Real Life™

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CIRM
CALIFORNIA'S STEM CELL AGENCY

Our Mission

OUR MISSION

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

Proposed DISC0 and DISC2 Concept Amendments

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DISCOVERY Pillar Programs

Foundational Knowledge → Single Product Candidate → Pre-IND Meeting or Equivalent → Approved Therapy

DISC0 FOUNDATION AWARDS

DISC2 QUEST AWARDS

TRAN1/2/3/4 AWARDS

CLIN1/2 AWARDS

DISC4 ReMIND AWARDS

Main Changes to DISC2 Concept

1. Award Tracks
2. Award Budgets

DISC2 Awards: Changes in Track

Current Tracks	Proposed Tracks
• Therapeutic Candidate • Diagnostic/Tool/Device Candidates	• Therapeutic Candidate • Biomarker Candidate

Rationale

- Tool/Device development and proof of concept is already supported by DISC0 mechanism
- Biomarker track: Includes Diagnostic + Expands scope to high unmet need in Tx Dev of Regenerative Medicine treatments (and CNS diseases)

DISC2 Awards: Changes in Budget

Current Budget *	Proposed Budget *
• Therapeutic **$1.5M**, 3yr	• Therapeutic **$1.75M**, 3yr • Biomarker **$1.5M** 3yr

* Direct project costs for entire award

Rationale

- Increased award accounts for higher costs of trainees/research
- $200K special supplement expanded to all therapeutic applications via higher base budget
- Budget and duration for biomarker track comparable to similar awards

Main Changes to DISC0 Concept

1. Award Tracks
2. Award Budgets
3. PI Percent Effort

DISC0 Awards: Changes in Track

Current Track *	Proposed Track *
• Single PI	• Single PI • **PI + 1-2 Co-I (Team)**

Rationale

- Team track will support synergistic, multidisciplinary collaborations with larger scope
- Teams drive innovation, creativity, and risk-taking with the support of a group

DISC0 Awards: Changes in Budget

Current Budget *	Proposed Budget *
• Single PI **$1.0M**, 3yr	• Single PI **$1.5M** , 3yr (0.5M/year) • Team (2-3) PIs **$3.0M**, 3yr (1M/year)

Rationale

- Budget increased to account for higher costs of trainees/research
- Budget and duration in line with similar awards for Team Track

DISC0 Awards: Changes in Percent Effort

Current % Effort	Proposed % Effort *
Single PI Track • PI – **20%**	Single PI Track • PI – **15%** Team Track • PI – **15%** • Co-Is – **10%**

Rationale

- Board feedback/alignment with other funding bodies

Requested Action

CIRM requests ICOC approval of these amendments

Proposed CLIN Concept Amendments and CLIN4 Concept Proposal

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CIRM
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Proposed CLIN Concept Changes

What is CIRM recommending?

1. Remove clinical track for medical devices

2. Increase maximum award amounts for CLIN1

3. Update CLIN2 PA to **highlight** specific allowable activities for product development

4. Introduce new CLIN4 PA to fund **Late-Stage Development activities** necessary to file a BLA and readiness for product launch

Clinical Programs Awards Overview

	Aim / Scope	Eligibility	Duration
CLIN 1	IND Enabling	Pre-IND Meeting / Start in 45 Days	24 Months*
CLIN 2	Clinical Trial	Active IND / Start in 45 Days	48 Months
CLIN 4	BLA Enabling	Active CLIN2 /End Of Phase 2 mtg	48 Months

* Up to 6 months additional for start-up activities

CLIN1 Awards: Changes in Award Amount

Maximum total CIRM award amount

Current Budget	Proposed Budget
• Non-profits, **$6 M** • For-profits, **$4 M**	• Non-profits, **$7.5 M** • For-profits, **$5 M**

Rationale

- Increased award amounts accounts for toxicology studies, manufacturing, and higher workers wages costs
- Duration for CLIN 1 remains at 24 months

Recommended CLIN2 Concept Changes

Why are changes needed?

- When CLIN2 was implemented, most CIRM-funded trials were in **Early-stage** Clinical Development
  - Phase 1 or Phase 2
- As the field has matured, more programs are entering **Late-stage** Development
  - Phase 3 or Pivotal/registration trial stage directly from phase1/2 dependent on the disease indication
- The current CLIN2 Program Announcement is not clear or explicit about the support of specific late-stage development activities
- To Ensure Best Practices Alignment with the FDA

Clarification of Eligible Activities in CLIN2

Activities that qualify for funding under CLIN2:

- Compilation of **alternative comparator data** acceptable to FDA for a marketing approval decision and intended to support the proposed interventional clinical trial in cases where placebo or sham controls are not possible.
  - Examples include **Natural History studies** or use of existing **data repositories**
  - Must have documented FDA agreement on the acceptability of the proposed comparator

- Compilation of **Patient-Reported Outcomes** (PRO) related to the conduct of the proposed trial

- Compilation of **Real -World Data** (RWD) and **Real- World Evidence** (RWE) related to the conduct of the proposed trial

- Activities that support **DEI** goals described in the proposal

‘New’ CLIN4 Concept Plan

What is the purpose of a CLIN4?

- Certain key activities required by FDA to get to **Biologics License Application** (BLA) filing and readiness for product Launch are not covered by the current CLIN2 PA
- The goal of a CLIN4 is to support CIRM-funded programs to achieve a **BLA filing** and advancement towards the goal of obtaining marketing approval
- Logical bridge to AAWG; demonstrating CIRM’s commitment to Access & Affordability

‘New’ CLIN4 Concept Plan

Who is ‘new’ CLIN4 for?

Eligibility Criteria:

- Must have an **active CLIN2 award**
- Must have completed 50% of milestones of an active CLIN2 award
- Must have completed an **End-Of-Phase 2** meeting **or equivalent** with FDA and have **concurrence** on requirements for a BLA filing

What will ‘new’ CLIN4 provide?

- Up to **$12M** to cover **Late-Stage Development activities** necessary for BLA filing but not included in the CLIN2 award

‘New’ CLIN4 Concept Plan

Late-Stage Development Activities that may be Funded under CLIN4:

- Activities necessary for **filing a BLA** such as:
  - conduct of a Pre-BLA meeting with FDA
  - compilation of an electronic common technical document (eCTD)
- **Product manufacturing** activities necessary to submit a BLA
- **Commercial development** activities such as pharmacoeconomic analysis, budget impact models (managed health-payer perspective)
- Development of a **supply chain** strategy
- Initiation of **pre-commercialization activities** such as production of a Payors’ cost-effectiveness Analysis Report, compilation of an AMCP Dossier
- **Compassionate use** of the investigational therapy for patients in the period after enrollment closed and Market Approval is awarded with FDA approval and agreement with the drug product supplier

Clinical Programs Awards Overview

	Aim / Scope	Eligibility	Duration	$$
CLIN 1	IND Enabling	Pre-IND Meeting / Start in 45 Days	24 Months*	6M to 7.5M** 4M to 5M
CLIN 2	Clinical Trial	Active IND / Start in 45 Days	48 Months	15M
CLIN 4	BLA Enabling	Active CLIN2 /End of Phase 2 Mtg	48 Months	12M

- Up to 6 months additional for start-up activities

** $7.5M for Non- profit; $5M for Profit

Requested Action

CIRM requests ICOC approval of these amendments and the CLIN4 concept plan