CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

# Memorandum

**To:** Members of the ICOC
**From:** Rosa Canet-Avilés, Chief Science Officer
**Re:** Revisions to CLIN2 Presentation
**Date:** March 27, 2025

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Please be advised of the following revisions to the CLIN2 Concept Presentation:

- Former slide 77, summarizing CLIN2 Concept design, has been removed for brevity.
- "*In vivo*" was italicized and "Breakthrough" was capitalized on slide 79.
- The definition of "Subsequent Trials" was added to slide 83 and footnote references were revised.
- The description of eligible candidates was revised on slide 84 to include all stem cell-based and genetic therapies.
- The co-funding requirements on slide 84 were revised to align with the Concept Plan and remove co-funding requirements for non-profit applicants at Phase 2 or subsequent trial phases.

# CLIN2 Funding Opportunity: Concept Overview

March 27, 2025

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# CLIN2 I Outline

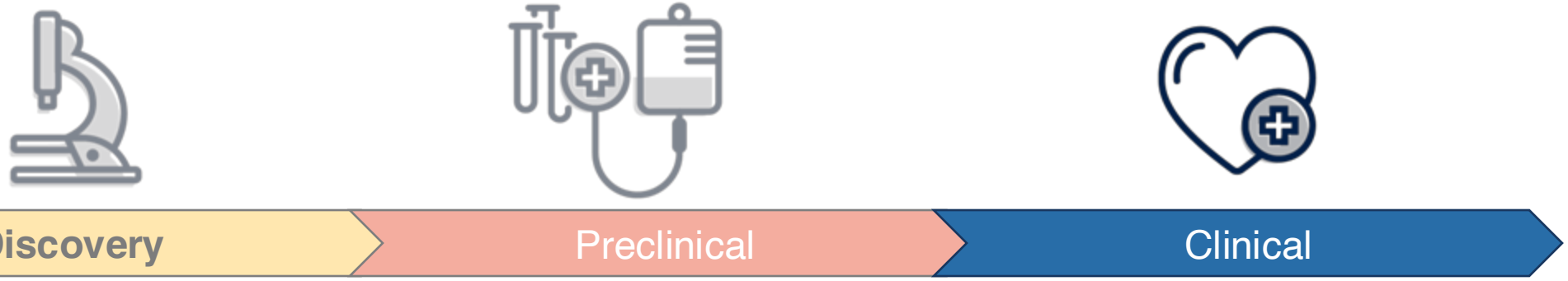
1. Background
2. Objective
3. Scope
4. Structure
5. Timeline
6. Request for Motion

# Goal 4 I Recommendations (CLIN2)

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

## Update CLIN2

- Allow for support of emerging **novel clinical trial designs** in CLIN2 program
- Incentivize stage-appropriate **market access strategy** development and **pre-commercialization** activities in CLIN2 program
- Incorporate **prioritization of innovative therapies for diseases that affect Californians**




* “late-stage trials” are Ph2 or beyond

# CIRM Clinical Programs: Challenges and Opportunities

## CIRM clinical trial award challenges

- Delays
- Lack of advancement to next phase
- Lack of partnerships
- Lack of emphasis on commercialization planning

## Landscape analysis conclusions

- ~50% of marketed CGTs originating in academia or emerging biopharma are launched by a larger company*

➢ CIRM's programs must depend on partnering for BLA/commercialization

**Opportunity:** Enhance success of CLIN2 programs with earlier development of clinical and manufacturing strategies, a market access strategy, & stage-appropriate pre-commercialization activities

* Emerging biopharma is defined as <$200M in R&D spend and <$500M in annual sales

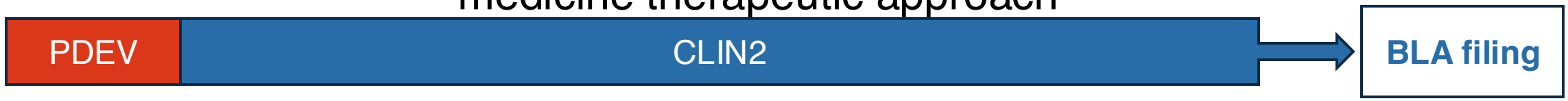
Source: IQVIA Institute for Human Data Science. Strengthening Pathways for Cell and Gene Therapies: Current State and Future Scenarios. March 2024

# CLIN2 I Objective

Accelerate clinical development of **stem cell-based and genetic therapies** to late-stage trials by encouraging innovative clinical trial designs and incentivizing stage-appropriate market access strategies and pre-commercialization activities

# CLIN2 I Scope

Phase 1, 2, or 3 clinical trials, including registrational trials, using a regenerative medicine therapeutic approach




## Required activities

- Clinical trial completion including those with accelerating trial designs
- Establishment and regular convening of a Strategic Planning Committee (SPC)
- Data sharing
- Outreach and inclusion activities
- Stage-appropriate commercialization and access and affordability activities

## Allowable activities

1. Natural history studies (FDA-approved) needed for baseline or control data
2. Manufacturing for next phase trial:
   Activity gated based on:
   a) Evaluation of current trial data, and
   b) Ability of awardee or partner to provide 50% co-funding

# Recall I SAF Recommendations (CLIN2)

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

## Update CLIN2

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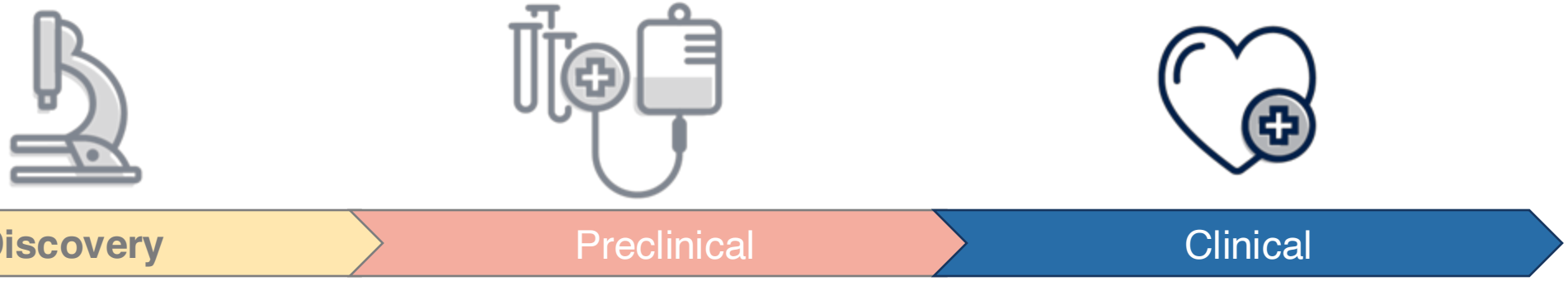


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# CLIN2 | Prioritizing to achieve SAF Goal

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

To achieve the SAF goal, the CLIN2 Program will incorporate program preferences

## Guiding Principles:

- Fund therapies that
  - Offer potential for transformative clinical impact
  - Address bottlenecks to access and affordability
  - Are not adequately supported by federal funding or private investment

## Implementation Plan:

- Build a diverse portfolio of therapeutic approaches
- Priorities informed by internal portfolio and external landscape analyses
- Approved on a fiscal year basis by the ICOC

# CLIN2 I Preferences for FY25/26

Preferences will be factored in during Qualification and ARS review

| Concept Preferences | Rationale |
|---|---|
| Pluripotent stem cell-derived therapies | • Propositions 71 and 14<br>• Potential to address patient access & affordability barriers |
| *In vivo* genetic therapies | • Potential to address patient access & affordability barriers |
| Non-viral nucleic acid delivery | • Potential to address patient access & affordability barriers |
| Diseases of the brain and CNS (Prop 14) | • Proposition 14 priority |
| CA organizations | • CA taxpayer-funded initiative |
| Progressions from IND-enabling or pipeline trial awards | • Advance CIRM-funded therapies |
| Fast Track, RMAT, or Breakthrough designations | • Leverage greater FDA access |
| Pivotal trials | • Fastest route to BLA |

# CLIN2 | Application & Review

## CLIN2 will incorporate a pre-review process to:

- Exclude ineligible applications
- Assess application completeness (verifying patient access and commercialization requirements are addressed)
- Prioritize applications using objective program preferences
- Manage high application volumes

# CLIN2 I Qualification Process Workflow

**1 Submission**

Applicant completes application in GMS (estimate ~10 per cycle)

**2 CIRM Qualification**

CIRM rank orders applications based on preferences and related objective criteria

**3 Full Review**

CIRM moves selected applicants to full review

# CLIN2 I Qualification Rubric

| Criteria | | Key Considerations |
|---|---|---|
| 1 | **Prop 14 Preferences** | • PSC-derived therapies, in vivo gene therapies, diseases of the brain and CNS |
| 2 | **Other Preferences** | • Non-Viral Nucleic Acid Delivery<br>• Progression from Pipeline Program<br>• CA organization<br>• Fast Track, RMAT, or Breakthrough Designation<br>• Pivotal Trial |
| 3 | **Novelty of therapeutic approach** | • Differentiation compared to CIRM active awards portfolio |
| 4 | **Under-represented therapeutic/disease area** | • Targeting a therapeutic/disease area under-represented in CIRM active awards portfolio |

# CLIN2 | Structure

| | CLIN2 | | |
|---|---|---|---|
| | **First-in-Human** | **Phase 2 or subsequent*** | **Phase 3 or pivotal** |
| **Recurrence** | 4x per year | | |
| **Max Duration** | 4 years | | |
| **Applicant** | California or non-California organizations | | |
| **Co-funding**** | 30% (for-profit)<br>None (non-profit) | 50% (for-profit)<br>None (non-profit) | 50% |
| **Max Award (Total Cost)** | $8M (for-profit)<br>$12M (non-profit) | $15M | $15M |
| **Awards/Year** | 9-16*** | | |
| **Projection** | 9 x $15M = $135M | | |
| **Total Funds/Year** | $135M | | |

* Subsequent trials are Ph1 trials following a First-in-Human trial with the same candidate, disease indication and route of administration
** Co-funding is a percentage of total Allowable Project Costs
*** Number of awards is dependent on how many at each stage and organization status. Avg. CLIN2/year 2022-2024 = 13

# CLIN2 I Eligibility

| | Eligibility Requirements |
|---|---|
| **Applicant** | • California and non-California organizations |
| **Eligible Candidates** | • Stem cell-based therapies and genetic therapies |
| **Candidate Readiness** | • New program to CIRM: IND cleared by FDA before CLIN2 application<br>• CIRM pipeline program*: IND filed before CLIN2 application and cleared by FDA before moving to GWG review |
| **Expected Outcome** | • Completion of a clinical trial and program prepared to advance to next stage |
| **Award Start** | • Must be ready to start within 60 days of award approval |
| **PI/PM Effort** | • PI – 15% average maintained through duration of award<br>• PM – 50% average maintained through duration of award |
| **Co-Funding**** | • FIH: 30% (For-profit only)<br>• Ph2 or Ph1 subsequent to FIH: 50% (For-profit only)<br>• Ph3: 50% For-profit or Non-profit |

* Pipeline program: progressing from an IND-enabling stage or earlier phase clinical trial CIRM award
** Co-funding is a percentage of total allowable project costs

# CLIN2 I Access & Data Sharing Requirements

## Access and Affordability

- Require patient access and affordability planning

## Clinical Data Sharing

- Require a Data Sharing and Management Plan and coordination with CIRM's data sharing initiatives

# CLIN2 I Proactive Award Management

## Proactive Award Management

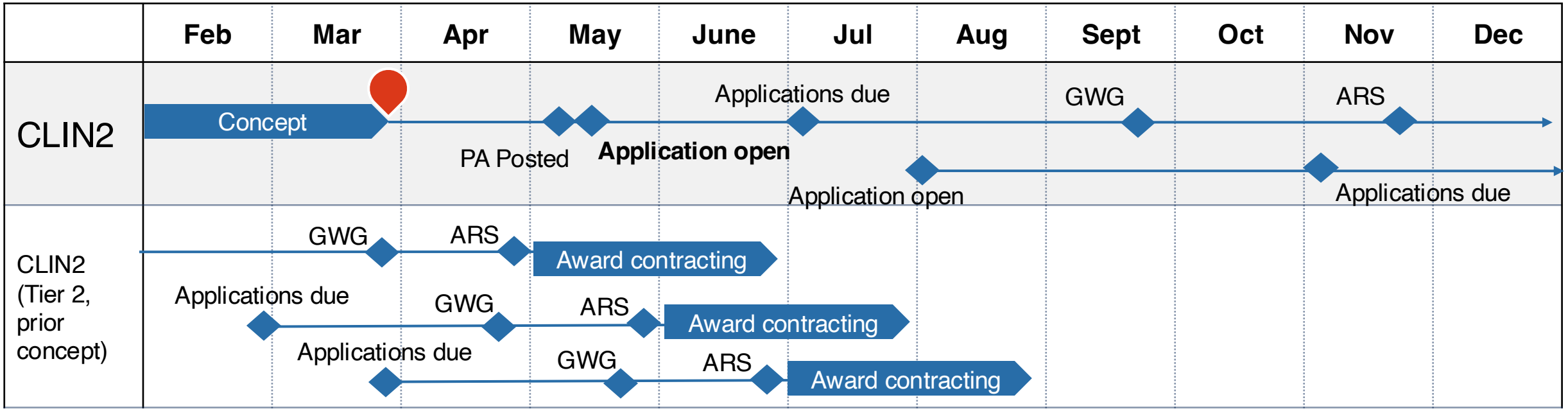
- Quarterly scientific progress reports and follow-up calls with CIRM
- Inclusion of CIRM in FDA meetings
- Inclusion of CIRM in Strategic Planning Committee meetings

## Performance Driven Milestone Structure

- Operational milestone (OM)-driven awards
- Contingency funding required if CIRM funding tranche is exhausted
- OM delay of more than 4 months triggers evaluation, with right to terminate award

# CLIN2 | Timeline

## Application to award start ~ 8 months
## First cycle awards start in February 2026



# Request for Motion

CIRM requests that the ICOC approve the proposed CLIN2 Concept Plan