lead to more compelling DISC4 portfolio. Therefore, CIRM concurs with the GWG recommendations to not fund them at this time.

Application Assessments:

1. Application number: DISC4-19391
Title: Dissecting cell-specific genetic and molecular drivers of amyotrophic lateral sclerosis for therapeutic insights

GWG Outcome:

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	84	87	80	11	3

CIRM Team Recommendation:

In concurrence with the GWG, CIRM **does** recommend that the ARS fund application DISC4-19391. This application tied for the 6th highest median score, ranked 6th in mean GWG scores, and ranked 6th in recommendations to fund with strong majority (11 of 14) providing scores to fund.

DISC4-19391 is focused on the identification, characterization, and therapeutic targeting of genetic drivers of amyotrophic lateral sclerosis (ALS). The GWG noted the breadth of expertise of the team, including industry partners. They also highlighted its potential for broad impact through the generation of large-scale multi-omic datasets and for findings that inform translation. CIRM team believes that a minor concern raised around patient sample acquisition could be readily addressed at award launch.

2. Application number: DISC4-19196
Title: Reprogramming the Spatial Transcriptome for Precision Neurodegenerative Therapies

GWG Outcome:

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	82	86	70	8	6

CIRM Team Recommendation:

CIRM **does not** recommend that the ARS fund application DISC4-19196 due to insufficient budget to support all recommended (median >85) applications. DISC4-19196 tied for the 6th highest median score and ranked 7th in mean GWG scores with a slight majority recommending to fund.

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. However, a significant risk was noted: while RNA mis-localization is 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. Given this perceived risk, and the lesser consensus for recommendation compared to the sixth ranked application that is also on focused on ALS, CIRM team recommends not to fund this project at this time.

3. Application number: DISC4-19226
Title: The immune system of the human brain: A platform for neuroimmunotherapies

GWG Outcome:

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	80	88	50	8	6

CIRM Team Recommendation:

CIRM **does not** recommend that the ARS fund application DISC4-19226 due to insufficient budget to support all recommended (median >85) applications. DISC4-19226 tied for the 6th highest median score and ranked 8th in mean scores with a slight majority voting to fund.

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, this 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. Given these risks and the lesser consensus for recommendation, the (8:6), CIRM team recommends not to fund this project at this time.