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

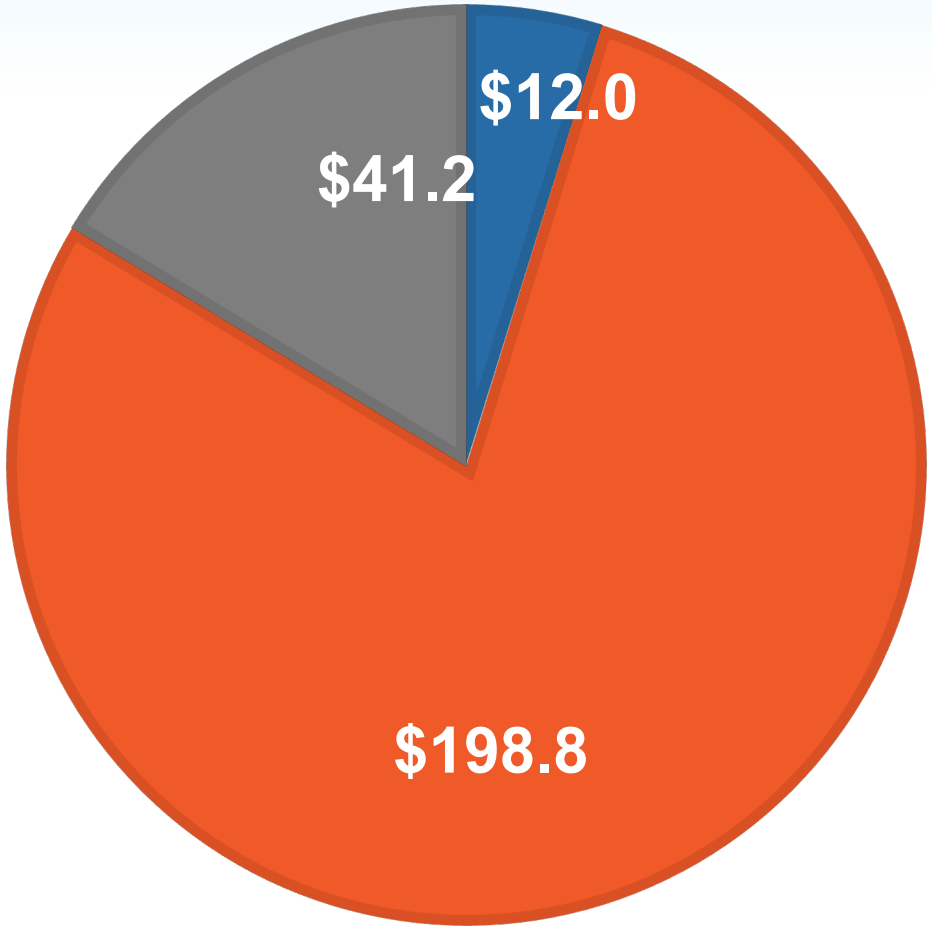
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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

Board Members with Conflicts of Interest

Board Members with Conflicts of Interest for Application CLIN1-14770
Maria Bonneville
Ysabel Duron
Steve Juelsgaard

CLIN1-14770

Title	Autologous Gene Corrected Sinus Basal Cells to Treat Serious Cystic Fibrosis Sinus Disease
Therapy	Gene corrected autologous sinus airway basal stem cells from patients with Cystic Fibrosis.
Indication	Chronic sinusitis in Cystic Fibrosis
Goal	IND filing
Funds Requested	$6,000,000 Co-funding: $0 (None required) California organization

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

CLIN1-14770: Background Information

Clinical Background: Cystic fibrosis (CF) is a genetic disease that impacts over 30,000 people in the US. Cystic fibrosis causes lung damage, chronic respiratory infections, and ultimately leads to lung failure in addition to other complications. Small molecule modulators can provide significant benefit but do not work for all patients, and many non-responders are ethnic minorities.

Value Proposition of Proposed Therapy: A treatment that provides stable restoration of the corrected cystic fibrosis gene in the airway could improve the quality of life for people with CF.

Why a stem cell or gene therapy project: The therapy is composed of autologous gene corrected airway stem cells.

CLIN1-14770: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing Cystic Fibrosis.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
DISC2	Cystic Fibrosis	Candidate discovery	2 years	$1,968,456	All five proposed milestones were completed. A protocol was established for gene correction of the same therapeutic under development.
CLIN1	Sickle cell disease	IND filing	3 years	$4,849,363	All three proposed milestones were completed. IND was filed with FDA.
CLIN2	Fanconi anemia	Clinical trial	4 years	$10,642,420	Five milestones are planned, two have been completed. The award is currently active.
CLIN2	Hematologic malignancies	Clinical trial	4 years	$9,740,000	Five milestones are planned, three have been completed. The award is currently active.
PC1 Preclinical development	SCID	Pre-IND meeting	3 years	$874,877	Six milestones were planned, three completed and two were delayed at the time of award completion.
INFR4	n/a	Alpha Stem Cell Clinic	5 years	$6,920,810	Six milestones are planned, one has been completed. The award is currently active.

CLIN1-14770: 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: $ 6,000,000*

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

Board Members with Conflicts of Interest for Application CLIN1-15399

Karol Watson

CLIN1-15399

Title	Development of a therapeutic monoclonal antibody for the treatment of myocardial infarction and heart failure
Therapy	Monoclonal antibody targeting human ectonucleotide pyrophosphatase/phosphodiesterase (ENPP1)
Indication	Heart disease
Goal	IND filing
Funds Requested	$5,999,998 Co-funding: $0 (None required) California organization

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

CLIN1-15399: Background Information

Clinical Background: Heart disease is the leading cause of death globally. After a heart attack, the body tries to repair the damaged area with scar tissue (fibrosis). The scar tissue stresses the remaining heart muscle, which over time, leads to heart failure. Standard of care for this indication does not address complications of fibrosis or enhance cardiac repair.

Value Proposition of Proposed Therapy: A one-time treatment of a drug that could either enhance repair and/or decrease fibrosis after a heart attack would be a significant advancement over standard of care.

Why a stem cell or gene therapy project: The therapy targets cardiac scar forming progenitor cells.

CLIN1-15399: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1	IND enabling	Q2 2026	Heart failure	Extracellular vesicles derived from cardiosphere derived cells	The vesicles aim to improve cardiac function, scar volume, and electrical stability
CLIN1	Phase 1 Clinical Trial	Q3 2025	Heart failure	Human embryonic stem cell-derived cardiomyocytes	Cardiomyocytes generated from hESCs are administered to the site of heart muscle damage, and aim to improve heart function

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN1	Heart failure	Pre-IND meeting	2 years	$4,791,428	Finished milestones well ahead of schedule and received pre-IND feedback.
DISC1	Heart failure	Basic research	2 years	$230,400	The award concluded without identifying a target unique to scar-forming progenitor cells and did not meet milestone 2. Subsequent studies validated ENPP1 as a useful target for the therapeutic that is under development.

CLIN1-15399: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI Score: 10 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 5,999,998*

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