Real Life™

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Grants Working Group Recommendations CLIN

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CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

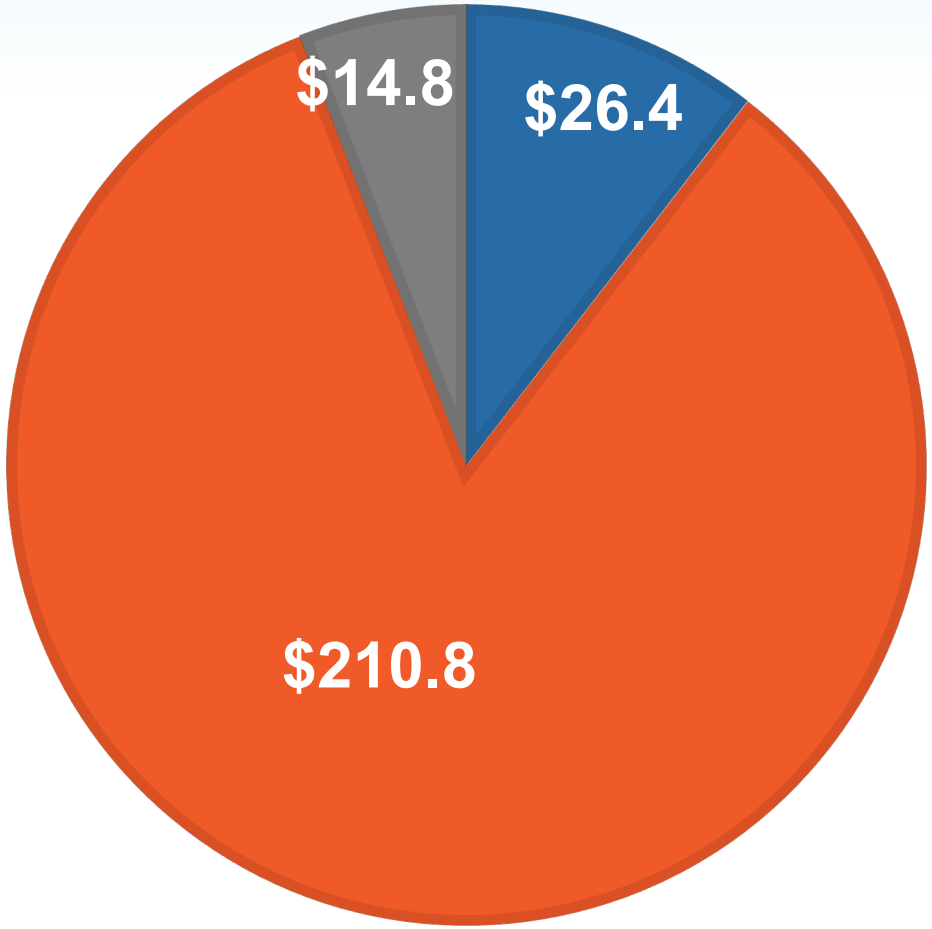
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

2023/24 Clinical Budget Status

Annual Allocation: $ 252 million

- Amount Requested Today
- Approved Awards
- Unused Balance

Amounts are shown in millions



Scientific Scoring System

- **Score of "1"**

  Exceptional merit and warrants funding.

  May have minor recommendations and adjustments that do not require further review by the GWG

- **Score of "2"**

  Needs improvement and does not warrant funding at this time but could be resubmitted to address areas for improvement.

  GWG should provide recommendations that are achievable (i.e., "fixable changes") or request clarification/information on key concerns.

- **Score of "3"**

  Sufficiently flawed that it does not warrant funding and the same project should not be resubmitted ***for at least 6 months****.*

Applications are scored by all scientific members of the GWG with no conflict.

Scientific Review Criteria

1. Does the project hold the necessary significance and potential for impact? *(what value does it offer; is it worth doing?)*
2. Is the rationale sound? *(does it make sense?)*
3. Is the project well planned and designed?
4. Is the project feasible? *(can they do it?)*
5. Does the project uphold principles of diversity, equity, and inclusion (DEI)? *(e.g., does it consider patient diversity?)*

CLIN DEI Scoring

CIRM CLIN Program DEI Rubric				
CRITERIA	Score of 0 to 2 Not Responsive	Score of 3 to 5 Not Fully Responsive	Score of 6 to 8 Responsive	Score of 9 to 10 Outstanding Response
1. Commitment to DEI	Fails to address how success of this project would lead to a therapy that positively impacts underserved or disproportionately affected communities.	Inadequately addresses how success of this project would lead to a therapy that positively impacts underserved or disproportionately affected communities.	Adequately describes how success of this project would likely lead to a therapy that positively impacts underserved or disproportionately affected communities.	Convincingly and clearly describes how success of this project would lead to a therapy that positively impacts underserved or disproportionately affected communities.
	Does not set goals for diverse trial population enrollment and provides no justification for the target enrollment.	May set trial population enrollment goals that are inappropriate or infeasible relative to the population affected or at risk for the indication.	Sets adequate goals for trial population enrollment relative to the population affected or at risk for the indication.	Trial population goals are based on a deep understanding of health disparities and disease burden.
	Inadequate personnel/expertise or budget to implement DEI-oriented activities.	May have inadequate personnel/expertise or budget to implement DEI-oriented activities.	Adequate personnel/expertise or budget to implement DEI-oriented activities.	Strong personnel/expertise and appropriate budget to implement DEI-oriented activities.
2. Project Plans	Planned activities do not reflect a good faith effort and are unlikely to be effective in outreach and engagement.	Planned activities are incomplete or inadequate and may not reflect a good faith effort for outreach and engagement.	Planned activities reflect a good faith effort and have the potential to be effective in outreach and engagement.	Planned activities reflect an outstanding and comprehensive effort for outreach and engagement.
	Does not demonstrate an understanding of the potential barriers to participation in the clinical trial.	Does not fully demonstrate an understanding of the potential barriers to participation in the clinical trial.	Demonstrates an understanding of the potential barriers to participation in the clinical trial.	Demonstrates a clear understanding of the potential barriers to participation in the clinical trial.
	Inadequate plan to address potential barriers to participation.	May not have an adequate plan to address potential barriers to participation.	Has an adequate plan to address potential barriers to participation.	Has a strong plan to address potential barriers to participation.
	Unlikely to achieve the recruitment of trial participants from underserved or disproportionately affected populations.	May not be able to achieve the recruitment of trial participants from underserved or disproportionately affected populations.	Likely to achieve the recruitment of trial participants from underserved or disproportionately affected populations.	Very likely to achieve the recruitment of trial participants from underserved or disproportionately affected populations.
3. Cultural Sensitivity	Does not include activities to increase cultural sensitivity on the team or at partner institutions, or activities proposed are not appropriate.	Proposed activities may not be effective or sufficient to increase cultural sensitivity on the team or at partner institutions. Activities may not match the needs of the project.	Has appropriate plans to increase cultural sensitivity on the team or at partner institutions. Activities match the needs of the project.	Outstanding plans to increase cultural sensitivity on the team or at partner institutions. Activities are well matched to the needs of the project.

DEI Scores

Applications are scored for adherence to principles of DEI by all GWG Board Members with no conflict.

- DEI Score of 9-10

  Outstanding Response

- DEI Score of 6-8

  Responsive

- DEI Score of 3-5

  Not Fully Responsive

- DEI Score of 0-2

  Not Responsive

GWG Composition and Roles

Scientific GWG Member	Scientific evaluation (disease area expert, regulatory, CMC, product development) Provides scientific score on all applications
GWG Board Member (Patient Advocate/Nurse)	DEI evaluation, patient perspective on significance and potential impact, oversight on process Provides DEI score on all applications Provides a suggested scientific score
Scientific Specialist (non-voting)	Scientific evaluation (specialized expertise as needed) Provides initial but not final scientific score

CLIN1-14792

Title	Superior forward-oriented b-globin vector for treating Sickle Cell Disease
Therapy	Gene-modified blood stem cells
Indication	Severe sickle cell disease
Goal	Complete IND-enabling studies, file IND
Funds Requested	$4,619,455 Co-funding: $0 (none required) California organization

Maximum funds allowable for this category: $6,000,000

CLIN1-14792: Background Information

Clinical Background: SCD affects approximately 100,000 Americans. SCD is particularly common in those with sub-Saharan African ancestry affecting 1 in 365 African-American births. Globally, over 300,000 babies are born with SCD every year.

Value Proposition of Proposed Therapy: Although similar gene editing approaches have advanced to FDA approval, the proposed therapy offers to better address the ongoing challenge of affordability and accessibility as well as a potentially more effective product for patients.

Why a stem cell or gene therapy project: The therapy involves genetic modification of blood stem cells.

CLIN1-14792: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 (NHLBI) $8,333,581	Phase 2	Dec 2024	Sickle Cell Disease	Autologous gene-modified CD34+ cells	Expression of a gene to induce anti-sickling fetal hemoglobin and silence beta-sickle globin
CLIN2 $8,389,407	Phase 1	May 2028	Sickle Cell Disease	Autologous CRISPR-edited hematopoietic stem cells	Virus-free CRISPR editing to correct the pathogenic hemoglobin S allele mutation in HSC

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN2	HIV/AIDS	Phase 1 clinical trial	4 years	$8,521,441	4 milestones proposed. All completed; 1 delayed, others early or on time.
Alpha Clinics	N/A	Clinical resource	5 years	$8,585,671	7 milestones. All completed early or on time.
Alpha Clinics	N/A	Clinical resource	6 years	$7,999,997	6 milestones. 1 completed, 1 on track, 4 not yet started.

CLIN1-14792: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	12
2	0
3	3

DEI Score: 9 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 4,619,455*

*Final award shall not exceed this amount and may be reduced contingent on CIRM's final assessment of allowable costs and activities.

CLIN1-14825

Title	Development of a Gene Therapy for the Treatment of WWOX related epileptic encephalopathy (WOREE)
Therapy	AAV gene therapy
Indication	WWOX-related epileptic encephalopathy
Goal	Complete IND-enabling studies, file IND
Funds Requested	$4,000,000 Co-funding: $1,000,000 (20% required) California organization

Maximum funds allowable for this category: $4,000,000

CLIN1-14825: Background Information

Clinical Background: WWOX related epileptic encephalopathy (WOREE) syndrome is an ultra rare disease that results in severe seizures, significant developmental delays, and frequent respiratory infections and complications. The disease manifests within the first days of life with a mean onset age of 1.6 months.

Value Proposition of Proposed Therapy: WOREE syndrome results from a deficiency in the WWOX protein, a transcriptional regulator found in many tissues including the CNS. The proposed AAV gene therapy offers the potential to restore the production and function of the missing gene to significantly reduce the burden of disease.

Why a stem cell or gene therapy project: The treatment is an AAV gene therapy approach.

CLIN1-14825: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing WWOX-related epileptic encephalopathy.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14825: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	12
2	1
3	2

DEI Score: 8 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 4,000,000*

*Final award shall not exceed this amount and may be reduced contingent on CIRM's final assessment of allowable costs and activities.

CLIN2-15218

Title	A Phase 2 Study Evaluating the Efficacy and Safety of IV Administered rAAV Gene Therapy in Male Patients with Danon Disease
Therapy	AAV gene therapy
Indication	Danon disease
Goal	Complete phase 2 clinical trial
Funds Requested	$5,808,735 Co-funding: $32,916,165 (40% required) Non-California organization

Maximum funds allowable for this category: $15,000,000

CLIN2-15218: Background Information

Clinical Background: Danon disease is a rare X-linked disorder that primarily affects the heart but also skeletal muscle and the brain, which results in limited cognitive impairment. There are no curative treatments currently available with the most definitive option being heart transplantation.

Value Proposition of Proposed Therapy: The proposed gene therapy approach restores expression of the missing LAMP2B gene to relieve patients of their symptoms and reduce the need for heart transplantation. The applicants hope that the approach may offer the possibility of a cure.

Why a stem cell or gene therapy project: The treatment is an AAV gene therapy approach.

CLIN2-15218: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1 $5,180,389	Pre-IND	Jul 2026	Danon disease	Autologous gene-modified blood stem cells	Transplanted cells deliver missing LAMP2B protein to heart, liver, muscle, & brain

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN2	LAD-1 deficiency	Phase 1 clinical trial	4 years	$6,567,085	6 milestones proposed and completed; 3 on time, 3 delayed.
CLIN2	Osteopetrosis	Phase 1 clinical trial	3 years	$3,728,485	5 milestones proposed. 4 completed with delays, 1 not completed.

CLIN2-15218: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	12
2	1
3	1

DEI Score: 8 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 5,808,735*

*Final award shall not exceed this amount and may be reduced contingent on CIRM's final assessment of allowable costs and activities.

CLIN2-16156

Title	Selective, Off-the-Shelf Logic Gated CAR NK Cell Therapy Targeting CD33 and/or FLT3 Expressing Hematologic Malignancies
Therapy	CAR-NK cell therapy
Indication	Hematologic malignancies, including acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS)
Goal	Complete phase 1 clinical trial
Funds Requested	$8,000,000 Co-funding: $4,804,127 (30% required) California organization

Maximum funds allowable for this category: $8,000,000

CLIN2-16156: Background Information

Clinical Background: Acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) are types of blood cancer that affect about 20,000 Americans each year. The 5-year survival rate is about 32% with current treatments. Patients with recurring and relapsing AML undergo various chemotherapy approaches or clinical trial treatments with median survival of only 3-6 months.

Value Proposition of Proposed Therapy: With limited effective therapeutic options, additional approaches are needed. The proposed CAR NK therapy uses a targeted approach that is potentially more durable and effective. The therapy may double the median life expectancy for patients with recurring/relapsing AML.

Why a stem cell or gene therapy project: The therapy involves gene modification of NK cells.

CLIN2-16156: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1 $3,200,000	IND-enabling	Jul 2025	Leukemia, AML	Small molecule inhibitor of ADAR1	Molecule inhibits ADAR1 splicing and selectively eradicates therapy-resistant cancer stem cells in blood cancers.
CLIN1 $6,000,000	IND-enabling	Jan 2025	AML	Vaccine	Patient AML cells are genetically modified to stimulate the immune system. Cells injected as a vaccine.
CLIN2 $11,983,547	Phase 1 clinical trial	Aug 2027	AML	CAR T cell therapy	Adoptive transfer of patient specific immune T cells expressing CAR that targets CD33.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-16156: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	12
2	0
3	0

DEI Score: 9.5 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 8,000,000*

*Final award shall not exceed this amount and may be reduced contingent on CIRM's final assessment of allowable costs and activities.

CLIN1-16244

Title	Novel Gene Therapy Targeting Multiple Pathological Drivers of Desmoplakin Associated Arrhythmogenic Cardiomyopathy
Therapy	AAV gene therapy
Indication	Desmoplakin-related arrhythmogenic cardiomyopathy
Goal	Complete IND-enabling studies, file IND
Funds Requested	$4,000,000 Co-funding: $11,266,899 (20% required) California organization

Maximum funds allowable for this category: $4,000,000

CLIN1-16244: Background Information

Clinical Background: Desmoplakin-associated arrhythmogenic cardiomyopathy is a rare genetic heart condition that typically manifests in young adults. This condition results in a high risk of life-threatening ventricular arrhythmias, sudden cardiac death, and progression to heart failure.

Value Proposition of Proposed Therapy: Currently, no disease-modifying therapies exist for this condition and therefore the proposed therapy addresses a clear unmet need. The approach utilizes an AAV gene therapy to induce liver specific expression of FGF21 that circulates to the heart and restores functions in heart cells caused by inherited variants in the genes of desmosomal proteins.

Why a stem cell or gene therapy project: The treatment is a AAV gene therapy approach.

CLIN1-16244: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing Desmoplakin-related arrhythmogenetic cardiomyopathy.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-16244: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	14
2	0
3	0

DEI Score: 9 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 4,000,000*

*Final award shall not exceed this amount and may be reduced contingent on CIRM's final assessment of allowable costs and activities.