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CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Early Development (EDEV) Concept

Concept Overview for Science Subcommittee

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Our Mission

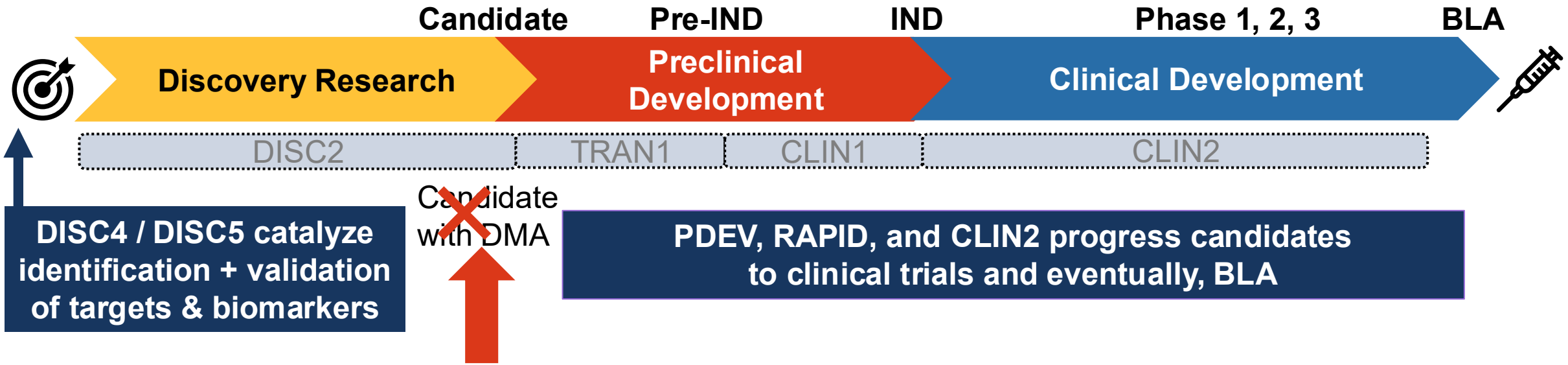
To accelerate world-class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and the world

Concept Outline

1. Background: Problem Statement & Rationale
2. Objective & Expected Outcome
3. Guiding Principles
4. High-Level Scope & Structure
5. Eligibility
6. Application & Review
7. Timeline & Request for Motion

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EDEV | Supporting Critical Transitions through CIRM's Pipeline



No CIRM programs support candidate discovery

EDEV will bridge **targets to candidates** and **position them** for rapid and **successful progression**

DMA = Disease Modifying Activity

How Can CIRM Address This Gap and De-risk Projects Earlier?

Proposed Solution

- Leverage **successes and lessons from CIRM's history with** candidate discovery funding
- Develop a program that will rapidly and efficiently transition a **validated disease target to a translatable, therapeutic candidate**
- Incorporate **product value drivers** to better anticipate risk and inform design strategies for future success

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DISC2 to EDEV: SAF Alignment and Expediency

Approach: Adapt DISC2 mechanism to EDEV by focusing scope and accelerating integration into preclinical and clinical pipelines through novel support mechanisms.

	DISC2	EDEV	Rationale
Scope	Therapeutics, biomarkers, devices, diagnostics, tools	Therapeutics only	SAF priorities, CIRM runway
Outcome	Single candidate	Single candidate	No change
Duration	1, 2, or 3 years to deliverable	2 years to deliverable	Focus on critical path; best suited for value planning
Critical Roles	Principal Investigator	Principal Investigator Project Manager	Support maintained focus on critical path
Value Add	Proactive award management	Proactive award management with product value planning	Improved derisking for future investment; increased probability of success

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EDEV | Objective and Expected Outcome

Objective:

To accelerate the progression of stem cell-based and genetic therapy[1] candidates and ready them for transition into preclinical development

Expected Outcome:

A translatable lead therapeutic candidate with reproducible disease-modifying activity, and a progression plan that includes refined product value drivers

1. CIRM's definition of genetic therapy: a human therapeutic intervention that: 1) alters the genomic sequence of cells or 2) introduces or directly manipulates nucleic acids (such as mRNAs, antisense oligonucleotides) in cells

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EDEV | Guiding Principles

Guiding the overall EDEV portfolio

1. Have potential to deliver transformative improvements in patient outcomes, through candidates that are differentiated from existing approaches and have a credible development path
2. Anticipate barriers to patient access to stem cell-based and genetic therapies and account for them early in product design
3. Broadly address both prevalent and rare diseases affecting Californians

Reminder that guiding principles are used to inform: 1) **GWG selection**, 2) **Review criteria**, and 3) **Program recommendations**

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EDEV | Scope

EDEV	
Scope	✓ Applicants may request funds to support all activities needed to achieve expected outcome ✓ To maximize the impact of EDEV projects, CIRM requires that applicant teams appropriately manage, preserve, and share data and knowledge generated over the course of an EDEV award
Out of Scope	X Preclinical and clinical development activities that are targeted by CIRM's later stage programs including PDEV, RAPID, CLIN2 X Exploratory research to identify new therapeutic or disease targets

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EDEV | High-Level Eligibility

	EDEV
Applicant	Must meet CIRM's definition of a California Organization
Critical Role & Minimum Effort	Principal Investigator (20%); Project Manager (25%)
Key Personnel with Required Expertise	Data Project Manager

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EDEV | Project Eligibility and Readiness

To be eligible for consideration

- The applicant must propose a project that is in scope and designed to culminate in the expected outcome, which is to accelerate the progression of stem cell-based and genetic therapy[1] candidates and ready them for transition to preclinical development

- The application must demonstrate readiness by meeting the below criteria:
  - Human genetic, cellular or patient-derived data support the relevance of the therapeutic target to the disease; AND
  - Modulating the target affects a disease-relevant cellular or biological process in an experimental model

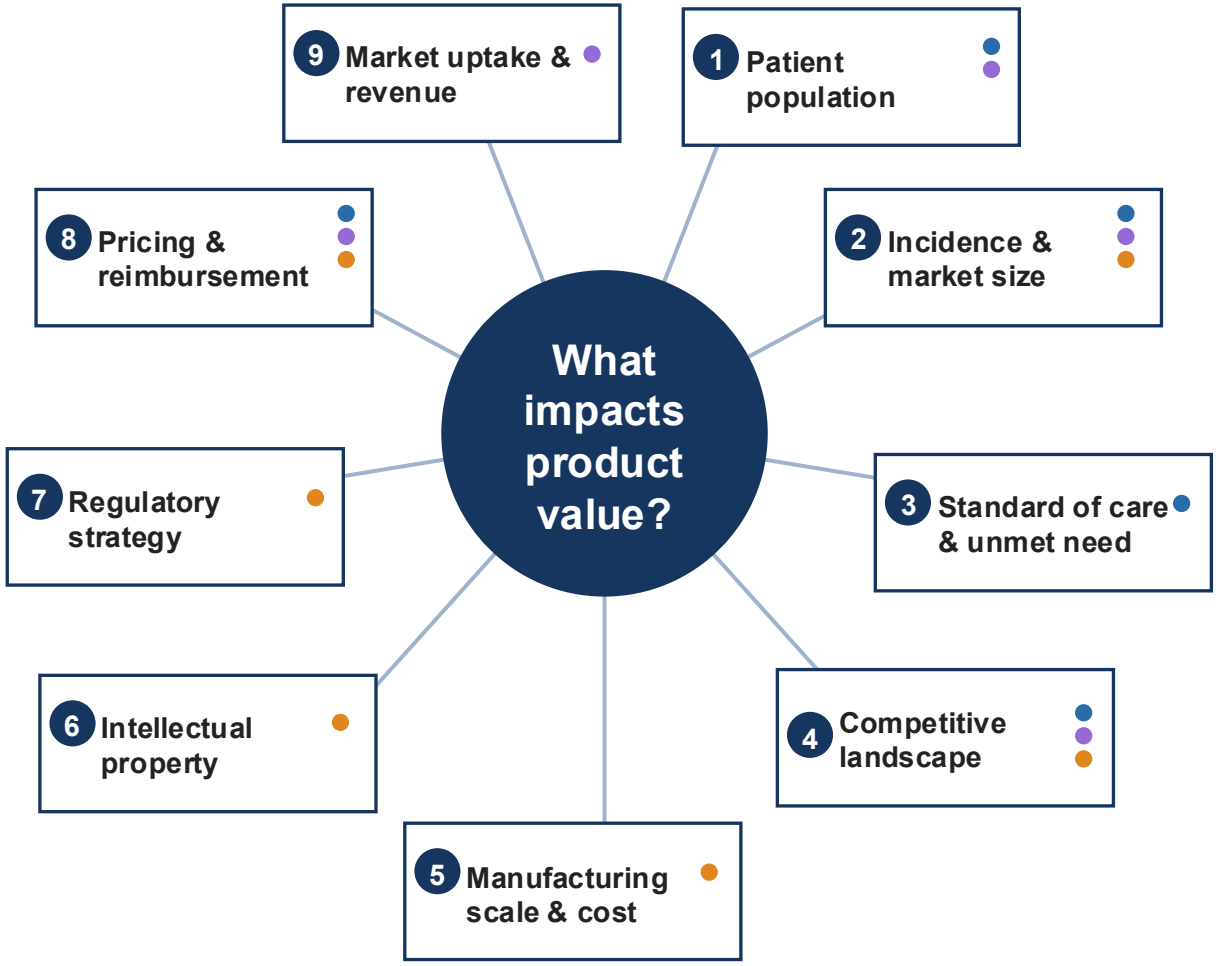
For cell replacement approaches, the target is the cell or function that the product is intended to restore.

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Early Planning of Product Value Helps to Drive Later Investments

Extend product value drivers required in PDEV & CLIN2 back into EDEV



Existing components in PDEV/RAPID/CLIN2 application



Each value driver corresponds to at least one section in the current PDEV and CLIN2 application

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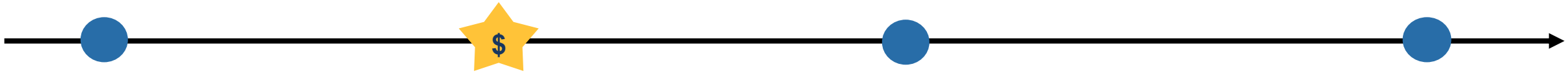
Stage-Appropriate Product Value Planning Feeds into PDEV

Value driver	EDEV entry at application *(basic info; prepared by applicant)*	EDEV exit in final deliverable* *(refined and expanded; with support of consultant)*
1 Patient population	✓	✓
2 Incidence & market size	✓	✓
3 Standard of care & unmet need	✓	✓
4 Competitive landscape	✓	✓
5 Manufacturing scale & cost	—	✓
6 Intellectual property	—	✓
7 Regulatory strategy	—	✓
8 Pricing & reimbursement	N/A — *begins in PDEV*	N/A — *begins in PDEV*
9 Market uptake & revenue	N/A — *begins in CLIN2*	N/A— *begins in CLIN2*

Value drivers 1 – 4 drafted at application, refined by end of award, along with other drivers that become the **starting point for the PDEV (or RAPID) application**

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Funds for Consultant Support to Refine Value Drivers



EDEV Application:
Preliminary plan
Applicant prepares value drivers 1–4 from their knowledge of the disease without CIRM funds.

EDEV Start:
50K made available to support value driver planning
To provide awardees with optimal flexibility, CIRM provides $50K in upfront funding for consultant support.

EDEV in Progress:
Gradual expansion and refinement of value drivers
In parallel with identifying a viable therapeutic candidate, awardees use the consulting funds to support the required update of value drivers by EDEV exit.

EDEV Exit:
Comprehensive plan
Awardee submits updated product value drivers as a final deliverable. CIRM release final payments and close award.

CIRM provides $50K at start of award period to provide awardees with maximum flexibility as they refine their product value drivers

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EDEV Award Structure and Budget

	EDEV
Recurrence	Annual, starting FY 27/28
Max Duration	Up to 2 years
Award Amount	Up to $1.85M in total costs
Award Structure	Project Milestones
Awards/Year	13-16
Total Funds/Year	$25M

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EDEV Justification for $1.85M Proposed Budget

- ✓ Benchmarked to most recent DISC2 burn rates using high-end of range
- ✓ Transitioned from direct cost cap to total cost cap
- ✓ Adjusted for 9% CPI[1] (Jan 2024 - August 2026)
- ✓ Added a conditional line item for product value driver activities

EDEV Budget Proposal	$1.85M Total Costs
Total Costs adjusted for CPI and 2-year duration (high-end)	$1.8M
Conditional allowance for value driver consultations	$50K

A $1.85M total costs budget aligns with **standard practice** for new programs and is sufficient to support **projects at the targeted scope**

1. CPI: consumer price index

Application and Review

EDEV will adopt a GWG selection process to:

- Allow GWG to select applications that are most responsive to the funding opportunity and hold the greatest potential for impact
- Allow CIRM pre-planning for improved scientific and technical review

EDEV will adopt a 1-100 numerical GWG scoring system to:

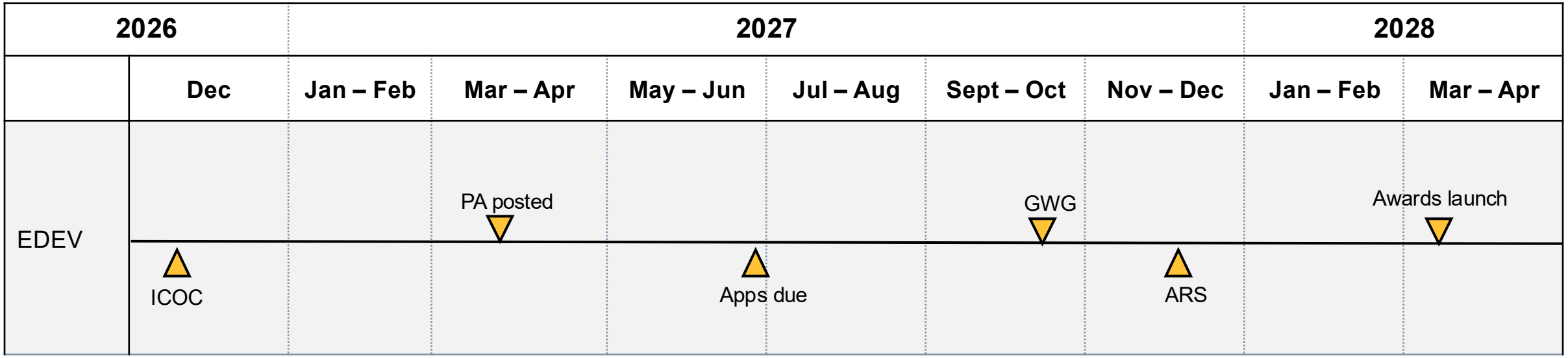
- Align across CIRM programs
- Improve granularity and visibility for score driving decisions

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EDEV First Cycle Timeline

First cycle: FY2027/2028

First cycle of EDEV awards start in March 2028



Request for Motion

CIRM requests the Science Subcommittee endorse the proposed EDEV program concept with an allocation of **$25M** per year