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

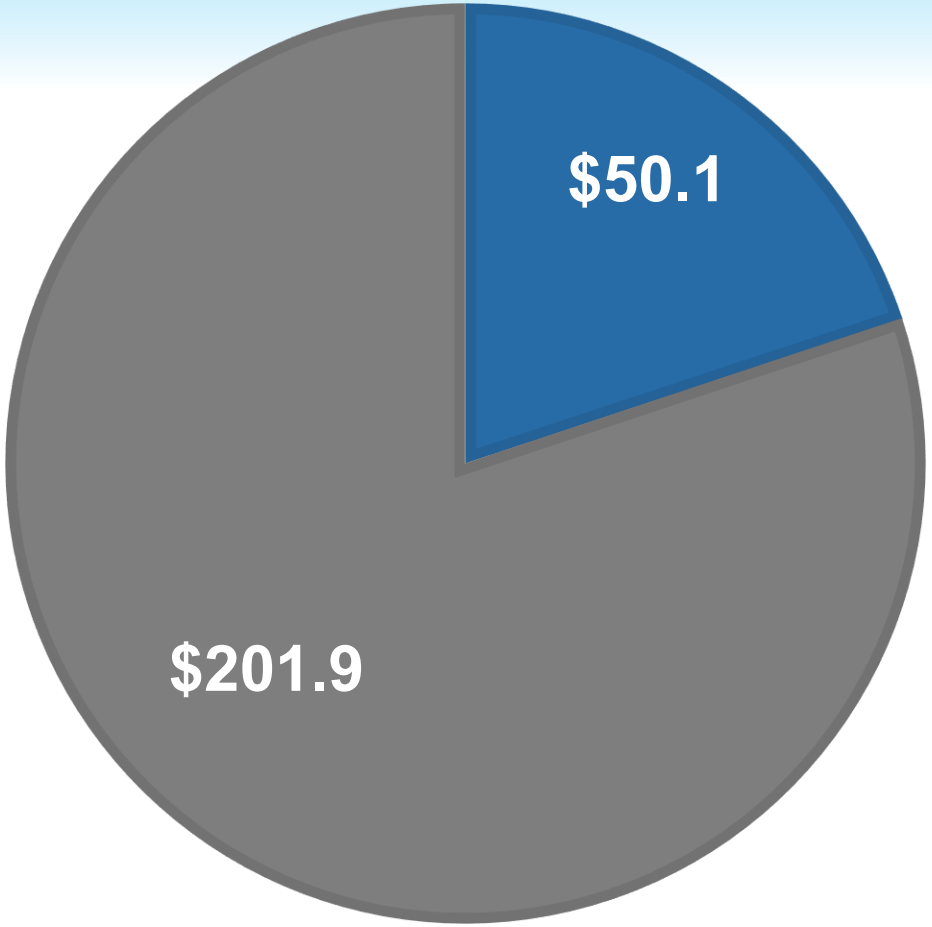
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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 the 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

CLIN2-14068

Title	Treatment of Severe Aplastic Anemia (SAA) by induction of mixed chimerism using CD4+ T cell depleted haploidentical donor stem cell transplant (SCT)
Therapy	Donor blood stem cell transplant with a low-toxic conditioning regimen
Indication	Severe Aplastic Anemia (SAA)
Goal	Complete phase 1 (first–in-human) clinical trial
Funds Requested	$9,054,216 Co-funding: $0 (None required)

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

CLIN2-14068: Background Information

Clinical Background: Severe aplastic anemia (SAA) is a life-threatening disease of the immune system in which blood lymphocytes destroy other blood cells resulting in severe anemia and bone marrow damage. The condition can be cured with a bone marrow transplant, but this approach is much less effective in older patients who experience a higher incidence of graft failure and GVHD. Additionally, patients without a fully matched donor (often from underserved groups) are associated with inferior survival outcomes.

Value Proposition of Proposed Therapy: The proposed therapy offers a potential for improved outcomes by significantly decreasing the occurrence of GVHD and eliminating the need to have a fully matched donor.

Why a stem cell or gene therapy project: The therapy involves a blood stem cell transplant.

CLIN2-14068: Similar CIRM Portfolio Projects

CIRM does not currently have any active awards addressing severe aplastic anemia.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN2	Sickle Cell Disease	Phase 1 clinical trial	Apr 2018 – Jun 2023	$4,352,180	6 milestones proposed to enroll/dose patients, apply for RMAT designation, and complete study. Only 3 milestones completed and CIRM terminated award in 2023.

CLIN2-14068: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	11
2	2
3	0

DEI Score: 8.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 9,054,216*

*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 CLIN1-14607 application
Mark Fischer-Colbrie

CLIN1-14607

Title	Cancer Stem Cell Interception with a Small Molecule Splicing Inhibitor
Therapy	Small molecule inhibitor of splicing that selectively eradicates therapy-resistant cancer stem cells
Indication	Secondary acute myeloid leukemia (sAML) or high-risk myelofibrosis (HR-MF)
Goal	Completion of IND-enabling studies and IND filing with FDA
Funds Requested	$3,200,000 Co-funding: $800,000 (20% required)

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

CLIN1-14607: Background Information

Clinical Background: Secondary acute myeloid leukemia (sAML) can develop from pre-existing high-risk myelofibrosis, a blood cancer that disrupts the body's normal production of blood cells. The five-year survival rate for patients with sAML is only 26%. Standard of care therapies are generally not curative and can result in significant morbidities. A key factor in the severity and recurrence of these cancers is the persistence of cancer stem cells.

Value Proposition of Proposed Therapy: The proposed therapy blocks a key RNA-modifying enzyme that promotes cancer stem cell persistence. As a small molecule drug, the approach could provide a clinically practical and feasible treatment option to patients.

Why a stem cell or gene therapy project: The therapeutic candidate is a small molecule that acts on cancer stem cells.

CLIN1-14607: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $6,000,000	Phase 1 clinical trial	Sep 2023	AML, CMML	Monoclonal antibody	Antibody targets LILRB4, an immune inhibitory receptor, to facilitate immune recognition of cancer cells .
CLIN1 $6,000,000	IND-enabling	Jan 2025	AML	Vaccine	Patient AML cells are genetically modified to stimulate the immune system. Cells injected as a vaccine.

8 additional active clinical stage projects related to blood cancers, but not addressing AML or MF

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
INFR5	N/A	Alpha Clinic	Feb 2023 – Jan 2028	$8,000,000	6 milestones proposed to expand and manage existing Alpha Clinics site.
TRAN1	Acute myeloid leukemia	Pre-IND	Mar 2018 – Nov 2020	$2,511,767	4 milestones proposed to conduct manufacturing and preclinical studies. All milestones achieved.
INFR	N/A	Alpha Clinic	May 2017 – Jul 2022	$7,999,137	5 milestones proposed and all completed on time.
Disease Team	Chronic lymphocytic leukemia	Phase 1 clinical trial	Jun 2014 – Nov 2017	$4,179,598	11 milestones proposed and all completed on time.
Candidate Discovery	Leukemia	Therapeutic candidate	May 2011 – Apr 2014	$3,103,041	4 milestones proposed and all completed on time.

3 additional CIRM awards

CLIN1-14607: 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: $ 3,200,000*

*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 CLIN2-14748 application
Maria Bonneville
Steve Juelsgaard

CLIN2-14748

Title	Evaluation of Safety and Feasibility of Cytomegalovirus-Specific, Anti-HIV Chimeric Antigen Receptor (CMV/HIV-CAR) T Cells in People with HIV
Therapy	Cytomegalovirus (CMV)-specific T cells that express a chimeric antigen receptor (CAR) which targets and eliminates HIV-infected cells
Indication	HIV/AIDS
Goal	Completion of phase 1 (first-in-human) clinical trial
Funds Requested	$11,299,976 Co-funding: $0 (none required)

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

CLIN2-14748: Background Information

Clinical Background: Human immunodeficiency virus (HIV) severely weakens the immune system and infected individuals become susceptible to infections and some types of cancer. Antiretroviral therapy (ART) is a life-long treatment to manage HIV infection, but it is not a cure and is associated with high morbidity and costs. More effective and potentially curative treatments are needed.

Value Proposition of Proposed Therapy: People with HIV maintain a high level of T cells specific to CMV despite their immune deficiency. The proposed approach leverages this fact to create a potentially curative CAR T cell therapy that can recognize and destroy HIV-infected cells and remain actively vigilant by way of CMV signaling.

Why a stem cell or gene therapy project: The therapeutic candidate contains blood progenitor cells and involves gene manipulation.

CLIN2-14748: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $6,852,486	Phase 1/2a clinical trial	Dec 2026	HIV/AIDS	Gene therapy	In vivo gene therapy used to excise the replication-competent proviral HIV from latently infected cells
CLIN2 $8,970,732	Phase 1/2 clinical trial	Sep 2024	HIV/AIDS	HIV-specific CAR T cells	CAR T cell therapy targeting HIV-infected cells
CLIN2 $8,414,265	Phase 1 clinical trial	Aug 2023	AIDS Lymphoma	Genetically modified blood stem cells	Modified blood stem cells are intended to replace the immune system with HIV resistant cells.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN1	HIV/AIDS	File IND	Dec 2018 – Dec 2022	$3,812,797	4 milestones complete, one on time and three with delays due to COVID-19 pandemic.
CLIN1	Glioblastoma	File IND	Aug 2018 – Jul 2023	$3,684,259	4 milestones proposed, 2 completed on time, one completed with minor delay and one pending.
INFR	N/A	Alpha Clinic	Feb 2015 – Oct 2022	$8,456,000	6 milestones proposed, 5 completed on time, 1 completed with minor delays.
Clinical trial	HIV/AIDS	Phase 1 clinical trial	Apr 2015 – Jun 2022	$5,583,438	4 milestones proposed, 1 completed on time, 3 completed with delay.
Disease Team	HIV/AIDS	Preclinical, IND-enabling	May 2010 – Sep 2014	$14,583,187	10 milestones proposed, 9 completed on time, and 1 completed with minor delay

1 additional CIRM award

CLIN2-14748: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	12
2	1
3	0

DEI Score: 10 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 11,299,976*

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

CLIN2-14787

Title	A Phase 2b, Randomized, Assessor-Masked Clinical Trial to Assess the Safety and Efficacy of a Retinal Pigmented Epithelial (RPE) Implant in Subjects with Geographic Atrophy
Therapy	A patch comprised of a layer of stem cell-derived retinal pigmented epithelial (RPE) cells on a supporting matrix
Indication	Geographic atrophy (GA), the late-stage form of age-related macular degeneration (AMD)
Goal	Completion of a phase 2b clinical trial
Funds Requested	$12,373,748 Co-funding: $8,250,000 (40% required)

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

CLIN2-14787: Background Information

Clinical Background: Age-related macular degeneration (AMD) is a leading cause of vison loss in the developed world. Geographic atrophy (GA), is the late-stage form of dry AMD, where supportive retinal pigment epithelium cells (RPE) degenerate over time. RPE loss contributes to the death of photoreceptors that then leads to visual impairment in late stages of the disease.

Value Proposition of Proposed Therapy: The proposed therapy would be a scalable approach to replace the diseased portion of GA and promote the survival and function of RPE cells, protecting the eye from disease progression and vision loss, and in some cases potentially improving vision.

Why a stem cell or gene therapy project: The therapeutic candidate is a combination therapy that contains stem cell-derived RPE.

CLIN2-14787: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1 $4,235,758	Preclinical	Mar 2024	Dry AMD	Allogeneic neural stem cell therapy product	The cells secrete factors and stimulate endogenous cells in target areas to restore function and prevent vision decline.
CLIN1 $6,000,000	Preclinical	May 2025	Maculopathies related to RPE atrophy	Autologous iPSC-derived RPE cells	A cell therapy intended to replace endogenous RPE cells.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
Disease Team	AMD	Clinical studies	Aug 2014 – Mar 2019	$16,339,827	Phase 1 clinical trial preparation and activities. 8 milestones proposed, 6 completed on time, 2 completed with delay.
Disease Team	AMD	IND enabling	Apr 2010 – Dec 2014	$18,904,916	IND enabling studies and activities. All proposed milestones were achieved. The project resulted in successful although delayed IND filing.

CLIN2-14787: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	9
2	5
3	0

DEI Score: 9.5 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $12,373,748*

*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 CLIN1-14933 application
Fred Fisher

CLIN1-14933

Title	Manufacturing an Antisense oligonucleotides for a Phase 1/2 Clinical Trial for Amyotrophic Lateral Sclerosis
Therapy	An antisense oligonucleotide
Indication	Amyotrophic Lateral Sclerosis
Goal	Completion of manufacturing activities and IND filing with FDA
Funds Requested	$2,199,782 Co-funding: $549,946 (20% required)

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

CLIN1-14933: Background Information

Clinical Background: ALS is a neurodegenerative disease that results in the death of nerve cells in the brain and spinal cord, causing the muscles in the body to gradually weaken, leading to loss of limb function, difficulty breathing, paralysis, and eventually death. There are medications that can slow down the progression of ALS, but unfortunately there is no cure for the disease.

Value Proposition of Proposed Therapy: The proposed therapy offers an opportunity to treat ALS patients with various underlying causes and have a greater impact on patient quality of life than the current standard of care.

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

CLIN1-14933: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $11,990,372	Phase 1 clinical trial	Oct 2025	ALS	Genetically engineered stem cells	The stem cells are transplanted into the brain and become support cells that help protect motor neuron function.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14933: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	13
2	1
3	0

DEI Score: 7.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $2,199,782*

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

CLIN2-15087

Title	Phase I Study of Chimeric Antigen Receptor Engineered T Cells targeting CD33 for the Treatment of Relapsed/Refractory Acute Myeloid Leukemia
Therapy	Immune T cells from a patient's transplant donor engineered for targeted leukemia killing
Indication	Relapsed or refractory acute myeloid leukemia
Goal	Completion of phase 1 clinical trial
Funds Requested	$11,983,547 Co-funding: $0 (none required)

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

CLIN2-15087: Background Information

Clinical Background: Relapsed or refractory acute myeloid leukemia (AML) is a type of leukemia that has either returned after prior treatment or has not responded to prior treatment. Available treatments are not very effective, and this type of leukemia is known to have poor outcomes.

Value Proposition of Proposed Therapy: The therapeutic options for refractory AML remain limited, and options for patients are needed. The proposed therapy uses a targeted approach to kill the cancer cells and lead to improved outcomes for AML patients.

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

CLIN1-15087: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $6,000,000	Phase 1 clinical trial	Sep 2023	AML, CMML	Monoclonal antibody	Antibody targets LILRB4, an immune inhibitory receptor, to facilitate immune recognition of cancer cells .
CLIN1 $6,000,000	IND-enabling	Jan 2025	AML	Vaccine	Patient AML cells are genetically modified to stimulate the immune system. Cells injected as a vaccine.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-15087: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	13
2	2
3	0

DEI Score: 10.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 11,983,547*

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