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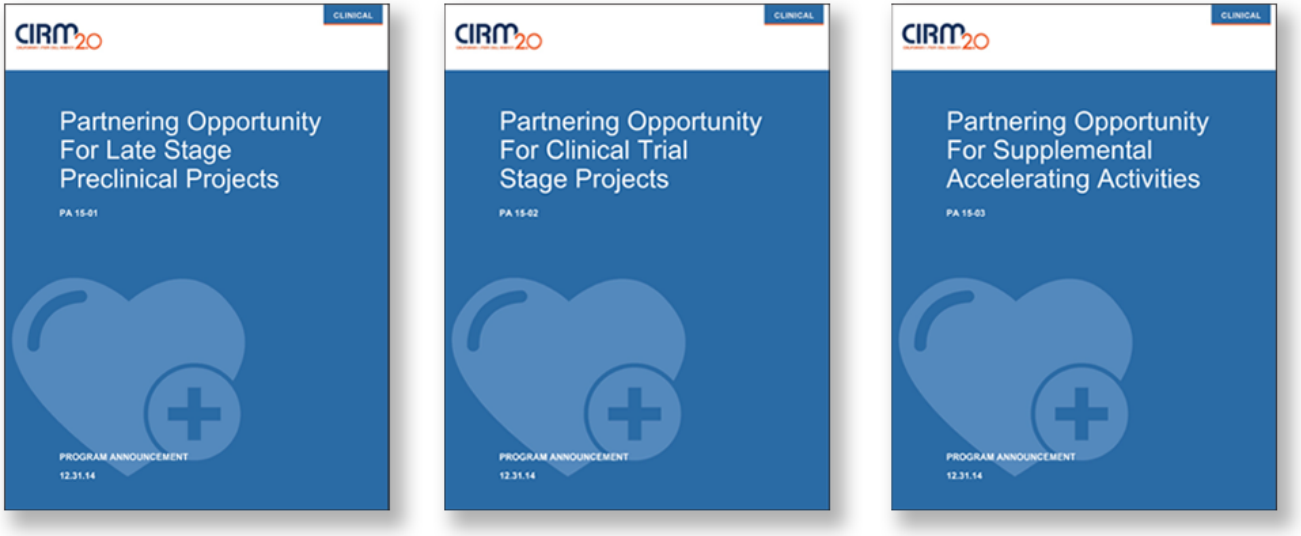
CIRM
CALIFORNIA'S STEM CELL AGENCY

Clinical Stage Programs

CLINICAL STAGE



CLIN 1 **CLIN 2** **CLIN 3**

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?)

CLIN 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 cannot be resubmitted for 6 months after the GWG review.

Applications are scored by all scientific members of the GWG with no conflict.

GWG Recommendations

General CLIN2 Applications	Number of Apps	Total Applicant Request
Recommended for funding Score of “1”	3	$21,695,691
Needs improvement Score of “2”	3	

CIRM Team Recommendation: Fund all projects with a score of “1”.

CLIN2-12095: Project Summary

Therapy	Autologous gene-corrected hematopoietic stem cells (HSC)
Indication	Infantile Malignant Osteopetrosis
Goal	Phase 1 trial completion
Funds Requested	$3,728,485 ($1,597,923 Co-funding)

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

CLIN2-12095: Background Information

Clinical Background: Infantile malignant osteopetrosis is an extremely rare (incidence ~1:250,000 live births) and lethal condition in young children resulting from mutations in the TCIRG1 gene, which is critical for bone resorption, and leads to blindness, deafness, bone marrow failure and death.

Value Proposition of Proposed Therapy: The standard of care when identified early is an allogeneic bone marrow transplant, which is associated with significant morbidity and mortality. The proposed therapy uses autologous HSC in which the TCIRG1 gene has been corrected and offers the potential to halt disease progression.

Why a stem cell project: The proposed therapy includes hematopoietic stem cells.

CLIN2-12095: Similar CIRM Portfolio Projects

CIRM is not currently funding any other project for this disease indication.

CLIN2-12095: Previous CIRM Funding

Applicant has received previous funding from CIRM for a project with an unrelated candidate and indication.

Project Stage	Project Outcome	Project Duration	Award Amount	Milestone Achievement
Clinical trial	Complete phase 1 trial	Jun 2019 – Jul 2023	$6,567,085	7 milestones: 1 on time, 2 minor delay

CLIN2-12095: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Score	GWG Votes
1	13
2	1
3	0

CIRM Team Recommendation: Fund (concur with GWG recommendation)

Award Amount: $3,728,485*

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

CLIN2-12090: Project Summary

Therapy	Autologous duoCAR T cells
Indication	HIV infection
Goal	Phase 1 trial completion
Funds Requested	$8,970,732 ($0 Co-funding)

Maximum funds allowable for this category: $9,000,000

CLIN2-12090: Background Information

Clinical Background: There are approximately 38 million people world-wide infected and living with HIV. An estimated 1.7 million acquired HIV in 2019. Standard of care involves anti-retroviral therapy (ART), which is successful in controlling HIV infection, but it requires lifelong adherence and is not a cure.

Value Proposition of Proposed Therapy: HIV persists in the body in long-lived cells and latent viral reservoir. The proposed therapy offers the potential to effectively cure patients of HIV infection by targeting and killing HIV-infected cells and persisting in the body to survey and kill any remaining HIV-infected cell.

Why a stem cell project: The proposed therapy includes T memory stem cells.

CLIN2-12090: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
Current Application	Phase 1 trial	N/A	HIV/AIDS	HIV-specific autologous duoCAR T cells	Targeting and killing of HIV-infected cells
CLIN1	IND	Feb 2021	HIV/AIDS	HIV-specific autologous CAR T cells	Targeting and killing of HIV-infected cells
Strategic Partnership Award	Phase 1	Mar 2021	HIV/AIDS	CCR5-modified autologous HSC	Provides a long-lasting source of HIV-resistant cells in patients
CLIN2	Phase 1/2	Aug 2021	HIV-related lymphoma, HIV/AIDS	Autologous HSC modified with combination of anti-HIV genes	Generate HIV-resistant immune cells in patients with HIV-related lymphoma

CLIN2-12090: Previous CIRM Funding

Applicant has not previously received funding from CIRM.

CLIN2-12090: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Score	GWG Votes
1	12
2	2
3	0

CIRM Team Recommendation: Fund (concur with GWG recommendation)

Award Amount: $8,970,732*

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

CLIN2-12129: Project Summary

Therapy	Placental-derived mesenchymal stem cells
Indication	Myelomeningocele (spina bifida)
Goal	Phase 1 trial completion
Funds Requested	$8,996,474 ($0 Co-funding)

Maximum funds allowable for this category: $9,000,000

CLIN2-12129: Background Information

Clinical Background: Myelomeningocele (MMC)is the most severe form of spina bifida, resulting from incomplete closure of the spinal cord during gestation which leaves a portion of the fetal spinal cord unprotected. Intrauterine chemical and mechanical trauma to the exposed spinal cord causes neuronal tissue damage that results in lifelong lower body paralysis and bowel and bladder dysfunction. Standard of care involves in utero surgical repair but 55% of children are still unable to walk independently and have bowel and bladder disabilities.

Value Proposition of Proposed Therapy: The proposed therapy would augment in utero repair by protecting motor neurons from damage and potentially improve quality of life for affected children.

Why a stem cell project: The proposed therapy includes mesenchymal stem cells.

CLIN2-12129: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
Current Application	Phase 1 trial	N/A	Myelomeningocele	Mesenchymal stem cells	Motor neuron protection
CLIN1	IND	Dec 2020	Myelomeningocele	Mesenchymal stem cells	Motor neuron protection

CLIN2-12129: Previous CIRM Funding

Applicant has received previous funding from CIRM for earlier stages of this project as described below.

Project Stage	Project Outcome	Project Duration	Award Amount	Milestone Achievement
Late Stage Preclinical	Filed IND	Jan 2019 – Dec 2020	$5,666,077	5 milestones: 3 on time, 1 on track, 1 minor delay
Preclinical	Pre-IND	Sep 2015-Aug 2018	$2,182,146	6 milestones: 3 on time, 3 minor delays

CLIN2-12129: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Score	GWG Votes
1	14
2	0
3	0

CIRM Team Recommendation: Fund (concur with GWG recommendation)

Award Amount: $8,996,474*

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

GWG Recommendations
Sickle Cell Disease Initiative

Sickle Cell Disease CLIN2 Applications	Number of Apps	Total Applicant Request
Recommended for funding Score of "1"	1	$8,333,581

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CLIN2SCD-12031: Project Summary

Therapy	Autologous gene-modified hematopoietic stem cells
Indication	Sickle Cell Disease
Goal	Phase 2 trial completion
Funds Requested	$8,333,581*

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

*Total cost of project is $34,393,842 with CIRM contributing to about 25% for California portion of the project and NHLBI contributing remainder.

CLIN2SCD-12031: Background Information

Clinical Background: SCD affects approximately 100,000 Americans. SCD is particularly common in those with sub-Saharan African ancestry affecting 1 in 365 African-American births. Globally, over 300,000 babies are born with SCD every year.

Value Proposition of Proposed Therapy: The only current cure is allogeneic HSC transplantation, but donor availability is very limited with high risk of complications such a GVHD. The proposed autologous therapy would avoid the medical risks of allogeneic transplant and need for donors while providing a potential cure.

Why a stem cell project: The therapy includes hematopoietic stem cells.

CLIN2SCD-12031: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1	IND	11/30/2020	Sickle Cell Disease	Autologous CRISPR-edited hematopoietic stem cells	Virus-free CRISPR editing to correct the pathogenic hemoglobin S allele mutation in HSC
CLIN1	IND	07/31/2020	Sickle Cell Disease	Autologous CRISPR-edited hematopoietic stem cells	CRISPR editing to correct the pathogenic hemoglobin S allele mutation in HSC
CLIN2	Phase 1	12/31/21	Sickle Cell Disease	Autologous lentiviral gene-modified hematopoietic stem cells	Expression of lentiviral transferred anti-sickling hemoglobin gene
CLIN2	Phase 1	10/31/23	Sickle Cell Disease	Allogeneic cord blood hematopoietic stem cells	Hematopoietic stem cell transplantation to replace patient sickle red blood cells
CLIN2	Phase 1	04/30/22	Sickle Cell Disease	CD4 T Cell depleted haploidentical HSC transplant	Achieving immune tolerance by inducing mixed chimerism

CLIN2SCD-12031: Previous CIRM Funding

Applicant has not previously received funding from CIRM.

CLIN2SCD-12031: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Score	GWG Votes
1	13
2	2
3	0

CIRM Team Recommendation: Fund (concur with GWG recommendation)

Award Amount: $8,333,581*

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