CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the Independent Citizens Oversight Committee (ICOC)
From: Rosa Canet-Avilés, PhD, Chief Science Officer; Gil Sambrano, Vice President, Review
Re: Funding Area Preferences: Rationale, Guiding Principles, Early Implementation Results
Date: January 29, 2026

---

1. Purpose of This Memorandum

This memorandum provides a detailed explanation of the rationale for funding area preferences, how they have been developed and applied across CIRM programs, and what early signals are emerging from initial funding cycles. It also responds to feedback from the Science Subcommittee and Board leadership regarding clarity, transparency, and communication of the preference framework.

The intent is to ensure that the Board, applicants, and other stakeholders share a common understanding of:

- What funding area preferences are intended to do;
- What they are not intended to do;
- How they relate to Proposition 14 and CIRM's Strategic Allocation Framework; and
- How early experience is informing potential refinements.

2. Context: Why preferences were introduced

CIRM is operating under three intersecting realities:

i. **Finite public funding and time horizon**
Proposition 14 provides a defined funding authorization and timeframe. CIRM must therefore make deliberate choices to maximize the likelihood that public investment results in therapies reaching patients within CIRM's remaining years.

ii. **Expanded statutory mandates**
Proposition 14 reaffirmed and expanded CIRM's responsibilities, including:
   a. Advancing treatments for diseases of the brain and central nervous system (CNS); and
   b. Addressing access, affordability, and scalability.

iii. **Persistent oversubscription across programs**
Across Discovery, Preclinical, and Clinical programs, CIRM consistently receives far more high-quality applications than can be funded. CIRM's challenge is no longer whether there is strong science to fund, but how to prioritize among many meritorious applications to maximize the likelihood of delivering impactful therapies to patients within CIRM's remaining years. Doing so requires looking beyond scientific merit alone to factors such as readiness, scalability, and statutory alignment.

3. What funding area preferences are intended to do

Funding area preferences are designed to:

- Focus limited review and funding capacity on applications most aligned with CIRM's impact goals and statutory priorities; and
- Shape the pool advancing to full peer review by prioritizing proposals with strong feasibility, readiness, and potential for downstream patient access.

4. What preferences are not intended to do

It is equally important to clarify what preferences are not intended to do. Funding area preferences do not:

- Function as eligibility requirements;
- Exclude entire disease areas, modalities, or approaches across all cycles; or
- Limit innovation or novelty.

All programs remain open to all qualified applicants unless the Board has explicitly approved a focused call (ex., DISC4 ReMIND-L program, neuropsychiatric disease focus, 2023).

5. Alignment with Proposition 14 and CIRM strategy

Preferences are grounded in guiding principles that reflect both Proposition 14 and CIRM's Strategic Allocation Framework. Collectively, these principles prioritize research that:

- Offers the potential for transformative patient impact;
- Addresses known bottlenecks to translation, including manufacturing, delivery, scalability, access, and affordability;
- Advances statutory priorities, including CNS diseases and pluripotent stem cell-derived therapies;
- Demonstrates a credible development and regulatory path achievable within CIRM's remaining runway; and
- Contributes to a balanced portfolio addressing diseases affecting Californians.

These principles were translated into program-specific preferences appropriate to the goals and stage of each program.

6. How preferences are applied in practice

CIRM's Discovery (DISC4), Preclinical Development (PDEV) and Clinical Development (CLIN2) funding opportunities utilize preferences tailored to the goals of each program and informed by the guiding principles above. Preferences are designed to be objective and quickly discernible by CIRM staff according to program-specific rubrics. In all cases, preference scoring occurs before scientific merit review by the GWG. Refer to **Appendix A** for a flow chart describing how preferences are implemented, **Appendix B** for a table of program-specific preferences and implementation details, **Appendix C** for scoring rubrics, and **Appendix D** for cycle-specific outcomes comparing the initial project pool with applications that advanced to full review.

7. Early results and signals from initial funding cycles

Staff reviewed outcomes from the first two cycles of PDEV, the first two cycles of CLIN2, and the FY25/26 DISC4 cycle to assess how the preference frameworks performed in practice. The observations below reflect early signals, with appropriate caveats regarding sample size, timing, and the preliminary nature of these data.

Preclinical Development (PDEV)

- **Cycle 1**
  CIRM received 168 PDEV pre-submissions and invited 33 applications (~20%) to submit full proposals. 97% of invited applications met three to four preferences, while 42% of non-invited applications met zero or one.
  Among the 12 funded awards, common features included strong translational readiness, disciplined progression from prior CIRM investments (over half of awards), and enrichment of disease areas previously under-represented in the preclinical portfolio.
  Overall, Cycle 1 suggests that PDEV preferences did not narrow the science but

supported more intentional portfolio balance across disease area, modality as well as Prop 14 statutory mandates.

- **Cycle 2 (ongoing)**
  Cycle 2 received 126 pre-submissions and invited 23 applications (~18%). All invited applications met three to five preferences, while roughly one-third of non-invited met zero or one. The invited pool reflected broad disease representation, including more cancer and hematology, and ~40% would represent portfolio progression if funded. While outcomes remain pending, Cycle 2 signals consistency with Cycle 1.

Clinical Development (CLIN2)

- **Cycle 1**
  Of 23 applications, seven advanced (one was subsequently ruled ineligible due to post-submission protocol changes) and four of the eligible six were funded. All advancing applications met three to four preference points; all targeted CNS indications; most involved pluripotent stem cell-derived or in vivo genetic therapies, and several held advanced FDA designations. Funded awards showed feasible delivery aligned with access and affordability considerations, and most represented progression from prior CIRM investments.
  These results indicate that the CLIN2 framework elevated programs aligned with CNS priorities, clinical readiness, and delivery feasibility, while also highlighting the importance of preference weighting as the clinical portfolio grows.
- **Cycle 2 (interim)**
  In Cycle 2, 21 applications were ranked using the same framework; seven advanced to full review, all meeting three to four preferences. Advancing applications again reflected CNS focus, portfolio progression, and PSC-derived or in vivo genetic therapies. Final funding decisions will follow GWG review.

Cross-Program Summary and Caveats

Across PDEV and CLIN2 Cycles 1 and 2, early signals are consistent with Board guidance: preferences are functioning as intended to prioritize alignment with innovation, readiness, access and affordability, and CNS priorities, without replacing peer review or excluding high-quality science.

These findings are preliminary. It is too early to assess long-term portfolio impact. At this stage, the evidence indicates that the framework is behaving as designed, supporting a more deliberate and strategically aligned portfolio while preserving scientific rigor and openness as evidenced by the fact that GWG recommended many of the invited or qualified proposals for funding.

Discovery (DISC4)

DISC4 serves a distinct role as a once-per-year, team-based discovery program. In 2024, the Board approved an **alternating preference structure**, under which some cycles reflect identified scientific needs and others reflect explicit Board-set preferences. All DISC4 cycles remain open to all applicants.
For FY25/26, the Board selected Neurological* Diseases (encompassing disorders of the brain, spinal cord, and peripheral nervous system) as the preference. This preference was the highest weighted in pre-submission scoring, and additional scored preferences addressed scientific

* Neurological diseases in this context includes neurodegenerative, neurodevelopmental, and neuropsychiatric conditions affecting the central and peripheral nervous systems.

substance (e.g., relevance to human disease biology, cross-disciplinary approaches, and innovation).

CIRM received 138 DISC4 pre-submissions for the FY25/26 cycle. Of these, 86 percent aligned with the preference, indicating that the priority signal was clearly received by the research community. From this pool, 24 applications were invited to submit full applications for GWG review. Importantly, 100 percent of the invited applications met the preference, confirming that the preference functioned as an effective enrichment mechanism.

Equally important, invited applications span a broad range of diseases within the preference criteria and reflect substantial diversity in mechanisms, model systems, and scientific approaches. There is no evidence of convergence on a single disease, modality, or research strategy. Instead, the pattern observed is one of enrichment within a priority area, while preserving scientific breadth and depth.

GWG review is ongoing, with funding decisions expected in March 2026. At this stage, conclusions are necessarily limited to pre-submission outcomes. Nevertheless, the available data indicate that the DISC4 preference structure is performing exactly as designed: shaping the applicant pool in alignment with Board direction, without narrowing the science or excluding high-quality discovery work.

8. Closing

Funding area preferences are a necessary tool for navigating the realities of expanded mandates, finite funds, and a limited runway. Early cycles suggest the system is behaving directionally as intended. Applications advancing to full merit review via the preferences continue to earn high marks from the GWG, and in some cases recommendations to fund more projects than we can support.

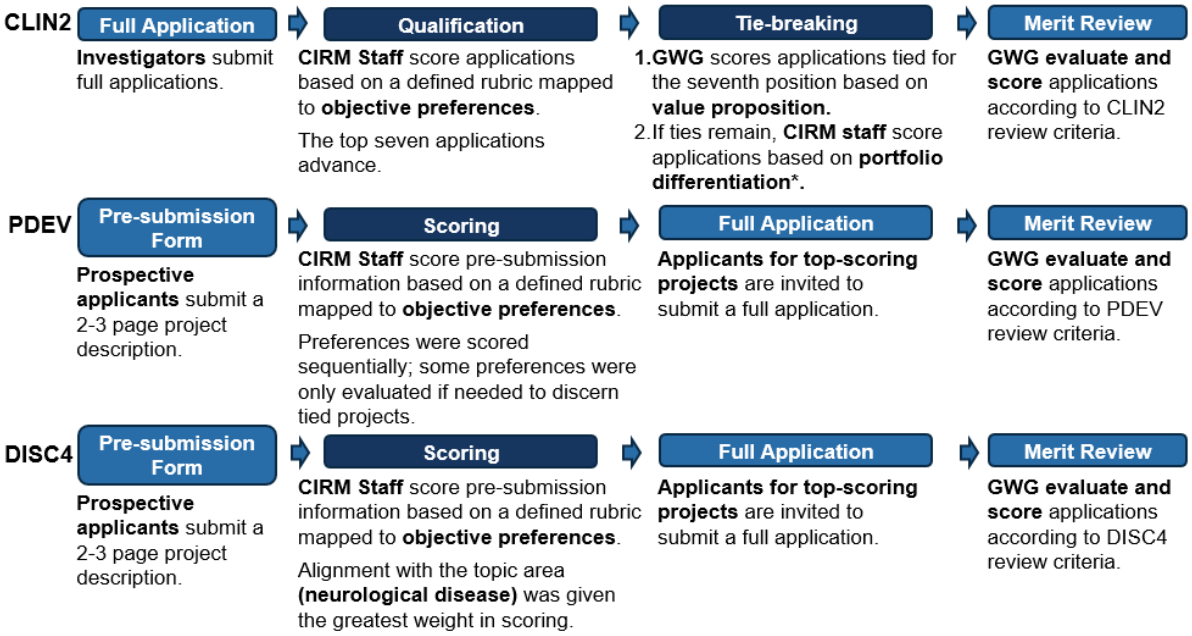
The work now is to ensure preferences are well understood, transparently communicated, and refined thoughtfully with Board guidance.

Requested Action: No formal action is requested at this time. This memo is provided to support the Board's discussion and to solicit guidance that will inform a portfolio-level analysis and any potential refinements to preferences or their implementation that will be brought to the Board for consideration in March 2026.

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Appendix A. Flow Chart of Pre-submission Scoring and Qualification Processes

Purpose of this Appendix:
This appendix provides a visual diagram of how preference scoring is implemented during a funding cycle for CLIN2, PDEV, and DISC4. Refer to Appendix B for lists of preferences evaluated at each stage.



*Refer to Appendix B, CLIN2 preferences, Step 4 for a detailed description.

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Appendix B. Program-Specific Preferences by Stage

Purpose of this Appendix
This appendix indicates when preferences were used at each step of the review process for each program.

Table B1. CLIN2 Preferences by Stage
The below table summarizes how preferences are applied at each stage after CLIN2 applications are received and who is responsible for each activity until funding is approved by the ICOC.

Stage		What is being assessed	Who is responsible
1	Applications Received		
2	Qualification: Preferences scored	Objective Preference Criteria: • PSC • Prop 14 CNS • In vivo genetic therapy • Non-viral nucleic acid • Progression • RMAT, Breakthrough or FastTrack accelerated regulatory designations • CA organization • Pivotal trial	CIRM Team
3	Qualification: GWG tie-breaking for top-scoring applications	Criteria: • Potential to provide a meaningful and substantial improvement in clinical outcomes • Expected impact of addressing unmet need • Feasibility and practicality of the therapy's uptake	GWG
4	*[Only if ties still remain]* Qualification: Preference tie-breaking for top-scoring applications	Objective Preference Criteria: • Under-represented disease area in CIRM's clinical portfolio • Novel therapeutic approach compared to CIRM portfolio	CIRM Team
6	Full applications scored by GWG	Scientific Merit	GWG
7	CIRM recommendations		CIRM Team
8	Final decisions for funding		ICOC

Table B2. PDEV Preferences by Stage

The below table summarizes how preferences are applied at each stage after PDEV pre-submissions are received and who is responsible for each activity until funding is approved by the ICOC.

	Stage	What is being assessed	Who is responsible
1	Pre-Submissions Received		
2	Preferences scored	Objective Preference Criteria: • PSC/Neuro/in vivo • Non-viral nucleic acid • Pre-IND/INTERACT meeting conducted • Progression • Under-represented disease area	CIRM Team
3	Novelty scoring for pre-submissions above cutoff*	Objective Preference Criteria: • Novelty compared to CIRM portfolio	CIRM Team
4	Tie-breaking for top-scoring pre-submissions	Objective Preference Criteria: • Neuro & Progression (Cycle 1) • Prevalence (Cycle 2)	CIRM Team
5	Top-scoring pre-submissions invited to full application		CIRM Team
6	Full applications scored by GWG	Scientific Merit	GWG
7	CIRM recommendations		CIRM Team
8	Final decisions for funding		ICOC

Table B3. DISC4 Preferences by Stage

The below table summarizes how preferences are applied at each stage after DISC4 pre-submissions are received and who is responsible for each activity until funding is approved by the ICOC.

	Stage	What is being assessed	Who is responsible
1	Pre-Submissions Received		
2	Preferences scored	Objective Preference Criteria: • Preference Topic: Neuro • Relevance to human disease biology • Cross disciplinary and systems biology • Stem cell or genetic research innovations	CIRM Team
3	Top-scoring pre-submissions invited to full application		CIRM Team

* Cutoffs were subtotal of 4 for cycle 1 & subtotal of 3 for cycle 2; cutoff varied by cycle depending on the pool of pre-submissions.

4	Full applications scored by GWG	• Scientific Merit	GWG
5	CIRM recommendations		CIRM Team
6	Final decisions for funding		ICOC

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Appendix C. Preference Scoring Rubrics and Descriptions

Purpose of this Appendix
For funding cycles in fiscal year 2025 – 2026, the following preferences were evaluated and scored for each program as described in each of the following tables.

Table C1. CLIN2 Qualification Rubric

Preference	Points
PSC-derived therapies	1
Diseases of the CNS	1
In vivo genetic therapies	1
Non-viral genetic therapy	1
Accelerated regulatory designation (RMAT, Breakthrough, Fast Track)	1
Progression from CIRM-funded IND-enabling or earlier phase clinical trial awards	1
California Organization	1
Pivotal clinical trial	2

Table C2. PDEV Pre-Submission Rubric

Preference	Points
At least one of the following: • PSC-derived therapies • In vivo genetic therapies • Diseases of the CNS	3
Non-viral nucleic acid delivery	1
Pre-IND or INTERACT meeting conducted	1
Progression from DISC2 or TRAN1	1
Targeting disease area under-represented in CIRM active awards portfolio	1*
Novelty of therapeutic approach compared to CIRM active awards portfolio	0-2**

*Under-represented disease area was worth up to 2 points in cycle 1 and up to 1 point in cycle 2. If disease area represented >10% of CIRM's active CLIN2 portfolio, then 0 points were awarded. In cycle 1, if disease area represented 5-10% of CIRM's active CLIN2 portfolio (infectious disease, metabolic, other), then 1 point was awarded, and if disease area represented <5% of CIRM's active CLIN2 portfolio (bone & cartilage, cardiovascular, muscle disorder, respiratory, and skin), then 2 points were awarded. In cycle 2, if disease area represented <10% of CIRM's active TRAN, CLIN1, and CLIN2 portfolio (bone & cartilage, cardiovascular, eye, infectious disease, metabolic, muscle disorder, respiratory, skin, other), then 1 point was awarded.

**Novelty was only scored for pre-submissions with the highest scoring subtotals (within range of invitation). 2 points were awarded if indication didn't exist in CIRM's active TRAN, CLIN1, & CLIN2 portfolio and the approach was differentiated from those in the same disease area. 1 point was awarded if the indication existed but the approach was still differentiated from those in the same indication.

Table C3. DISC4 Pre-Submission Rubric

Preference	Description	Maximum Points
Preference Topic: Neuro	Does the project align with the cycle-specific preference topic?	9
Relevance to human disease biology	Does the project hold strong relevance for understanding or addressing human disease?	6
Cross-disciplinary and systems biology	Does the project integrate cross-disciplinary approaches?	6
Stem cell or genetic research innovations	Does the project incorporate innovative approaches particularly in stem cell or genetic research?	4

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Appendix D. Preference Frequency Analysis (PDEV and CLIN2)

Purpose of this Appendix
This appendix summarizes how frequently individual funding area preferences were met across applicant pools, and how those preferences were **enriched in the invited or advancing cohorts**. The intent is to illustrate that the preference framework does not simply reward what is most common in the field, but selectively elevates **harder-to-find attributes aligned with CIRM's strategic goals**.

Table D1. PDEV Pre-Submission Preference Frequency - Round 1

Preference Category	All Pre-Submissions (n = 168)	Invited Pre-Submissions (n = 33)
PSC-derived therapies	23 (14%)	8 (24%)
CNS Indication	66 (39%)	9 (27%)
In vivo genetic therapies	67 (40%)	21 (64%)
Non-viral nucleic acid delivery	36 (21%)	16 (48%)
FDA meeting conducted	50 (30%)	15 (45%)
Progression from DISC2 / TRAN1	33 (20%)	15 (45%)

Table D2. PDEV Pre-Submission Preference Frequency - Round 2

Preference Category	All Pre-Submissions (n = 126)	Invited Pre-Submissions (n = 23)
PSC-derived therapies	23 (18%)	10 (43%)
CNS Indication	57 (45%)	8 (35%)
In vivo genetic therapies	51 (40%)	10 (43%)
Non-viral nucleic acid delivery	28 (22%)	10 (43%)
FDA meeting conducted	33 (26%)	6 (26%)
Progression from DISC2 / TRAN1	28 (22%)	9 (39%)

Table D3. CLIN2 Preference Frequency - Combined Cycles 1 and 2 Results

Preference Category	Applications Received (n = 44)	Advancing Applications (n = 13)
California-based organization	38 (86%)	13 (100%)
Progression from prior CIRM award	27 (61%)	8 (62%)
CNS indication	15 (33%)	10 (77%)
FDA regulatory designation	15 (33%)	6 (46%)
In vivo genetic therapy	10 (22%)	6 (46%)
PSC-derived therapy	5 (11%)	4 (30%)
Pivotal trial proposed	2 (5%)	0
Non-viral delivery	1 (2%)	1 (8%)