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

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

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Director, Portfolio Development and Review

ICOC/ARS Meeting

March 27, 2025

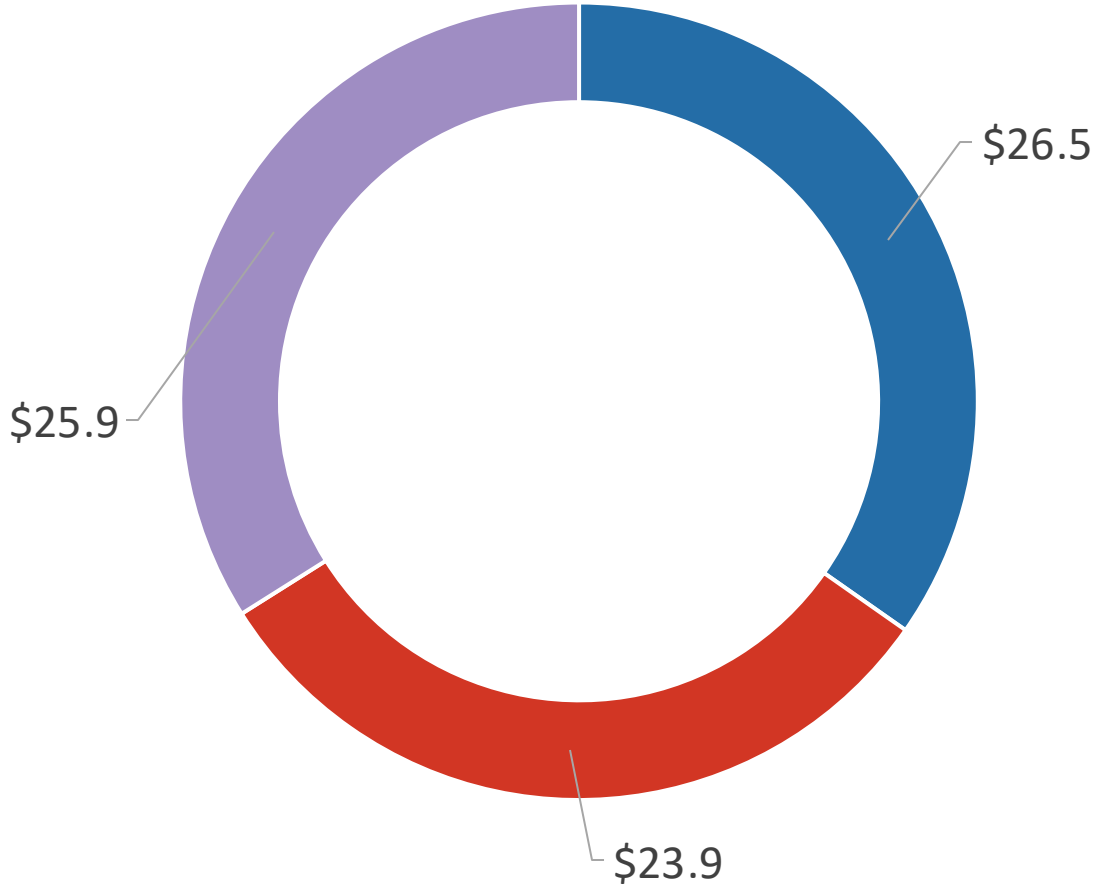
Our Mission

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

Clinical Budget Status

Budget Allocation: $76.7 million (Jan to June 2025)

- 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

CLIN1-17103

Expression of Ube3a by the hematopoietic system for the treatment of Angelman syndrome

FUNDS REQUESTED

$4,487,656

Co-funding: $0 (none required)

California organization

THERAPY

Autologous human CD34+ hematopoietic stem and progenitor cells transduced with a Ube3a expressing lentiviral vector

INDICATION

Angelman syndrome

GOAL

Submit an IND

CLIN1-17103 Background Information

Clinical background

Angelman syndrome (AS) is a rare genetic neurodevelopmental disorder that develops in early childhood. People with Angelman syndrome have seizures, movement and balance issues, and intellectual disabilities, including impaired speech. This is a progressive chronic condition that requires lifelong aid and the current standard of care treats symptoms only.

Value proposition of proposed therapy

The proposed product is a one-time treatment that modifies the patient's own hematopoietic stem and progenitor cells with a corrected Ube3a gene. The transplanted cells will then deliver functional Ube3a protein and have the potential to prevent, halt or reverse symptoms associated with AS.

Why a stem cell or gene therapy project

The therapy is a gene modified stem cell product.

CLIN1-17103 Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1 $5,276,765	Preclinical	Q2 2027	Angelman syndrome	Functional UBE3A expressing autologous hematopoietic stem cells	Autologus gene modified stem cells will be transplanted and provide the therapeutic protein, UBE3A

CLIN1-17103 Previous CIRM Funding to Applicant Team

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1 $4,048,253	IND enabling	Jan 2025	Tay-Sachs disease	HexA/HexB expressing-autologous hematopoietic stem cells	Autologous HSPC genetically modified with HexA/HexB engraft in the brain and deliver functional beta-hexosaminidase to affected neurons
TRAN1 $883,174	Preclinical	Sep 2019	Tay-Sachs disease	HexA/HexB expressing-autologous hematopoietic stem cells	Autologous HSPC genetically modified with HexA/HexB engraft in the brain and deliver functional beta-hexosaminidase to affected neurons

CLIN1-17103 GWG Review

Expression of Ube3a by the hematopoietic system for the treatment of Angelman syndrome

CIRM Award Amount:
$4,487,656*

*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)

CLIN2-17080

[redacted] for prevention of GvHD in patients receiving HLA mismatched HSCT for the treatment of hematologic malignancies

FUNDS REQUESTED

$8,000,000

Co-funding: $4,732,279 (40% required)

California organization

THERAPY

A CD4+ T cell investigational allogeneic, off-the-shelf cellular therapy product for the prevention of GvHD

INDICATION

Prevention of graft-versus-host disease

GOAL

Complete Phase 1 study

CLIN2-17080 Background Information

Clinical background

People undergoing mismatched hematopoietic stem cell transplants for the treatment of blood cancers are often affected by graft versus host disease (GvHD), where donor cells attack recipient tissue and organs. Standard of care treatments for GvHD often don't work, usually suppress the immune system which increases the risk of infections and can also impact the effectiveness of the cancer treatments. In some patients, GvHD can be potentially life threatening and cause tissue damage in multiple organ systems.

Value proposition of proposed therapy

The proposed allogenic, off the shelf, engineered regulatory T cell product could increase access to transplants for individuals who are candidates for transplants but lack a suitable matched donor, while reducing the burden of GvHD.

Why a stem cell or gene therapy project

The therapy is made from stem/progenitor cells.

CLIN2-17080 Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $11,996,634	Clinical Trial	Q4 2025	Children and young adults with leukemia receiving stem cell transplants	Immune cells enriched for type 1 regulatory T cells	Delivering the enriched cell product accelerates stem cell transplant recovery without GvHD, improving cancer outcomes
CLIN1 $3,457,858	IND enabling	Q1 2025	Acute GvHD resulting from stem cell transplantation	Cryopreserved interferon-gamma primed bone marrow mesenchymal stem cells (MSCs)	MSCs suppress the immune response of the transplant recipient through cell-cell contact and secreted factors to reduce GvHD

CLIN2-17080 Previous CIRM Funding to Applicant Team

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1 $4,000,000	IND enabling	Nov 2024	Prevention of GvHD	Allogeneic off-the-shelf CD4+ T cells	Suppress GvHD by secretion cytokines in target tissues and organs, and stimulate production of new Tr1 cells

CLIN2-17080 GWG Review

[redacted] for prevention of GvHD in patients receiving HLA mismatched HSCT for the treatment of hematologic malignancies

CIRM Award Amount:

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GWG RECOMMENDATION

Exceptional merit and warrants funding

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2	0
3	0

DEI SCORE

8 (scale 1-10)

CIRM TEAM RECOMMENDATION

Fund (concur with GWG recommendation)

CLIN2-17135

Inhibitory Interneuron Cell Therapy for the Treatment of Drug-resistant Bilateral Temporal Lobe Epilepsy

FUNDS REQUESTED

$13,999,983

Co-funding: $9,333,321 (40% required)

California organization

THERAPY

Inhibitory interneuron cell therapy derived from human embryonic stem cells

INDICATION

Focal epilepsy; bilateral drug-resistant mesial temporal lobe epilepsy (MTLE)

GOAL

Completion of a Phase 1/2 trial

CLIN2-17135 Background Information

Clinical background

Epilepsy impacts about 1% of adults in the US. Epilepsy is a neurological disorder that causes recurring seizures. Anti-seizure medications are the main way in which epilepsy is treated. However, one third or more of people living with epilepsy have drug-resistant seizures, impacting their quality of life. Current treatments for drug-resistant epilepsy include surgical methods which destroy tissue and can cause serious, irreversible adverse effects.

Value proposition of proposed therapy

The proposed product is targeted, non-tissue-destructive, one-time delivery of cells into the impacted brain regions. The cell replacement therapy aims to rebalance neural activity in the localized brain area and hopes to provide long-lasting seizure reduction.

Why a stem cell or gene therapy project

The therapy is made from stem/progenitor cells.

CLIN2-17135 Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $7,999,999	Clinical Trial	Q2 2026	Unilateral Mesial Temporal Lobe Epilepsy	Inhibitory interneuron cell therapy	The interneuron cells integrate and release inhibitory neurotransmitter GABA, reducing seizures
TRAN1 $3,828,714	Preclinical	Q1 2027	Temporal lobe epilepsy	Universal allogeneic inhibitory interneuron cell therapy	The interneuron cells integrate and release inhibitory neurotransmitter GABA, reducing seizures

CLIN2-17135 Previous CIRM Funding to Applicant Team

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $7,999,999	Clinical Trial	June 2026	Unilateral Mesial Temporal Lobe Epilepsy	Inhibitory interneuron cell therapy	The interneuron cells integrate and release inhibitory neurotransmitter GABA, reducing seizures
TRAN1 $4,848,505	Preclinical	Aug 2021	Chronic temporal lobe epilepsy	Inhibitory interneuron cell therapy	The interneuron cells integrate and release inhibitory neurotransmitter GABA, reducing seizures
DISC2 $1,616,536	Candidate Discovery	June 2019	Temporal lobe epilepsy	Inhibitory interneuron cell therapy	The interneuron cells integrate and release inhibitory neurotransmitter GABA, reducing seizures
TRAN1 $3,828,714	Preclinical	Feb 2027	Temporal lobe epilepsy	Universal allogeneic inhibitory interneuron cell therapy	The interneuron cells integrate and release inhibitory neurotransmitter GABA, reducing seizures

CLIN2-17135 GWG Review

Inhibitory Interneuron Cell Therapy for the Treatment of Drug-resistant Bilateral Temporal Lobe Epilepsy

CIRM Award Amount:
$13,999,983*

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GWG RECOMMENDATION

Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
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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