Grants Working Group Recommendations

PDEV Preclinical Awards

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

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Our Mission

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

Strategic Impact Goals

Accelerating Discovery & Translation

Goal 1: Catalyze the identification and validation of at least four novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California

Goal 2: Accelerate the development and utilization of 5-8 technologies that have the potential to improve safety, efficacy, and/or quality of cell and gene therapies

Cell & Gene Therapy Approvals

Goal 3: Advance 4-7 rare disease projects to Biologics License Application (BLA)

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

Accessibility & Affordability of Therapies

Goal 5: Ensure that every BLA-ready program has a strategy for access and affordability

Diverse Workforce Development

Goal 6: Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine

Strategic Impact Goals

Accelerating Discovery & Translation	Cell & Gene Therapy Approvals	Accessibility & Affordability of Therapies	Diverse Workforce Development
Goal 1: Catalyze the identification and validation of at least four novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California	**Goal 3:** Advance 4-7 rare disease projects to Biologics License Application (BLA)	**Goal 5:** Ensure that every BLA-ready program has a strategy for access and affordability	**Goal 6:** Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine
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PDEV

- Accelerate the preclinical development incentivizing multidisciplinary collaborations and rapid progression to IND
- Incorporate **prioritization of innovative therapies for diseases that affect Californians**

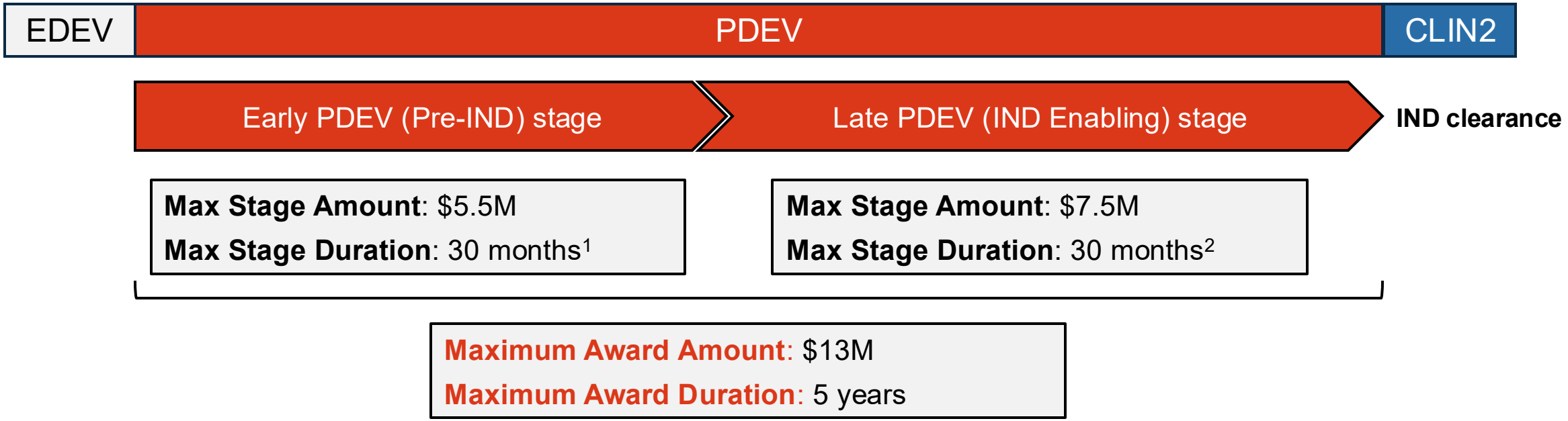
PDEV Program Objective

To accelerate completion of preclinical development, FDA IND clearance, and clinical trial startup for stem cell-based and genetic therapies

PDEV Program Structure

	PDEV (Preclinical Development)
Recurrence	2x per year
Applicant	California organizations only
Co-funding	None (Unpartnered Non-Profit) 20% (Non-profit with For-Profit partner) 20% (For-Profit)
Maximum Award Amount	$13 million
Maximum Award Duration	5 years
Awards/Year	12-21
Projection	7 Early (7x$13M), 9 Late (9x$7.5M)
Total Funds/Year	$160M

PDEV | Award Amount & Duration Vary by Entry Points

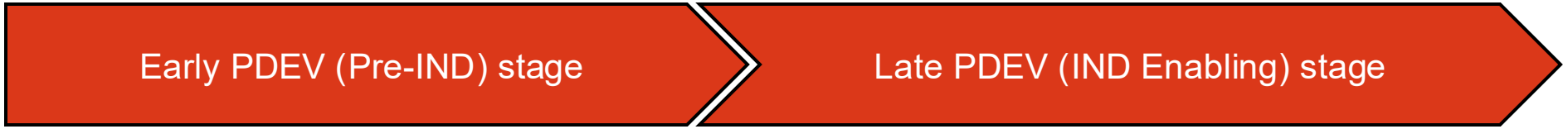


Singular Expected Project Outcome: IND Clearance

[1]Inclusive of optional candidate optimization activity (max 6 months)

[2]Inclusive of optional trial startup activity completion following IND clearance (max 6 months)

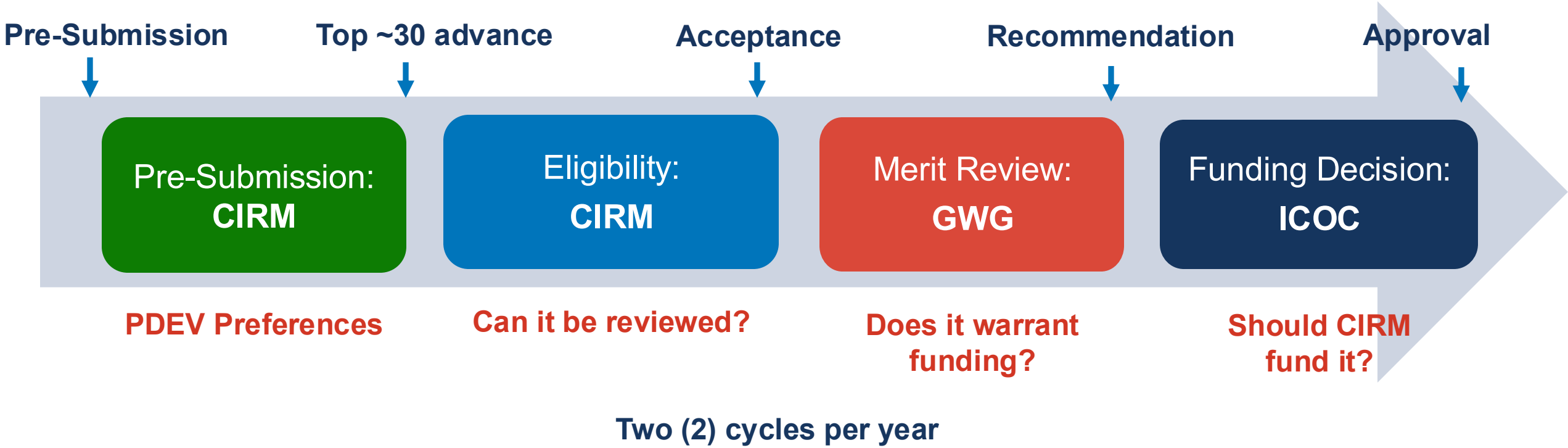
Applicants Requesting Funding for *Both* Early & Late PDEV Activities



CIRM Award Management

- CIRM will review pre-IND strategy and participate in pre-IND meeting
- After pre-IND meeting, CIRM will review alignment of IND-enabling activities with FDA pre-IND feedback and may modify Operational Milestones & Award Disbursements

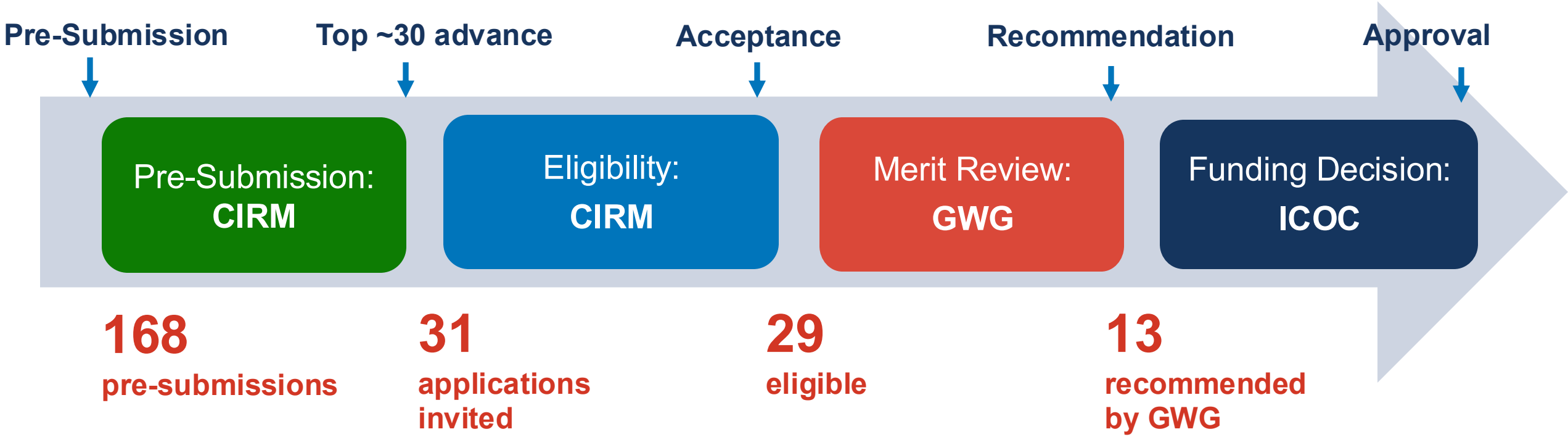
PDEV Application & Review Process



Two (2) cycles per year

GWG – Grants Working Group
ICOC – Independent Citizens' Oversight Committee

PDEV Preclinical Awards: Round 1



PDEV GWG Panel Composition and Roles

Who participates and how they contribute

Scientific GWG Members	Scientific evaluation (disease area expert, regulatory, CMC, product development)
GWG Board Members	Patient perspective on significance and potential impact, oversight on process
Scientific Specialists	Scientific evaluation based on specialized expertise

Scientific Scoring System

Using the 1 to 100 scale

- **Median score of 85-100:** *Exceptional merit and warrants funding, if funds are available.*
- **Median score of 1-84:** *Not recommended for funding.*
- Scoring is holistic and based upon all facets of the expert review.
- GWG are encouraged to make full use of the scoring range to signal their enthusiasm for each project.

PDEV Scientific Review Criteria

1. **Value Proposition** - Evaluate the extent to which the therapy offers a compelling value proposition
2. **Rationale** - Evaluate the scientific rationale for the proposed therapy and the strength of the supporting data
3. **Project Plan and Design** - Evaluate the project's plan and design to achieve an active IND
4. **Project Team and Resources** - Evaluate the expertise and resources that will be deployed to achieve the project deliverables
5. **Population Impact** – Evaluate the extent to which the project considers the potential impact of the proposed therapy across affected populations

Access & Affordability

Ensure that every BLA-ready program has a strategy for access and affordability

- Applicants describe their plans to fulfill Access and Affordability (A&A) requirements
- Access and affordability activities are assessed by GWG. Evaluations may inform scoring of the review criteria
- A&A activities and plans are expected to be forward looking at the PDEV stage, and evaluations can inform funding recommendations, applicant feedback, and award management
- Applicants are expected to conduct market landscape assessment and research, develop reimbursement and market access strategy by award close

GWG + CIRM Team Recommendations

Recommendation	Number of Apps	Total Applicant Request	Funds Available
Recommended for funding Score of 85-100	12	$117,591,750	$160,000,000
Not recommended for funding Score of 1-84	17		

Minority Reports

- Under Prop 14, any application that is not recommended for funding by the GWG, but which had 35% or more members score to fund the application must include a minority report.

- The minority report is included in the review summary and provides a brief synopsis of the opinion of reviewers that scored the application 85 or above.

No PDEV applications qualified for a minority report this cycle.

CIRM Team Recommendations Rationale

PDEV-19139 proposes an autologous lentiviral gene-modified iPSC-derived neural stem cell therapy to address Canavan disease.

- Competitive landscape: There are currently two products in late-stage clinical trials for Canavan disease.
- Delivery: The proposed therapy requires invasive surgery.
- Manufacturing: The proposed therapy requires a long and complex manufacturing process.
- Efficient use of funds: IND clearance has not been achieved despite existing NIH funding for the proposed therapy.