Real Life™

Gil Sambrano, PhD
Vice President, Portfolio Development and Review

Grants Working Group Recommendations CLIN

December 15, 2022

CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

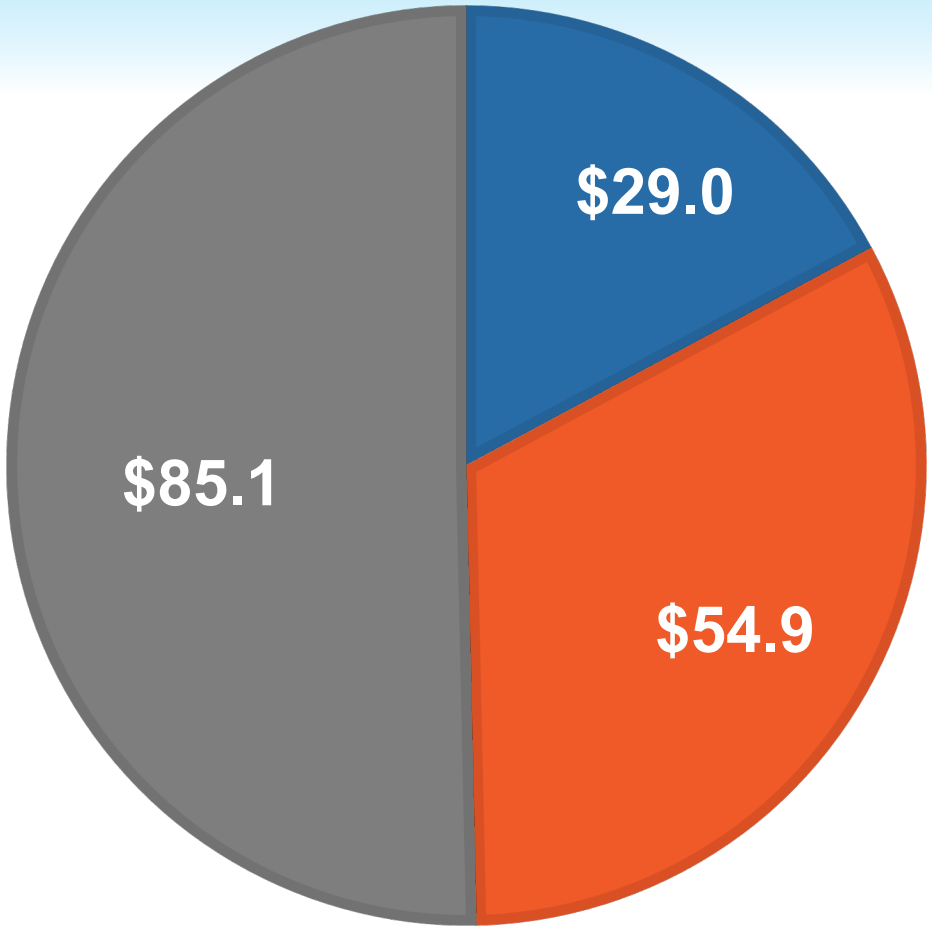
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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 CLIN1-13985
Haifaa Abdulhaq
Elena Flowers
Judy Gasson
Christine Miaskowski
Barry Selick
Karol Watson

CLIN1-13985

Title	Development of an Engineered Autologous Leukemia Vaccine for Stimulating Cytolytic Immune Responses to Residual Leukemic Stem Cells
Therapy	Genetically modified cancer cell vaccine
Indication	Acute myelogenous leukemia (AML)
Goal	Completion of IND-enabling studies and filing of IND
Funds Requested	$6,000,000 (co-funding: $0 – not required)

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

CLIN1-13985: Background Information

Clinical Background: About 20,000 new cases of acute myeloid leukemia (AML) are diagnosed each year in the US with a 5-year survival rate of ~29%. There is a significant unmet need as most patients relapse after treatment. Hematopoietic stem cell transplant can be curative, but many older patients do not qualify.

Value Proposition of Proposed Therapy: The proposed therapy utilizes a vaccine approach to stimulate an immune attack against the cancer via genetic modification and expression of three immune markers on the cancer cells. The approach holds the potential for long-term effectiveness as it targets both AML blasts and leukemic stem cells that are often the source of relapse.

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

CLIN1-13985: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	Sep 2023	AML, CMML	Monoclonal antibody	Monoclonal antibody to target monocytic leukemic stem cells
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

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN	AML	Pre-IND meeting	Feb 2019 – Dec 2022	$4,171,728	**M1-M2**: Manufacturing process development and SOPs (Completed on time) **M3**: Preclinical safety studies and GMP-compatible production (Completed with delay due to COVID issues) **M4**: Conduct pre-IND meeting (Completed on time)

CLIN1-13985: 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: $ 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

Board members with Conflicts of Interest for CLIN1-14006
Kim Barrett
Judy Gasson
Karol Watson

CLIN1-14006

Title	Hematopoietic stem cell gene therapy for the treatment of Tay-Sachs disease
Therapy	Autologous, gene-modified blood stem cells
Indication	Tay-Sachs disease
Goal	Completion of IND-enabling studies and filing of IND
Funds Requested	$4,048,253 (co-funding: $0 – not required)

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

CLIN1-14006: Background Information

Clinical Background: Tay-Sachs disease is a rare genetic disorder that causes an accumulation of gangliosides that build up to toxic levels and result in neurodegeneration. There are several manifestations of disease, including an infant, juvenile, and adult forms. Over a hundred mutations in the disease-causing Hex A gene have been identified that result in enzyme disfunction.

Value Proposition of Proposed Therapy: There are currently no effective therapies or cures for Tay-Sachs. The proposed therapeutic candidate has the potential to produce and deliver the Hex enzyme via an autologous blood stem cell transplant to restore function.

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

CLIN1-14006: Similar CIRM Portfolio Projects

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

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN	Tay-Sachs disease	Pre-IND meeting	Jun 2016 – Sep 2019	$883,174	**M1**: Produce and release GMP-compatible vector (Completed on time) **M2**: Preclinical safety and efficacy studies (Completed on time) **M3**: Conduct pre-IND meeting (Completed with delay)

CLIN1-14006: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	14
2	0
3	0

DEI Score: 7.5 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 4,048,253*

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

CLIN1-14140

Title	IND-Enabling activities for a masked immunocytokine
Therapy	Antibody and interferon alpha fusion protein
Indication	Advanced or metastatic solid tumors and multiple myeloma
Goal	Completion of IND-enabling studies and filing of IND
Funds Requested	$3,999,113 (co-funding: $999,779 - 20% required)

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

CLIN1-14140: Background Information

Clinical Background: Cancers with a prevalence of CD138 expression include multiple myeloma and several solid tumors such as pancreatic, bladder, breast, colorectal, ovarian, and prostate. Although approved treatments for these cancers exist, patients with advanced or metastatic disease will often relapse or are refractory to current treatments.

Value Proposition of Proposed Therapy: Interferon alpha therapies are currently available to treat multiple myeloma following first in line therapy but is limited by toxicities. If successful, the proposed therapy would provide a safer and effective therapeutic option for patients due to its targeted and masked delivery.

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

CLIN1-14140: 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
TRAN	Preclinical	Jan 2024	Multiple myeloma	Bi-specific CAR-T cell therapy	Therapy targets both BCMA and CS1 to prevent antigen escape in multiple myeloma
TRAN	Preclinical	Jan 2024	Multiple myeloma	CAR-iNKT cell therapy	Allogeneic natural killer T cell therapy that targets BCMA

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14140: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	11
2	3
3	1

DEI Score: 6.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 3,999,113*

*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

Board members with Conflicts of Interest for CLIN2-14302
Kim Barrett
Judy Gasson
Larry Goldstein
Linda Malkas
Barry Selick
Karol Watson

CLIN2-14302

Title	Phase 3 Trial and Related Activities to Support Clinical Development of Genetically Modified Human Umbilical Cord-Derived Vascular (Endothelial) Cells
Therapy	Genetically-modified endothelial cells
Indication	Severe regimen related toxicities from treatment for lymphoma
Goal	Completion of a phase 3 trial
Funds Requested	$15,000,000 (co-funding: $10,135,289 – 40% required)

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

CLIN2-14302: Background Information

Clinical Background: Cancer therapies often employ regimens that damage otherwise health tissues and organs. Severe regimen-related toxicities (SRRT) can become life-threatening and can limit the effectiveness of therapies, including hematopoietic stem cell transplants.

Value Proposition of Proposed Therapy: The standard of care for SRRT includes prophylactic supportive treatments to address symptoms. However, the proposed therapy aims to target the underlying cause of SRRT by acting on and restoring the endogenous stem cell vascular niches in organs. If successful, this approach could significantly improve outcomes for patients undergoing a variety of therapies for cancer.

Why a stem cell or gene therapy project: The candidate targets endogenous stem cells for its therapeutic effect.

CLIN2-14302: 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

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN2	Severe regimen related toxicities from treatment for lymphoma	Phase 1 trial	Feb 2019 – Apr 2021	$6,200,000	**M1-3**: Patient enrollment and dosing (Completed on time) **M4**: 100-day report (Completed on time) **M5**: Clinical data report (Completed on time)
CLIN2	Immune/blood cell reconstitution following myeloablation	Phase 1 trial	Oct 2017 – Mar 2022	$5,000,000	**M1**: Enroll first patient (Completed with delay) **M2-3**: Enrollment, transplantation of 3 cohorts (Completed on time) **M3**: Clinical study report (Completed with delay)
CLIN1	Immune/blood cell reconstitution following myeloablation	IND filing	Apr 2016 – Mar 2017	$3,800,000	**M1-2**: Comparability studies and release of GLP material (Completed on time) **M3**: File IND (Completed on time)

CLIN2-14302: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	10
2	3
3	0

DEI Score: 8.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 15,000,000*

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