CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the Application Review Subcommittee
From: CIRM Leadership
Re: CIRM Team Recommendations: Preclinical Development (PDEV)
Date: June 25, 2026

Executive Summary

This memo summarizes the CIRM program staff funding recommendations for applications submitted to the Preclinical Development (PDEV) Program for consideration by the Application Review Subcommittee (ARS) on June 25, 2026.

This is the second annual funding cycle for the PDEV Program. Following substantial utilization of the annual PDEV allocation in the first funding cycle, a limited portion of the annual budget remains available for award funding in the current cycle*. Eight applications received a fundable recommendation from the Grants Working Group (GWG), requiring CIRM staff to prioritize among fundable applications based on both GWG merit ranking and programmatic and portfolio considerations.

Among these eight applications, the GWG scores created a clear separation between the top four applications and the remaining fundable applications. CIRM staff reviewed all GWG recommended applications, including the lower-ranked fundable applications, to determine whether any programmatic or portfolio considerations would justify deviating from the GWG rank order. The review found that the top four applications provide strong portfolio diversification across therapeutic areas, technologies, and development approaches. Furthermore, the lower ranked applications did not provide a programmatic or portfolio benefit sufficient to justify advancing them ahead of higher scoring applications.

Accordingly, CIRM Program staff recommends funding the top four GWG recommended applications and does not recommend funding the remaining four fundable applications. This recommendation reflects both the GWG merit ranking and CIRM's programmatic and portfolio assessment. CIRM staff also does not recommend funding the application associated with a minority report.

The Appendix contains detailed application assessments, including portfolio and programmatic considerations where relevant, and the basis for the CIRM funding recommendations.

*Note: The PDEV program structure has subsequently been adjusted to better align future funding availability with anticipated demand.

I. Background

Introduction

The role of CIRM staff during the Application Review Subcommittee (ARS) meetings is to assist the ARS in making well-informed funding decisions by providing programmatic context alongside the outcomes of the Grants Working Group (GWG) recommendations. In developing these recommendations to ARS, CIRM evaluated all applications consistent with the following CIRM funding recommendation framework presented to the ICOC (March 2026):

1. Available program budget
2. GWG score & comments
3. Programmatic factors
4. Prior awardee performance
5. New information available to CIRM after GWG review

Summary of Program Budget Considerations

Available Program Budget (Annual)	$42,408,250
Budget Utilization – GWG Recommended	$89,618,311
Budget Utilization – CIRM Recommended	$40,479,339
Remaining Program Budget	$1,928,911

This second funding cycle of PDEV reflects limited remaining budget after substantial utilization of the annual PDEV allocation in the first funding cycle, In March 2026, the ICOC approved an updated program structure to mitigate this scenario going forward.

II. Proposal

After a review of the 8 GWG Recommended Applications, the CIRM team recommends:

1. To fund the top four applications PDEV-19735, PDEV-19727, PDEV-19742, PDEV-19725
2. To *not* fund applications PDEV-19718, PDEV-19835, PDEV-19729 and PDEV-19780 as there is neither a programmatic nor a portfolio benefit sufficient to justify moving them ahead of higher-scoring applications

Summary of Funding Recommendations

Application	Median Score	Scores to fund	Scores not to fund	CIRM Recommendation
PDEV-19735	91	14	0	Fund
PDEV-19727	90	14	0	Fund
PDEV-19742	90	14	1	Fund
PDEV-19725	87	12	3	Fund
PDEV-19718	85	12	2	Do Not Fund
PDEV-19835	85	12	3	Do Not Fund
PDEV-19729	85	11	4	Do Not Fund
PDEV-19780	85	8	6	Do Not Fund
PDEV-19728	84	6*	8	Do Not Fund

*Application PDEV-19728 includes a minority report.

Appendix: Application Assessments

1. Application number: PDEV-19735

Title: Hypoimmune Stem Cell–Derived Islets: A Next-Generation Cell Therapy Toward a Functional Cure for Type 1 Diabetes

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
91	92	95	90	14	0

CIRM Team Recommendation: Fund

PDEV-19735 proposes an allogeneic gene-modified iPSC-derived pancreatic beta cell therapy to address type 1 diabetes. The CIRM team recommendation is based on GWG scoring, patient access considerations, and that the application proposes a unique therapeutic approach in CIRM's portfolio and in comparison to the external type 1 diabetes landscape.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate could lead to transformative clinic benefit by providing a glucose responsive, insulin secreting, non-immunogeneic living cell-based transplant. • CIRM's active PDEV portfolio contains two awards that address type 1 diabetes, and the active CLIN2 portfolio contains one award that addresses type 1 diabetes. This approach would represent the only allogeneic gene modified cell therapy and also the only one that is PSC-derived in CIRM's portfolio. • Based on GlobalData, the external US-based cell and gene therapy landscape for type 1 diabetes includes 10 late-stage (phase 2 or 3) clinical programs and one approved treatment. PDEV-19735 represents a novel modality compared to these landscape programs.
Patient Access	The proposed therapeutic candidate is an off-the-shelf drug derived from engineered allogeneic-iPSC allowing it to delivered to a larger number of patients than cadaveric islet-based therapies without the requirement for lifelong immunosuppression.

Disease Representation	The application under consideration addresses a prevalent disease currently addressed by three programs in CIRM's active PDEV and CLIN2 portfolio.

2. Application number: PDEV-19727

Title: Regenerating the Acutely Infarcted Heart with iPSC-Ventricular Cardiomyocytes.

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
90	91	95	86	14	0

CIRM Team Recommendation: Fund

PDEV-19727 proposes an allogeneic iPSC-derived cardiomyocyte cell therapy to address heart failure due to acute myocardial infarction with cardiogenic shock. The CIRM team recommendation is based on GWG scoring, patient access considerations, and that the application proposes a unique therapeutic approach in CIRM's portfolio and in comparison to the external acute myocardial infarction landscape.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate could a meet a high unmet need for a heart failure condition with a high mortality rate. • CIRM's active PDEV portfolio contains two awards that address myocardial infarction, and the active CLIN2 portfolio contains one award that addresses downstream consequences of myocardial infarction. • Based on GlobalData, the external US-based cell and gene therapy landscape includes 5 late-stage clinical programs and no approved US treatments addressing myocardial infarction. PDEV-19727 represents a novel modality compared to these landscape programs.
Patient Access	The proposed therapeutic candidate is an off-the-shelf drug derived from allogeneic-iPSC allowing for cost effective manufacturing. Additionally, the PI proposes a reduced immunosuppression regimen increasing the likelihood of patient uptake.
Disease Representation	The application under consideration addresses a specific presentation of a prevalent disease currently addressed by three programs in CIRM's active PDEV and CLIN2 portfolio.

3. Application number: PDEV-19742

Title: Therapeutic Restoration of Immune Function through iPSC-derived Human Thymic Epithelial Cells

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
90	88	92	84	14	1

CIRM Team Recommendation: Fund

PDEV-19742 proposes an allogeneic iPSC-derived thymic epithelial cell therapy to address thymic immune defects in congenital athymia. The CIRM team recommendation is based on GWG scoring, patient access considerations, and that the application proposes a unique therapeutic approach in CIRM's portfolio and in comparison to the external congenital athymia landscape.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate offers a clear advantage over current therapies in terms of safety, efficacy and healthcare burden. • CIRM's active PDEV portfolio contains no awards that address congenital athymia and the active CLIN2 portfolio contains no awards that address congenital athymia. This application would be unique to the CIRM portfolio for this indication. • Based on GlobalData, the external US-based cell and gene therapy landscape for congenital athymia includes one approved US treatment. PDEV-19742 represents a novel modality compared to the current landscape.
Patient Access	The proposed therapeutic candidate is an off-the-shelf drug derived from allogeneic-iPSC allowing for cost effective manufacturing and greater access than the current treatment option.
Disease Representation	The application under consideration addresses an ultra-rare disease currently not addressed in CIRM's active PDEV and CLIN2 portfolio.

4. Application number: PDEV-19725

Title: Stem Cell-Engineered Off-The-Shelf CAR-NKT Cell Therapy for Multiple Sclerosis

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
87	87	90	80	12	3

CIRM Team Recommendation: Fund

PDEV-19725 proposes an allogeneic gene modified HSC-derived CAR-NKT cell therapy to address multiple sclerosis. The CIRM team recommendation is based on GWG scoring, patient access considerations, and that the application proposes a unique therapeutic approach in CIRM's portfolio and in comparison to the external multiple sclerosis landscape.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate offers a clear potential of a functional curative outcome and to reduce healthcare burden. • CIRM's active PDEV portfolio contains no awards that address multiple sclerosis, and the active CLIN2 portfolio contains no awards that address multiple sclerosis. This application would be unique to the CIRM portfolio for this indication. • Based on GlobalData, the external US-based cell and gene therapy landscape for multiple sclerosis includes 11 late-stage clinical programs and no approved treatments. PDEV-19725 represents a novel modality compared to these landscape programs in that no other program uses allogeneic NKT.
Patient Access	The proposed therapeutic candidate is an off-the-shelf drug derived from allogeneic-HSC allowing for cost effective manufacturing.
Disease Representation	The application under consideration addresses a prevalent neurological disease currently not addressed in CIRM's active PDEV and CLIN2 portfolio.

5. Application number: PDEV-19718

Title: A one-time gene therapy for rare and common forms of fibrotic kidney disease.

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	86	90	70	12	2

CIRM Team Recommendation: Do not fund

PDEV-19718 proposes an in vivo gene therapy to address nephrotic syndrome. The CIRM team recommendation is based on the GWG ranked order and that the team found that there is neither a programmatic nor a portfolio benefit sufficient to justify moving this proposal ahead of higher-scoring applications.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate could provide meaningful improvement and clinical outcomes over current treatments. • CIRM's active PDEV portfolio contains no awards that address nephrotic syndrome, and the active CLIN2 portfolio contains no awards that address nephrotic syndrome. This application is unique to the CIRM portfolio for this indication. • Based on GlobalData, there are no US-based clinical cell and gene therapy programs and no approved US treatments addressing nephrotic syndrome.
Patient Access	The proposed therapeutic candidate is an in vivo gene therapy; the costs associated with manufacturing will be high but overall costs for treatment may be lower than current standard of care for the patient population.
Disease Representation	The application under consideration addresses an ultra rare disease currently not addressed in CIRM's active PDEV and CLIN2 portfolio.

6. Application number: PDEV-19835

Title: Allogeneic, Immune-Evasive and Regenerative iPSC-Liver Organoid Therapy for Acute-on-Chronic Liver Failure

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	85	85	80	12	3

CIRM Team Recommendation: Do not fund

PDEV-19835 proposes an allogeneic iPSC-derived liver organoid cell therapy to address acute-on-chronic liver failure. The CIRM team recommendation is based on the GWG ranked order and that the team found that there is neither a programmatic nor a portfolio benefit sufficient to justify moving this proposal ahead of higher-scoring applications.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate could provide meaningful improvement and clinical outcomes due to the lack of availability of the standard of care (organ transplant). • CIRM's active PDEV portfolio contains one award that addresses liver failure, also utilizing iPSC-derived liver cells, and the active CLIN2 portfolio contains no awards that address liver failure. The PDEV portfolio award is still developing a final candidate. • Based on GlobalData, the external US-based cell and gene therapy landscape includes one late-stage clinical programs and no approved treatments addressing liver failure. PDEV-19835 represents a novel modality compared to these landscape programs in that the source of hepatocytes is iPSC.
Patient Access	The proposed therapeutic candidate is an is an off-the-shelf drug derived from allogeneic-HSC which allows for scalability to meet patient demand and potentially reduce ICU length of stay. As a bridge-to-transplant, this candidate would not remove the cost of standard of care (organ transplant) treatment.
Disease Representation	The application under consideration addresses a prevalent disease currently addressed by one program CIRM's active PDEV portfolio.

7. Application number: PDEV-19729

Title: Durable Islet Transplantation to Bridge Gap in Current Type I Diabetes Therapies

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund

85	83	87	70	11	4

CIRM Team Recommendation: Do not fund

PDEV-19729 proposes a combination product comprised of an implanted encapsulation device containing an iPSC-derived beta cell therapy to address type 1 diabetes. The CIRM team recommendation is based on the GWG ranked order and that the team found that there is neither a programmatic nor a portfolio benefit sufficient to justify moving them ahead of higher-scoring applications. Additionally, there is also a higher GWG ranked proposal addressing type 1 diabetes in this funding round.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate could a transformative clinic benefit by providing an iPSC-derived islet replacement in an clinically-tested immune protected implantable device. • CIRM's active PDEV portfolio contains two awards that address type 1 diabetes, and the active CLIN2 portfolio contains 1 award that addresses type 1 diabetes. This approach is novel to the portfolio in that it is an allogeneic PSC-derived cell therapy. • Based on GlobalData, the external US-based cell and gene therapy landscape for type 1 diabetes includes 10 late-stage clinical programs and one approved treatment. PDEV-19729's modality is similar to an external phase 2 program using an encapsulation device with an iPSC-derived beta cell therapy.
Patient Access	The proposed therapeutic candidate is an off-the-shelf drug derived from allogeneic-iPSC allowing it to delivered to a larger number of patients than cadaveric islet-based therapies. Encapsulation of the cells in an immune protected device removes the requirement for the patient of lifelong immunosuppression.
Disease Representation	The application under consideration addresses a prevalent disease currently addressed by three programs in CIRM's active PDEV and CLIN2 portfolio.

8. Application number: PDEV-19780

Title: Escape-Resistant Genetic Therapy for CMV Disease in Transplant Patients and Newborns

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	83	90	80	8	6

CIRM Team Recommendation: Do not fund

PDEV-19780 proposes a cell-free in vivo gene therapy to address sequelae of cytomegalovirus infections in transplant recipients and newborns. The CIRM team recommendation is based on the GWG ranked order and that the team found that there is neither a programmatic nor a portfolio benefit sufficient to justify moving this proposal ahead of higher-scoring applications.

Summary:

Transformative Clinical Impact	• GWG noted that the proposed therapeutic candidate could provide meaningful improvement and clinical outcomes as there are limited treatment options for this indication. • CIRM's active PDEV portfolio contains no awards that address cytomegalovirus infections, and the active CLIN2 portfolio contains no awards that address cytomegalovirus infections. This application is unique to the CIRM portfolio for this indication. • Based on GlobalData, the external US-based cell and gene therapy landscape includes 12 late-stage clinical programs and no approved treatments addressing cytomegalovirus infections. PDEV-19780 represents a novel modality compared to these landscape programs.
Patient Access	The proposed therapeutic candidate is a cell-free gene therapy; the costs of the therapy may be less than currently available options, but the exact reduction was unclear to GWG reviewers.
Disease Representation	The application under consideration addresses specific consequences of a prevalent disease currently not addressed in CIRM's active PDEV and CLIN2 portfolio. While CMV infection is prevalent, the prevalence of the sequelae targeted by this application is unclear.

9. Application number: PDEV-19728

Title: AAV gene therapy for brain metastases

GWG Outcome: Do Not Fund (Minority Report)

Median	Mean	High	Low	Scores to fund	Scores not to fund
84	81	88	60	6*	8

*The GWG summary for this application includes a minority report, issued when the GWG score is between 1-84 points and 35% or more scientific members of the GWG recommended the application for funding.

CIRM Team Recommendation: Do not fund

PDEV-19728 proposes an in vivo gene therapy to address adult brain cancer metastases. The CIRM team recommendation is based on the GWG ranked order and that the team found that there is neither a programmatic nor a portfolio benefit sufficient to justify moving them ahead of higher-scoring applications.

Summary:

Transformative Clinical Impact	• GWG concurred with the applicant that the proposed therapeutic candidate could a transformative clinic benefit by providing an in vivo gene therapy for a focal brain cancer metastasis where standard local therapy has failed. • CIRM's active PDEV portfolio contains 2 awards that address metastatic brain tumors, and the active CLIN2 portfolio contains one award that addresses metastatic brain tumors. This modality is unique to the CIRM portfolio for this indication. • Based on GlobalData, the external US-based cell and gene therapy landscape includes one late-stage clinical program and no approved US treatments addressing metastatic brain tumors.
Patient Access	The proposed therapeutic candidate is an in vivo gene therapy; the costs associated with manufacturing are considered by the applicant and the proposal utilizes an approach that may ultimately lower costs.
Disease Representation	The application under consideration addresses a prevalent disease currently addressed by three programs in CIRM's active PDEV and CLIN2 portfolio. Although brain cancer metastasis is common, the occurrence of focal metastasis is unclear.