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Grants Working Group Recommendations CLIN

November 28, 2023

CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

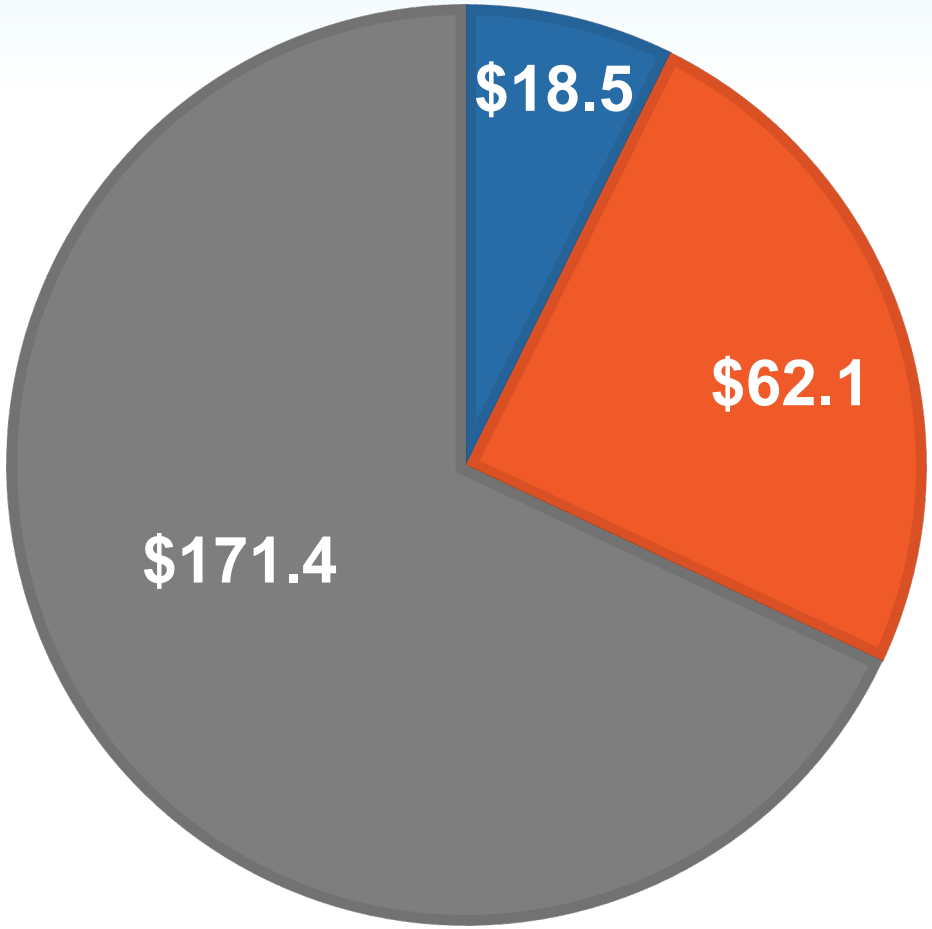
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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

CLIN1-14945

Title	Pre-Clinical to Clinical Gene Therapy Development for CMT4J
Therapy	AAV9 Gene Therapy
Indication	Patients with CMT4J (FIG4 Gene) mutation
Goal	Complete IND-enabling activities and file an IND
Funds Requested	$3,930,964 Co-funding: $982,741 (20% required)

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

CLIN1-14945: Background Information

Clinical Background: Charcot-Marie-Tooth disease type 4J (CMT4J) is a rare, debilitating, progressive hereditary motor and sensory neurological disease caused by heteroallelic FIG4 loss of function alleles. It is characterized by progressive motor weakness with sensory involvement resulting in quadriplegia, respiratory failure, and a shortened lifespan. There are currently no treatments available to slow or halt disease progression.

Value Proposition of Proposed Therapy: The proposed gene therapy approach utilizes the AAV9 vector to target affected neurons and provide the missing FIG4 gene. The approach has the potential to significantly improve quality of life for affected patients by halting the progression of disease.

Why a stem cell or gene therapy project: The therapeutic candidate is a gene therapy.

CLIN1-14945: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing CMT4J.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14945: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI Score: 9 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $3,930,964*

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

CLIN1-15060

Title	A 1XX-enhanced and fully non-viral BCMA chimeric antigen receptor (CAR) T cell therapy for Relapsed and Refractory Multiple Myeloma
Therapy	Cryopreserved autologous TRAC locus 1XX BCMA-CAR T cells
Indication	Relapsed and Refractory Multiple Myeloma
Goal	Complete IND-enabling studies and file an IND
Funds Requested	$4,585,501 Co-funding: $0 (None required)

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

CLIN1-15060: Background Information

Clinical Background: Multiple myeloma is the second most common malignancy among blood cancers and primarily affects individuals over the age of 60. The median survival is 7-10 years. Although there are several treatments available, patients will typically relapse and become refractory to additional lines of therapy.

Value Proposition of Proposed Therapy: CAR T therapies that target BCMA have demonstrated significant promise for treating relapsed and refractory multiple myeloma, but current approaches still have some limitations. The proposed therapy aims to overcome these limitations to produce a CAR T therapy with improved persistence and reduced relapse.

Why a stem cell or gene therapy project: The therapy is composed of T memory stem cells.

CLIN1-15060: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing multiple myeloma.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-15060: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	11
2	3
3	0

DEI Score: 9 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $4,585,501*

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

CLIN2-15085

Title	Personalized antisense oligonucleotide therapy for rare pediatric genetic disease: SCN2A
Therapy	Personalized antisense oligonucleotide drug
Indication	SCN2a-associated genetic disorder
Goal	Complete first-in-human trial
Funds Requested	$985,713 Co-funding: $0 (None required)

Maximum funds allowable for this category: $12,000,000

CLIN2-15085: Background Information

Clinical Background: SCN2A-related disorders are caused by mutations in the SCN2A gene. SCN2A-related disorders result in a range of neurodevelopmental conditions mainly characterized by the severity of epilepsy. Severe forms of the disorder cause seizures beginning in infancy, and anti-seizure medications are often not effective.

Value Proposition of Proposed Therapy: The proposed personalized therapy would treat a patient with a severe epilepsy and severe neurodevelopmental delay. If successful, other people with similar disorders could benefit from equivalent precision therapies.

Why a stem cell or gene therapy project: The therapeutic candidate is a gene therapy.

CLIN2-15085: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing SCN2A-related disorders.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
DISC2	Neurodevelopmental diseases	Candidate discovery	Aug 2022 – July 2024	$1,180,654	Seven milestones proposed, two completed with delay, three on track, two not yet started.

CLIN2-15085: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	8
2	6
3	0

DEI Score: 8.5 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $985,713*

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

CLIN2-15115

Title	The CuRe Trial: Cellular Therapy for In Utero Repair of Myelomeningocele
Therapy	Allogeneic mesenchymal stem cells on a matrix graft
Indication	Myelomeningocele (MMC) - or spina bifida - diagnosed prenatally
Goal	Complete a Phase 2a clinical trial
Funds Requested	$8,996,477 Co-funding: $5,997,653 (40% required)

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

CLIN2-15115: Background Information

Clinical Background: Myelomeningocele (MMC) is a birth defect that occurs due to incomplete closure of the developing spinal cord, resulting in neurological damage to the exposed cord. This damage leads to lifelong lower body paralysis, and bladder and bowel dysfunction. Current in utero surgery improves the quality of life of children born with MMC, but over half cannot walk independently.

Value Proposition of Proposed Therapy: The proposed therapy could improve the motor outcomes of children born with MMC compared to surgery alone, and if successful will result in more children who are able to walk.

Why a stem cell or gene therapy project: The therapy is composed of mesenchymal stem cells together with a matrix material.

CLIN2-15115: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $8,996,474	Phase 1 clinical trial	April 2024	MMC	Mesenchymal stem cells on a graft	The graft with cells will be applied *in utero* to promote proper spinal cord formation.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN2	MMC	Phase 1 clinical trial	Jan 2021-April 2024	$8,996,474	Enroll, treat, and complete evaluations of six patients. Five milestones proposed, two achieved on time, two delayed, one on track.
CLIN1	MMC	Preclinical	Jan 2019 – Jan 2021	$5,666,077	Complete IND enabling studies and manufacturing. File IND and complete trial startup activities. 5 milestones proposed, 4 completed on time, one with delay.
Preclinical	MMC	Preclinical	Sep 2015-Aug 2018	$2,182,146	Complete activities culminating in a Pre-IND meeting. 6 milestones proposed, 3 achieved on time, 3 delayed.

CLIN2-15115: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	14
2	0
3	0

DEI Score: 9.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $8,996,477 *

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