GWG Recommendations: Clinical Program (CLIN1, CLIN2, CLIN4)

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

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Associate Director, Portfolio Development and Review

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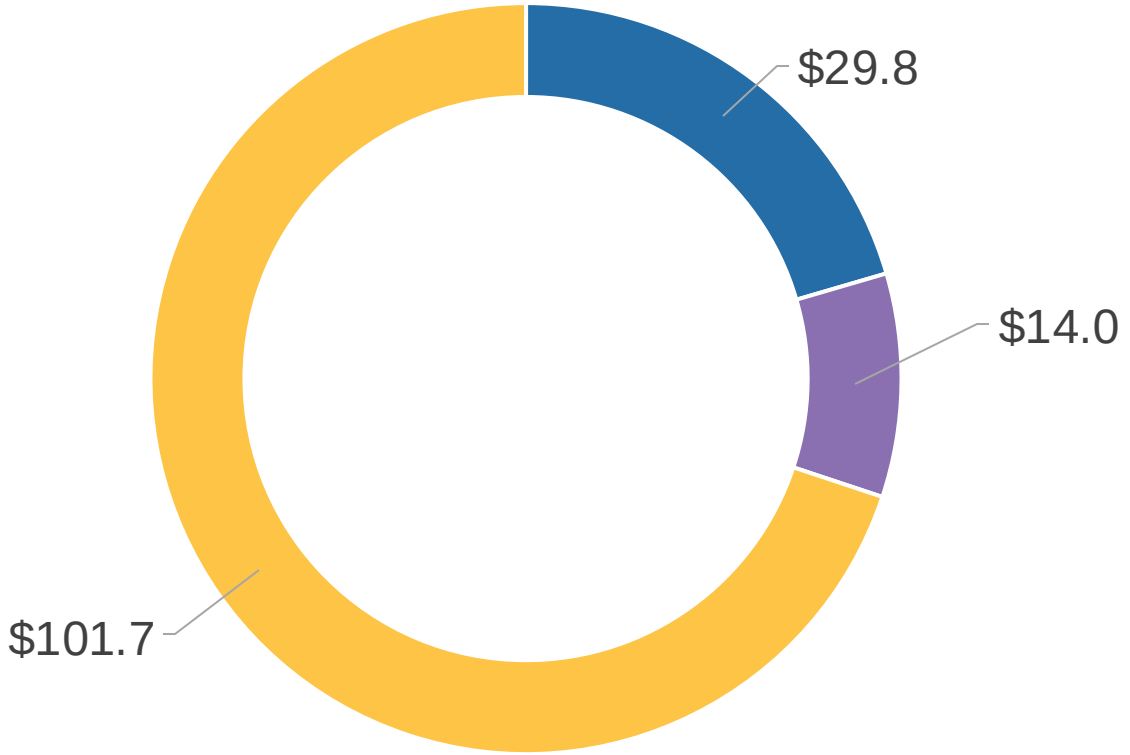
Our Mission

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

Clinical Budget Status

Annual Allocation: $145.5 million (July to December 2024)

- Amount Requested Today
- Approved Awards
- Unused Balance



Clinical 

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.

Clinical 

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 principles of diversity, equity, and inclusion (DEI)? *(e.g., does it consider patient diversity?)*

Clinical 

Diversity, Equity and Inclusion Scoring System

- 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*

Applications are scored for adherence to principles of DEI by all GWG Board Members with no conflict.

The criteria used to measure adherence fall under overarching categories of: Commitment to DEI, Project Plans and Cultural Sensitivity.

Clinical

Review Panel Roles

Scientific GWG Members	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

Board Members with Conflicts of Interest

Board Members with Conflicts of Interest for CLIN2-17078

Dan Bernal

Elena Flowers

Chris Miaskowski

Karol Watson

CLIN2-17078

Efficacy and safety of cryopreserved autologous CD34+ HSC transduced with EFS-ADA lentiviral vector encoding for human ADA gene in ADA-SCID subjects

FUNDS REQUESTED

$14,798,337

Co-funding: $9,865,558 (40% required)

California organization

THERAPY

Autologous CD34+ hematopoietic stem cells gene edited to express ADA enzyme

INDICATION

Children with Adenosine Deaminase-Deficient Severe Combined Immunodeficiency

GOAL

Establish commercial manufacturing of lentivirus vector and drug product

CLIN2-17078 Background Information

Clinical background

Babies born with Adenosine Deaminase-Deficient Severe Combined Immunodeficiency (ADA-SCID) do not have a functioning immune system, and the condition is fatal if not treated. The current ideal treatment is a stem cell transplant with a matched related donor, but this is available for only 20% of patients.

Value proposition of proposed therapy

For patients without an ideal donor, there is a significant risk of transplant rejection and long-term side effects of treatment. The proposed therapy to correct the patient's copy of the ADA enzyme is a potentially curative treatment that would not have rejection risk and lowers the risk of long-term side effects.

Why a stem cell or gene therapy project

The therapy is a gene edited stem cell product.

CLIN2-17078 Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $18,572,670	Phase 2 Clinical Trial	Q2 2027	ADA-SCID	Autologous CD34+ HSPC transduced by the EFS-ADA lentiviral vector to express ADA enzyme	Transplantation of the gene corrected cells expressing ADA enzyme aims to restore protective immunity

CLIN2-17078 Previous CIRM Funding to Applicant Team

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $18,572,670	Phase 2 clinical trial	Q2 2027	ADA-SCID	Autologous CD34+ HSPC transduced by the EFS-ADA lentiviral vector to express ADA enzyme	Transplantation of the gene corrected cells expressing ADA enzyme aims to restore protective immunity
TRAN1 $4,309,973	Preclinical	Jan 2026	X-linked Agammaglobulinemia (XLA)	BTK gene edited autologous CD34+ HSPC	Transplantation of the gene corrected cells aims to restore normal B cell and antibody production
DISC2 $1,177,739	Candidate discovery	Feb 2025	Alpha Thalassemia	Autologous CD34+ HPSC transduced with the α-globin lentiviral vector (AGLV)	Transplantation of the gene corrected cells aims to restore normal hemoglobin production

CLIN2-17078 Previous CIRM Funding to Applicant Team (continued)

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $7,083,364	Phase 1/2 clinical trial	Sep 2024	X-linked Chronic Granulomatous disease (X-CGD)	Autologous CD34+ hematopoietic stem cells transduced with the G1XCGD lentiviral vector	Transplantation of the gene corrected cells aims to restore the immune system
TRAN1 $4,751,297	Preclinical	Dec 2024	Pulmonary arterial hypertension	Autologous MPO Knock-Out Hematopoietic Stem and Progenitor Cells (HSPCs)	Gene edited HPSCs aim to prevent the progression/worsening of pulmonary arterial hypertension
DISC2 $219,230	Candidate discovery	Jun 2022	X-linked Agammaglobulinemia (XLA)	BTK gene edited autologous CD34+ HSPCs	Transplantation of the gene corrected cells aims to restore normal B cell and antibody production
DR3 $13,145,465	Phase 1/2 clinical trial	Dec 2025	Sickle Cell Disease	Autologous gene corrected hematopoietic stem cells	Transplantation of hemoglobin gene corrected cells that blocks sickling of the red blood cells

CLIN2-17078 GWG Review

Efficacy and safety of cryopreserved autologous CD34+ HSC transduced with EFS-ADA lentiviral vector encoding for human ADA gene in ADA-SCID subjects

CIRM Award Amount:

$14,798,337*

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

GWG RECOMMENDATION

Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI SCORE

8.5 (scale 1-10)

CIRM TEAM RECOMMENDATION

Fund (concur with GWG recommendation)

Board Members with Conflicts of Interest

Board Members with Conflicts of Interest for CLIN2-17127

Maria Bonneville

Dan Bernal

Ysabel Duron

Elena Flowers

Chris Miaskowski

CLIN2-17127

Gene Therapy for Artemis-Deficient Severe Combined Immunodeficiency Using a Self-Inactivating Lentiviral Vector

FUNDS REQUESTED

$14,999,999

Co-funding: $0 (none required)

California organization

THERAPY

The gene for Artemis inserted into hematopoietic stem cells from patients with Artemis deficient SCID

INDICATION

Artemis-deficient severe combined immunodeficiency (ART-SCID)

GOAL

Complete Phase 2 trial and submit BLA

CLIN2-17127 Background Information

Clinical background

Babies born with Artemis-deficient severe combined immunodeficiency (ART-SCID) do not have a functioning immune system. This rare genetic condition is fatal if not treated and disproportionately impacts Native American populations. The current standard of care bone marrow transplant has more complications than other types of SCID, and many still need frequent expensive immune globin treatments because their immune systems are not fully restored.

Value proposition of proposed therapy

The project aims to genetically modify the patient's own blood stem cells with a functional copy of Artemis, with the goal of restoring a healthy immune system. Using the patient's own cells reduces many of the risks with transplantation, such as graft rejection, and has more complete restoration of the immune system.

Why a stem cell or gene therapy project

The therapy is (made from stem-cell derived/a gene therapy product).

CLIN2-17127 Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $12,000,000	Phase 1 clinical trial	Q4 2024	Artemis-Deficient SCID	Lentiviral Gene Therapy for Artemis-Deficient SCID	Restore production of normal Artemis protein to restore the adaptive immune system

CLIN2-17127 Previous CIRM Funding to Applicant Team

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $12,000,000	Phase 1 clinical trial	Nov 2024	Artemis-Deficient SCID	Lentiviral Gene Therapy for Artemis-Deficient SCID	Restore production of normal Artemis protein to restore the adaptive immune system
CLIN1 $4,268,865	IND enabling	April 2018	Artemis-Deficient SCID	Lentiviral Gene Therapy for Artemis-Deficient SCID	Restore production of normal Artemis protein to restore the adaptive immune system
TR3 $3,862,367	Preclinical	Oct 2016	Artemis-Deficient SCID	Lentiviral Gene Therapy for Artemis-Deficient SCID	Restore production of normal Artemis protein to restore the adaptive immune system

CLIN2-17127 GWG Review

Gene Therapy for Artemis-Deficient Severe Combined Immunodeficiency Using a Self-Inactivating Lentiviral Vector

CIRM Award Amount:

$14,999,999*

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

GWG RECOMMENDATION

Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	14
2	0
3	0

DEI SCORE

8 (scale 1-10)

CIRM TEAM RECOMMENDATION

Fund (concur with GWG recommendation)

CIRM

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Thank You

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