CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the Application Review Subcommittee
From: CIRM Team
Re: CIRM Team Recommendations: **PDEV**
Date: December 11, 2025

Introduction:

The CIRM Team's role during Application Review Subcommittee (ARS) meetings is to assist the ARS in making well-informed funding decisions. The ARS is provided the funding recommendations of the GWG, which include the final scores, assessment against the review criteria, and summary of specific strengths and weaknesses. Beyond these recommendations, the ARS may consider additional factors such as:

1. Programmatic factors (such as budget, portfolio balance, relevance to CIRM's mission, urgency, and unmet need)
2. Recommendations from the CIRM team
3. Public comment

This memo details the CIRM Team recommendations for applications to PDEV which the ARS will consider on December 11, 2025. CIRM assessed all applications with a median GWG score of 80 or above based on pipeline portfolio balance, the external clinical development landscape, and other factors that could impact on the success of projects under consideration.

CIRM Team Recommendations

The CIRM Team concurs with the GWG recommendations to fund the 12 top ranking applications with a score of 85 or higher. However, the CIRM Team recommends **not** funding application **PDEV-19139**, which had a median score of 85 and ranks 13th among all applications.

Budget Considerations:

Available PDEV Budget (Annual, 2 cycles)	**$160,000,000**
Budget Utilization – GWG Recommended	**$121,985,050** ($38,014,950 remaining)
Budget Utilization – CIRM Recommended	**$117,591,750** ($42,408,250 remaining)

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Rationale for CIRM Recommendation on PDEV-19139

Application Title: *Develop a human iPSC-based cell therapy for Canavan disease*

GWG Scores:

Median	Mean	Highest	Lowest	Scores to fund	Scores not to fund
85	81	90	60	9	5

Application PDEV-19139 proposes an autologous lentiviral gene-modified iPSC-derived neural stem cell therapy to address Canavan disease. Canavan disease is a rare inherited disorder caused by mutations in the ASPA gene. The disease is classified as a leukodystrophy, a group of diseases that disrupt the growth or maintenance of the neural myelin sheath. Among a multitude of symptoms, Canavan disease results in developmental delays, weak muscle tone, intellectual disability, seizures, and difficulty eating and swallowing. Patients with the severe form of the disease often do not survive past childhood.

The CIRM Team considered the following factors in making a recommendation to not fund this application:

- CIRM's active PDEV and CLIN2 portfolios contain no awards that address Canavan disease.
- Assessment of the external competitive landscape (based on Globaldata) indicates there are 2 late-stage clinical programs but no approved US treatments addressing Canavan disease. An intracerebroventricularly delivered AAV gene therapy being developed by Myrtelle has published interim clinical results (Nature Medicine), and is part of the FDA START pilot. The second late-stage clinical program, an intravenously delivered AAV gene therapy being developed by BridgeBio has also released interim clinical results. The two late-stage AAV gene therapies and the proposed candidate in this PDEV application are all designed to deliver a functional ASPA gene. In contrast to the off-the-shelf in vivo gene therapy landscape programs, the proposed candidate in PDEV-19139 is an autologous lentiviral gene-modified iPSC-derived neural progenitor cell therapy that requires neurosurgical delivery to multiple brain regions.
- The proposed autologous genetically-modified cell therapy requires a time and resource-intensive manufacturing process as well as a complex invasive neurosurgical procedure for delivery to patients. Compared to the external landscape of late-stage AAV gene therapies, the proposed therapy has significant access and affordability challenges for Canavan disease patients.
- The inability to achieve IND clearance with existing NIH U01 funding raises concerns about timely execution of project activities and efficient use of the CIRM requested funds toward achievement of the expected outcome of the PDEV award.
- GWG reviewer comments on value proposition, manufacturing process and surgical procedure.