CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the ICOC
From: Rosa Canet-Avilés, Chief Science Officer, CIRM
Re: Update on the Strategic Allocation Framework Implementation: Phase 1 - New and Amended Concepts
Date: March 27, 2025

Dear Members of the ICOC,

On March 27th, we will present four concept proposals -DISC4, DISC5, PDEV, and CLIN2- for your consideration and recommendation to the ICOC for approval on March 27th. These concepts represent the first phase of implementation of the Strategic Allocation Framework (SAF), approved by the ICOC in September 2024, which prioritizes CIRM's resource allocations with defined programmatic recommendations to maximize CIRM's impact.

As part of the SAF implementation, CIRM has established a structured preference-setting process to ensure that funding priorities remain responsive to emerging portfolio, scientific, and clinical needs while addressing gaps in the cell and gene therapy (CGT) landscape and fulfilling Proposition 14's Neuro mandate (**see Exhibit A**). Anchored in annual portfolio reviews and landscape analyses, this process systematically will inform funding decisions, aligning CIRM's investments with emerging opportunities in neuroscience and regenerative medicine to drive transformative change in CNS therapeutic development.

This preference-setting process originated with the work of the Neuro Task Force (NTF) and was established to guide CIRM's neuroscience investments under Proposition 14. The NTF served as the foundation for this structured approach, ensuring that funding priorities are strategically aligned to maximize impact. Its analysis identified a critical gap in neuropsychiatric research, leading to the development of the ReMIND-L pilot in 2023, which fostered multidisciplinary, innovative approaches to neuro diseases. This effort culminated in approval of $84M in 2024 for neuropsychiatric diseases through the ReMIND-L program, further cementing CIRM's commitment to high-need, high-impact CNS research.

The approach used by NTF will now be applied to the broader regenerative medicine field. As the driving force behind CIRM's preference-setting approach, the NTF has been fully integrated into this process, ensuring that funding priorities remain responsive to emerging portfolio, scientific, and clinical needs. Through this deliberate, data-driven strategy, CIRM is not only fulfilling the Neuro mandate under Proposition 14 but also leveraging it to drive lasting, transformational impact in CNS research and regenerative medicine. This approach ensures that CIRM's investments continue to be strategically aligned with the most pressing scientific and clinical opportunities, ultimately benefiting Californians and advancing the field of cell and gene therapy.

I. Summary of New and Updated Funding Concepts

1. Discovery Programs (DISC4 & DISC5)

- **DISC4 – Funding Opportunity for Discovery Stage Research (Updated Concept)**
  - Supports expansive, cross-disciplinary, and integrated studies led by large collaborative teams to address knowledge gaps or bottlenecks in disease biology
  - Encourages the integration of diverse sources of evidence to strengthen validity and reproducibility of novel targets and biomarkers
  - Builds on the ReMIND-L framework for neuropsychiatric disorders and expands to a broader set of disease areas and mechanistic insights while continuing to prioritize gaps identified by the NTF
  - Implements a pre-submission process to identify and prioritize applications that align with program objectives while maintaining a point of entry for unique proposals with the potential to be transformative
- **DISC5 – Funding Opportunity for Discovery Stage Research (New Concept)**
  - Supports exploratory and innovative foundational research focused on novel stem cell and genetic therapy applications
  - Designed for smaller, high-risk research collaborations applying a range of technologies and approaches to address critical gaps in stem cell biology and regenerative medicine
  - Encourages high-gain pursuits that leverage CIRM-funded networks and infrastructure

Portfolio Considerations: The Discovery Programs have been instrumental in seeding innovative approaches. These refinements enhance CIRM's ability to support early-stage research that identifies and validates high-impact therapeutic targets and biomarkers, fostering the next generation of stem cell and genetic medicine breakthroughs.

2. Preclinical Development Program (PDEV) (New Concept)

- Integrates part of DISC2, TRAN and CLIN1 into a single, agile program that supports projects from pre-IND through IND-enabling activities.
- Key Enhancements:
  - Allows flexible entry points based on project maturity to optimize funding efficiency
  - Prioritizes transformative therapies aligned with regulatory and clinical translation pathways
  - Embeds commercialization and patient access planning to enhance long-term sustainability and impact

Portfolio Considerations: Analysis indicates that many promising early-stage therapeutic candidates face funding and translational gaps. The PDEV program addresses these gaps by providing milestone-driven support to accelerate readiness for clinical trials.

3. Clinical Trial Acceleration Program (CLIN2) (Updated Concept)

- Expands support for:
  - Innovative clinical trial designs, including adaptive, basket, and seamless Phase 2/3 approaches
  - Data-sharing requirements to improve transparency and regulatory alignment
  - Patient access planning, ensuring equity in enrollment and affordability considerations
- Introduces structured co-funding and commercialization planning requirements for late-stage trials to ensure sustainability beyond CIRM funding
- Expands eligibility for pivotal trials and regulatory designations (e.g., RMAT, Breakthrough, Fast Track) to ensure that therapies advance efficiently toward approval and patient access

Portfolio Considerations: CLIN2 remains CIRM's primary tool for advancing cell and gene therapies to pivotal trials. However, limitations in trial design flexibility and commercialization strategy have been identified as barriers to progression to approval. These refinements directly address those challenges.

II. Next Steps and Request for Board Approval

Requested Action: We seek approval from the ICOC to launch these funding initiatives as part of SAF Phase 1 implementation. The proposed allocations and award structure are as follows:

Program	Proposed Budget	Expected Awards
DISC4	$84M	6 awards
DISC5	$50M	15-20 awards
PDEV	$160M	12-21 awards
CLIN2	$135M	9-16 awards

These programs have been designed to ensure a balanced and strategic investment across the discovery, preclinical, and clinical development pipeline. The preference-setting process (**Exhibit A)** will guide the implementation of programmatic priorities, ensuring alignment with CIRM's impact goals and Proposition 14 mandates.

We look forward to your feedback and approval to move forward with these critical initiatives.

Attachments:

- Exhibit A - Funding Area Preferences: Fiscal Year 25/26

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EXHIBIT A

Funding Area Preferences: Fiscal Year 25/26

Preference-setting Process

The Strategic Allocation Framework (SAF), approved by the ICOC on September 26, 2024, established a structured approach for prioritizing CIRM's resource allocations. As part of this framework, CIRM has implemented a systematic preference-setting process to ensure funding priorities remain dynamic, data-driven, and responsive to both emerging scientific opportunities and portfolio needs.

This process builds upon the work of the Neuro Task Force (NTF), which served as the foundation for structured decision-making in neuroscience investments under Proposition 14. By leveraging annual portfolio reviews and landscape analyses, CIRM aligns its funding strategies with cutting-edge advancements, regulatory trends, and critical gaps in cell and gene therapy (CGT). This ensures that CIRM's investments continue to drive therapeutic innovation, accelerate development pathways, and address unmet medical needs for Californians.

To achieve these objectives, CIRM will conduct an annual portfolio review and preference-setting process, occurring near the end of each fiscal year. This structured process will include:

- A comprehensive report from CIRM staff to the Science Subcommittee and ICOC, providing an overview of portfolio trends, programmatic progress, and key award outcomes in the broader context of the regenerative medicine landscape.
- Refinement of funding area preferences based on portfolio analysis, ensuring alignment with scientific and clinical advancements.
- ICOC review and approval of proposed preference adjustments, which will then be incorporated into Program Announcements (PAs) for the relevant funding cycles in the upcoming fiscal year.

The goal of this process is to ensure that preferences are continuously optimized to maximize impact in regenerative medicine and align with the SAF's long-term strategic vision.

Fiscal Year 2025/2026 Preference Setting

DISC4 Preferences

DISC4 Awards are open to all applications that fulfill the eligibility requirements detailed in the DISC4 concept document, without restrictions in research topics or disease indications.

To align with CIRM's Proposition 14 mandate, optimize synergy across teams, leverage external partnerships, and remain responsive to an evolving research landscape, funding areas will be selected on an annual basis. These preferences will be approved by the ICOC based on recommendations from CIRM staff and implemented through the pre-submission process. CIRM recommends that, for FY 25/26, preference be given to applications addressing neurodegenerative diseases.

PDEV Preferences

The PDEV Program aims to enrich the clinical pipeline with innovative stem cell-based and genetic therapies that have the potential for transformative clinical impact, and which address barriers to access and affordability. This goal will be achieved through preferences for certain modalities that show strong potential to achieve these goals. CIRM recommends that, for FY 25/26, preference be given to applications to the PDEV program that:

- Propose the development of a pluripotent stem cell (PSC)-derived cell therapy
- Propose the development of an in vivo genetic therapy
- Propose the development of a therapy using non-viral nucleic acid delivery
- Propose a therapy to treat a disease of the brain and/or central nervous system as defined in Proposition 14
- Are CIRM "pipeline" programs progressing from existing CIRM DISC2 and TRAN1 awards
- Have conducted an FDA INTERACT or Pre-IND meeting

CLIN2 Preferences

The CLIN2 Program aims to advance clinical candidates that have the potential for transformative patient impact and that address barriers to access and affordability. This goal will be achieved through preferences for certain modalities and project features that show strong potential to achieve these goals. CIRM recommends that, for FY 25/26, preference be given to applications to the CLIN2 program that:

- Propose the development of a pluripotent stem cell (PSC)-derived cell therapy
- Propose the development of an in vivo genetic therapy
- Propose the development of a therapy using non-viral nucleic acid delivery
- Propose a therapy to treat a disease of the brain and/or central nervous system, as defined in Proposition 14
- Come from a California organization
- Are CIRM “pipeline” programs progressing from existing CIRM IND-enabling stage award or earlier phase clinical trial award
- Have received a Regenerative Medicine Advanced Therapy (RMAT) or Breakthrough designation from the FDA
- Propose a registrational clinical trial