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

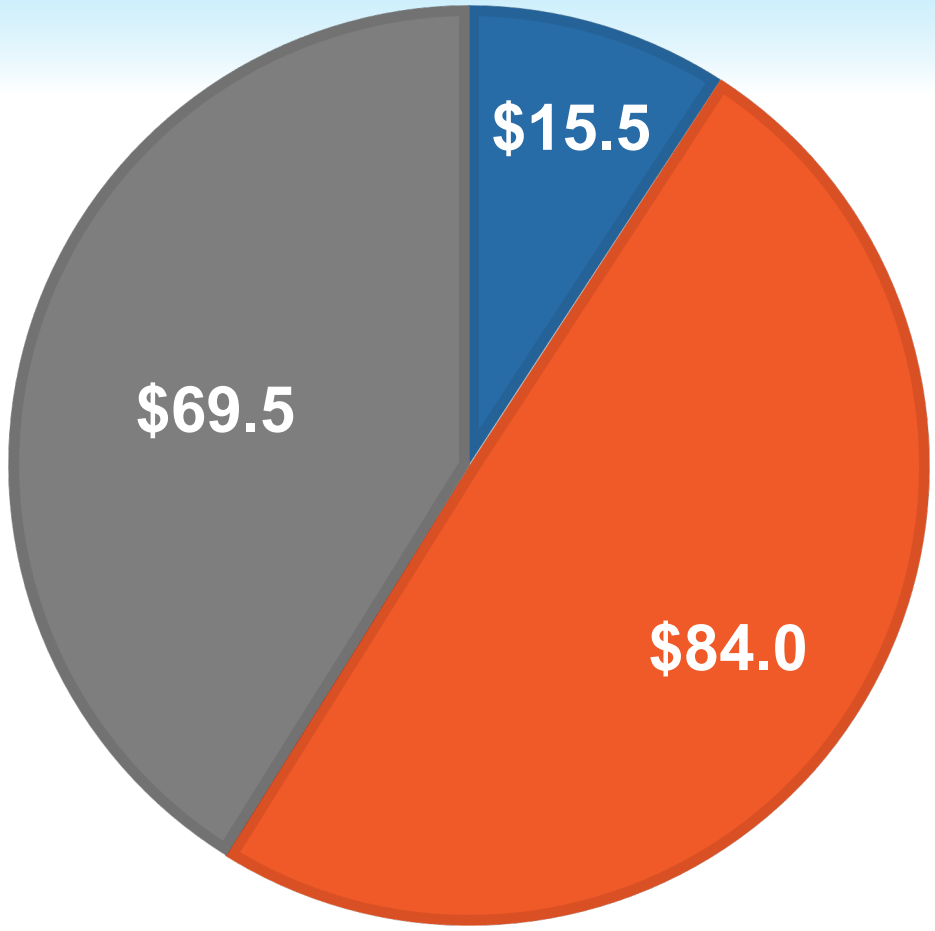
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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

CLIN1-14070

Title	Development of cryopreserved interferon-gamma primed allogeneic MSCs, for treatment of steroid refractory acute graft versus host disease
Therapy	Cryopreserved, interferon-gamma-primed bone marrow mesenchymal stem cells
Indication	Acute graft versus host disease (aGVHD)
Goal	Completion of studies to remove clinical hold on IND
Funds Requested	$3,457,858 (co-funding: $865,000 – 20% required)

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

CLIN1-14070: Background Information

Clinical Background: Allogeneic stem cell transplants can be life-saving and curative treatments for blood cancers, blood disorders, and other conditions. However, there are significant risks including acute graft versus host disease, which is a life-threatening condition where donor cells attack the host tissues. Furthermore, many patients with aGVHD can become refractory to immune suppressing steroids used to manage this serious complication.

Value Proposition of Proposed Therapy: The proposed MSC therapy, that provides immunomodulatory effects, has the potential to eliminate or reduce the severity of aGVHD and improve overall survival.

Why a stem cell or gene therapy project: The therapeutic candidate is composed of mesenchymal stem cells.

CLIN1-14070: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	Dec 2023	GVHD related to B cell cancers, leukemia, AML	T cell immunotherapy	Administration of donor T cells following HSCT transplant

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14070: 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: $ 3,457,858*

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

CLIN1-14300

Title	Allogeneic iPSC derived Dopaminergic Drug Product for Parkinson's disease
Therapy	Allogeneic iPSC-derived dopamine progenitor cells
Indication	Idiopathic Parkinson’s disease
Goal	Completion of IND-enabling studies and filing of IND
Funds Requested	$4,000,000 (co-funding: $3,000,000 – 20% required)

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

CLIN1-14300: Background Information

Clinical Background: Parkinson's disease (PD) is the second-most common neurodegenerative disease after Alzheimer's disease affecting approximately one million people in the U.S.. PD is characterized by a loss of dopaminergic neurons that result in motor symptoms, such as dyskinesias, and non-motor effects such as dementia, depression and sleep disorders.

Value Proposition of Proposed Therapy: PD at its early stages can be treated with medication such as levodopa to treat symptoms but these become less effective as the disease progresses. The proposed cell therapy offers the potential to restore dopamine neurons and repair some of the lost brain circuits to greatly improve quality of life.

Why a stem cell or gene therapy project: The therapeutic candidate is manufactured from induced pluripotent stem cells.

CLIN1-14300: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1	IND-enabling studies	Feb 2023	Parkinson's disease	Gene-modified neural progenitor cell therapy	Transplantation of GDNF-secreting cells in the brain to protect dopamine neurons and induce repair
CLIN2	Clinical trial	Nov 2023	Parkinson's disease	Gene therapy vector	Delivery of GDNF gene to the putamen to stimulate regeneration of terminals of dopamine producing neurons.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14300: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	11
2	3
3	0

DEI Score: 7.0 (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.

CLIN2-14416

Title	A Phase I Open Label Study to Evaluate the Safety and Tolerability of a Candidate in Patients with Mucopolysaccharidosis Type I
Therapy	Gene corrected B cells
Indication	Mucopolysaccharidosis I (MPSI)
Goal	Completion of phase 1 clinical trial
Funds Requested	$8,000,000 (co-funding: $3,514,654 - 30% required)

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

CLIN2-14416: Background Information

Clinical Background: Mucopolysaccharidosis type I (MPS I) is a lysosomal storage disease caused by the enzymatic deficiency of alpha-L-iduronidase (IDUA). This results in lysosomal accumulation of glycosaminoglycans (GAG) and multi-system disease. 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 effective. The proposed autologous therapy holds the potential for a safer and more effective treatment of patients with MPS I.

Why a stem cell or gene therapy project: The therapeutic candidate is manufactured from progenitor cells that differentiate into plasma cells.

CLIN2-14416: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1	IND-enabling studies	Dec 2024	MPS I	Gene-edited autologous hematopoietic stem cells	Transplantation of gene-corrected stem cells to restore production of alpha-L-iduronidase

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN	MPS II	Pre-IND meeting	Feb 2022 – Jan 2024	$3,994,676	**M1**: Complete two-month dose-ranging study (Completed on time) **M2-M5**: Process development, pharmacology and pilot safety studies, pre-IND (On Track)

CLIN2-14416: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	11
2	2
3	0

DEI Score: 6.0 (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.