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

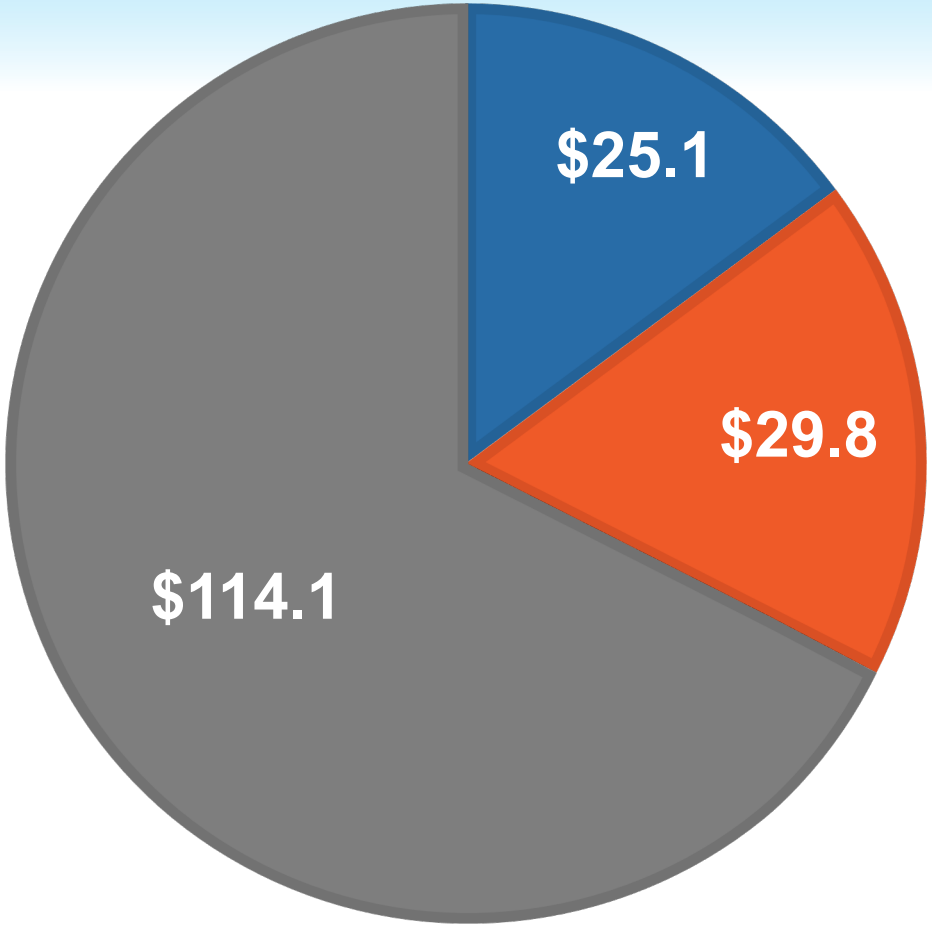
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

2022/23 Clinical Budget Status

Annual Allocation: $169 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.

Review Criteria

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

GWG Composition and Roles

Scientific GWG Member	Scientific evaluation (disease area expert, regulatory, CMC, product development) Provides scientific score on all applications
Patient Advocate or Nurse GWG Member	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 CLIN applications

Ysabel Duron

CLIN1-13988

Title	Genome Editing of Autologous Hematopoietic Stem Cells to Treat Severe Mucopolysaccharidosis type 1 (Hurler Syndrome)
Therapy	Autologous blood stem cells edited to restore iduronidase expression
Indication	Severe Mucopolysaccharidosis type 1
Goal	Completion of IND-enabling studies and filing of IND
Funds Requested	$5,999,919 (co-funding: $0)

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

CLIN1-13988: Background Information

Clinical Background: Mucopolysaccharidosis type 1 (MPS1) is a lysosomal storage disease affecting children that results in neurologic, musculoskeletal, and cardiorespiratory deterioration. The severe form of this disease is diagnosed at infancy and is fatal within the first 10 years of life.

Value Proposition of Proposed Therapy: The current standard of care involves enzyme replacement therapy and allogeneic blood stem cell transplant but is not adequately effective. The proposed autologous therapy holds the potential for a safer and more effective treatment of patients with MPS1.

Why a stem cell or gene therapy project: The therapeutic candidate is composed of blood (hematopoietic) stem cells.

CLIN1-13988: Similar CIRM Portfolio Projects

CIRM portfolio does not currently have any active awards addressing this or similar indications.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-13988: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	13
2	0
3	0

DEI Score: 8.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 5,999,919*

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

CLIN2-14024

Title	Sequential same donor αβdepleted-HSCT from an HLA-partially matched donor allowing immunosuppression free kidney transplant
Therapy	Allogeneic blood stem cells depleted of TCRαβ+ T cells/CD19+ B cells
Indication	Renal failure due to one of four genetic and/or immunological diseases
Goal	Completion of a phase 1 study to assess feasibility and safety
Funds Requested	$11,998,188 (co-funding: $0)

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

CLIN2-14024: Background Information

Clinical Background: Improvement of long term outcomes for pediatric and young adult kidney transplantation remains an unmet medical need due to immune-mediated graft rejection and infections. Most children requiring a kidney transplant will need an additional transplant and requires life-long immunosuppression.

Value Proposition of Proposed Therapy: The proposed therapy has the potential to reduce the risk of chronic transplant rejection, the need for repeat transplantation, and the need for immunosuppression by retraining the immune system to develop tolerance to donor kidney.

Why a stem cell or gene therapy project: The therapeutic candidate is composed of blood (hematopoietic) stem cells.

CLIN2-14024: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	Dec 2022	Kidney Failure	Blood stem cells and T cells	Donor stem cells and T cells combine to induce tolerance and minimize GVHD for kidney transplantation
CLIN2	Phase 3 clinical trial	Dec 2023	Kidney Failure	Blood stem cells and T cells	Donor stem cells and T cells combine to induce tolerance and minimize GVHD for kidney transplantation
CLIN2	Phase 1 clinical trial	Nov 2023	Kidney Failure	Blood stem cells and Treg cells	Donor stem cells and T cells combine to induce tolerance and minimize GVHD for kidney transplantation
CLIN2	Phase 1/2 clinical trial	Jul 2023	Cystinosis & Related kidney failure	Cell and gene therapy	Autologous transplant of gene corrected blood stem cells to restore functional cystinosin

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-14024: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI Score: 9.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 11,998,188*

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

CLIN2-14232

Title	A Potent, First-In-Class KDM4 Inhibitor for Advanced Cancers
Therapy	Small molecule inhibitor of KDM4 histone demethylase
Indication	Colorectal Cancer
Goal	Completion of a phase 1 trial to assess safety and initial efficacy
Funds Requested	$7,141,843 (co-funding: $3,060,790)

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

CLIN2-14232: Background Information

Clinical Background: Colorectal cancer remains an unmet medical need and was the second leading cause of cancer death in the U.S. in 2020. About 15 percent of colorectal cancer patients are not responsive to chemotherapy due to a deficiency in DNA repair mechanisms.

Value Proposition of Proposed Therapy: The standard of care for advanced colorectal cancer that is unresponsive to first line therapy includes immune checkpoint inhibitors and/or agents that target angiogenesis/vascularization. Still, a significant fraction of patients are refractory to these therapies and additional approaches needed. If successful, the proposed therapy would provide an effective therapeutic option for patients.

Why a stem cell or gene therapy project: The therapeutic candidate targets cancer stem cells.

CLIN2-14232: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	May 2025	Solid tumors	Cytokine Induced Killer cells containing oncolytic virus	Cytokine Induced Killer cells target tumor cells to deliver oncolytic virus

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-14232: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	7
2	6
3	0

DEI Score: 9.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 7,141,843*

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