CLIN2 Funding Opportunity: Concept Overview

February 2025

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

CLIN2 I Outline

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

Goal 4 | 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

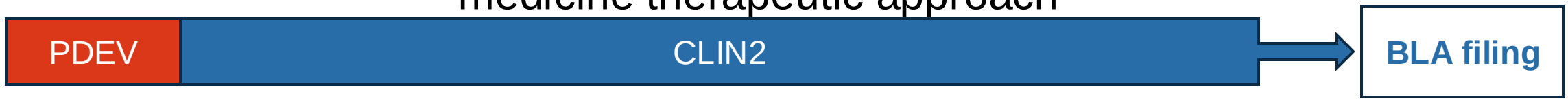
Accelerate clinical development of **stem cell-based and genetic therapies** to late-stage trials by encouraging innovative clinical trial designs, incentivizing stage-appropriate market access strategies and pre-commercialization activities

CLIN2 | Scope

Objective	Accelerate clinical development of stem cell-based and genetic therapies to late-stage trials (Ph2 or later)
Prioritization	Enrich clinical pipeline with innovative CGT that have potential for transformative clinical impact and address barriers to access and commercialization
Outcome	The expected outcome of all CLIN2 awards is completion of a clinical trial for the CGT candidate
Allowable Activities	All necessary activities to complete a Ph1, 2 or 3 clinical trial, including manufacturing for the trial, regulatory interactions, developing a market access strategy and conducting pre-commercialization activities

CLIN2 | 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 | SAF Recommendations (CLIN2)

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

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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 | Preferences for FY25/26

Goal: Accelerate progression of CGT therapies to late-stage clinical trials

Concept Preferences	Rationale
Pluripotent stem cell-derived therapies	• Propositions 71 and 14 • 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
RMAT or breakthrough designations	• Leverage greater FDA access
Pivotal trials	• Fastest route to BLA

CLIN2 | Structure

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

*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 | Eligibility

	Eligibility Requirements
Applicant	• California and non-California organizations
Eligible Candidates	• Stem cell-based cell therapies and genetic therapies • MSCs, small molecule and biologic therapies if a pipeline program*
Candidate Readiness	• New program to CIRM: IND cleared by FDA before CLIN2 application • 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 • PM – 50% average maintained through duration of award
Co-Funding**	• Ph1: 30% For-Profit only; Ph2 or 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 | Application and 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 will adopt a 1-100 numerical GWG scoring system to:

- Align across CIRM programs
- Improve granularity and visibility for score driving decisions

CLIN2 I Access and 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

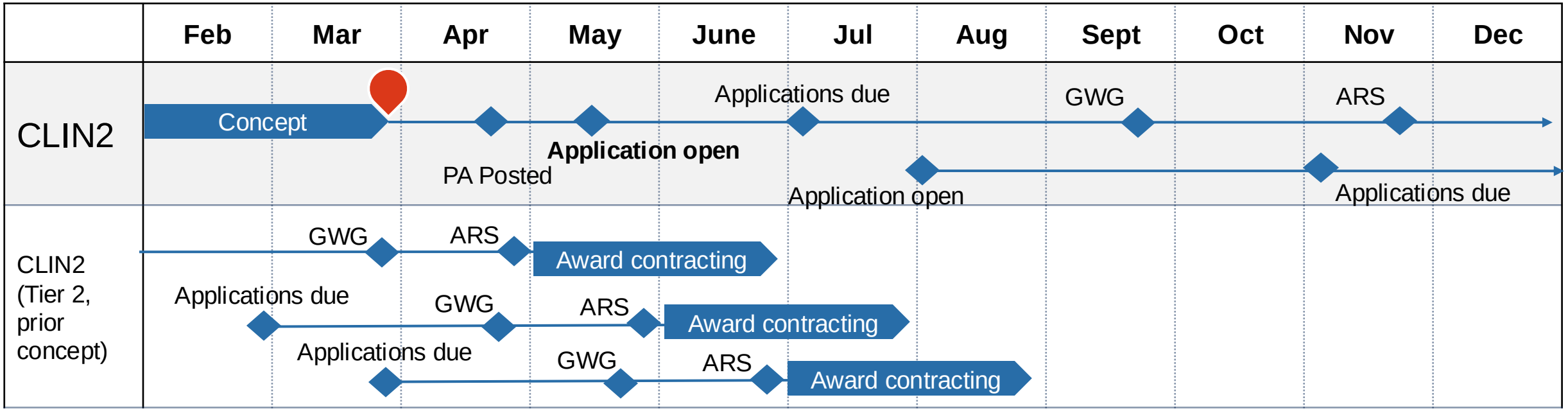
- Quarterly scientific progress reports and follow-up calls with CIRM
- Inclusion of CIRM in FDA meetings
- Inclusion of CIRM in Strategic Planning Committee meetings

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



CLIN2: Formal Request for Funding

CIRM requests that the ICOC approve the proposed CLIN2 Program Concept, with an initial allocation of **$135M for FY25/26**