

# Real Life™

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Vice President, Portfolio Development and Review

Grants Working Group Recommendations CLIN

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**CIRM**  
CALIFORNIA'S STEM CELL AGENCY

## OUR MISSION

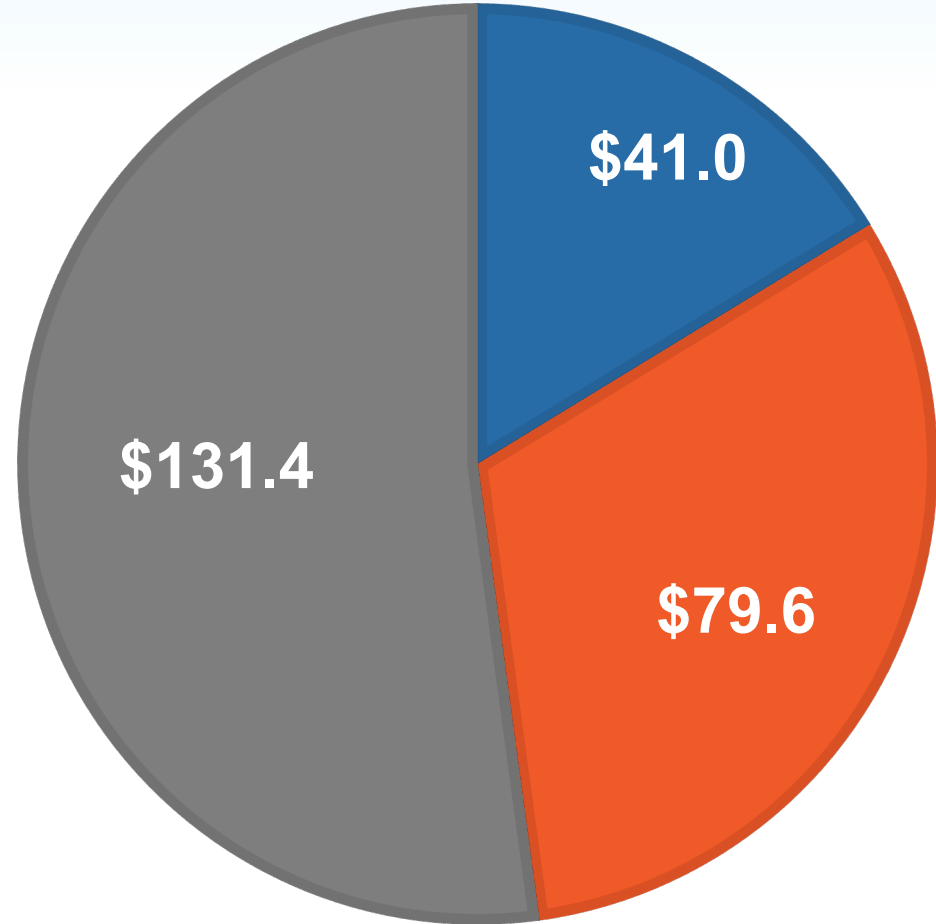
Accelerating world class science  
to deliver transformative  
regenerative medicine treatments  
in an equitable manner to a  
diverse California and world



**Annual Allocation: \$ 252 million**

- Amount Requested Today
- Approved Awards
- Unused Balance

Amounts are shown in millions



- **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.

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?*)

CIRM CLIN Program DEI Rubric				
CRITERIA	Score of 0 to 2	Score of 3 to 5	Score of 6 to 8	Score of 9 to 10
	Not Responsive	Not Fully Responsive	Responsive	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*

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

<b>Title</b>	Prevention of GvHD in patients receiving HLA mismatched related or unrelated allogeneic HSCT for the treatment of hematologic malignancies.
<b>Therapy</b>	Allogeneic regulatory T cells
<b>Indication</b>	Patients with hematologic malignancies at risk of GvHD from stem cell transplant
<b>Goal</b>	Complete IND-enabling activities and file an IND
<b>Funds Requested</b>	\$4,000,000 Co-funding: \$1,000,000 (20% required)

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



**Clinical Background:** Hematologic malignancies (such as acute leukemias and lymphomas) are the most common types of cancer in children and young adults.

**Value Proposition of Proposed Therapy:** The current standard of care for high-risk or refractory cancers is chemotherapy and allogeneic hematopoietic stem cells transplant. However, there is often a lack of matched donors as well as a high risk of rejection or GVHD for these patients. The proposed therapy offers the opportunity for greatly improving outcomes for patients undergoing HSCT.

**Why a stem cell project:** The therapeutic candidate is manufactured from CD4+ T-cell progenitor cells and is combined with a hematopoietic stem cell transplant.

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	Oct 2025	Hematologic malignancies	T-cell immunotherapy	Regulatory T-cell product decreases GvHD related to stem cell transplant

# Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN2	Hematologic malignancies	Complete Phase 1 trial	Nov 2021 – Oct 2025	\$10,563,822	Five milestones proposed, three completed on time, and two on track.

**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:** \$4,000,000\*

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

<b>Title</b>	Personalized antisense oligonucleotide therapy for rare pediatric genetic disease: SCN2A
<b>Therapy</b>	Personalized antisense oligonucleotide drug
<b>Indication</b>	SCN2a-associated genetic disorder
<b>Goal</b>	Complete first-in-human trial
<b>Funds Requested</b>	\$985,713 Co-funding: \$0 (None required)

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

**Clinical Background:** SCN2A-related disorders are caused by mutations in the SCN2A gene. SCN2A-related disorders result in a range of neurodevelopmental conditions mainly characterized by the severity of epilepsy. Severe forms of the disorder cause seizures beginning in infancy, and anti-seizure medications are often not effective.

**Value Proposition of Proposed Therapy:** The proposed personalized therapy would treat a patient with a severe epilepsy and severe neurodevelopmental delay. If successful, other people with similar disorders could benefit from equivalent precision therapies.

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

CIRM does not currently have any active TRAN or CLIN awards addressing SCN2A-related disorders.

# Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
DISC2	Neurodevelopmental diseases	Candidate discovery	Aug 2022 – July 2024	\$1,180,654	Seven milestones proposed, two completed with delay, three on track, two not yet started.



**GWG Recommendation:** Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	8
2	6
3	0

**DEI Score: 8.5 (scale 1-10)**

**CIRM Team Recommendation:** Fund (concur with GWG recommendation)

**CIRM Award Amount: \$985,713\***

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

<b>Title</b>	A Phase 2b Study of the Efficacy of a Novel Pro-Neurogenesis/Pro-Plasticity Drug for Bipolar Depression Using a Precision Psychiatry Approach
<b>Therapy</b>	Neurogenic small molecule
<b>Indication</b>	Bipolar depression
<b>Goal</b>	Complete a Phase 2b clinical trial
<b>Funds Requested</b>	\$15,000,000 Co-funding: \$13,202,842 (40% required)

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

**Clinical Background:** Bipolar disorder, particularly the depressive phase (BD-D), is a severe, life-long psychiatric condition associated with a high burden of illness and risk of suicide. Approved treatments are limited to antipsychotic drugs with limited efficacy and poor tolerability.

**Value Proposition of Proposed Therapy:** The proposed therapy could provide a novel therapeutic option that, unlike available antipsychotics, addresses disease-related pathophysiology, offers better tolerability, and includes a diagnostic approach to identifying patients who are most likely to benefit.

**Why a stem cell or gene therapy project:** The therapy is a small molecule drug that acts on neural progenitor cells and causes neurogenesis.

CIRM does not currently have any active TRAN or CLIN awards addressing bipolar depression.

Applicant has not previously received a CIRM award.

**GWG Recommendation:** Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	10
2	4
3	0

**DEI Score: 9.0 (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.

<b>Title</b>	Human Embryonic Stem Cell-Derived Neural Stem Cells for Severe Spinal Cord Injury (SCI)
<b>Therapy</b>	Human embryonic stem cell-derived neural stem cells
<b>Indication</b>	Sub-acute spinal cord injury
<b>Goal</b>	Complete IND-enabling studies and file an IND
<b>Funds Requested</b>	\$6,000,000 Co-funding: \$0 (None required)

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

**Clinical Background:** More than half a million Americans are living with spinal cord injury (SCI) and no approved therapies for promoting recovery of lost function after SCI are currently available. SCI can result in a loss of movement, sensation, bowel and bladder function but also chronic neuropathic pain and disabling bouts of autonomic dysreflexia leading to dangerous elevations of blood pressure and risk of cerebral hemorrhage.

**Value Proposition of Proposed Therapy:** The proposed therapy offers an opportunity to restore function in patients with SCI by implanting neural stem cells at the injury site to regenerate and repair damaged axons. The applicants note this as a fundamental difference from other approaches that simply aim to remyelinate spared host axons.

**Why a stem cell or gene therapy project:** The therapy is composed of neural stem cells.



Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1	Pre-IND meeting	Oct 2025	Spinal cord injury	Neural stem cells	Integration of transplanted cells to form new oligodendrocytes, increase repair, and improve locomotor function

# Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN1	Spinal cord injury	Pre-IND meeting	Nov 2019 – Aug 2023	\$6,235,897	Six milestones proposed, all were achieved on time.
DISC2	Spinal cord injury	Candidate discovery	Apr 2018 – Oct 2019	\$1,905,173	Two aims proposed, all achieved on time.
DISC	Spinal cord injury	Candidate Discovery	Nov 2012 – Oct 2015	\$4,600,447	Three aims proposed, all completed on time.

**GWG Recommendation:** Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	13
2	0
3	0

**DEI Score: 8 (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 for CLIN2-15607 Application

Maria Bonneville

<b>Title</b>	Phase 3 (Pivotal) Clinical Trial for SPG50
<b>Therapy</b>	Gene therapy utilizing adeno-associated virus encoding a codon-optimized human AP4M1 transgene
<b>Indication</b>	Spastic Paraplegia Type 50 (SPG50)
<b>Goal</b>	Complete a phase 3 clinical trial
<b>Funds Requested</b>	\$15,000,000 Co-funding: \$10,159,703 (40% required)

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

**Clinical Background:** Spastic paraplegia type 50 (SPG50) is a rare genetic neurodegenerative disease caused by a mutation in the adapter protein complex 4 (AP-4). The disease is characterized by the gradual onset of spastic paraplegia during the initial decade of life, which escalates to quadriplegia during adolescence or early adulthood. About 16 individuals in North America are affected by this specific disorder.

**Value Proposition of Proposed Therapy:** The proposed therapy offers the potential to correct the gene mutation in SPG50 patients and to develop a framework for applying this approach to other ultra-rare monogenic diseases.

**Why a stem cell or gene therapy project:** The proposed therapy is a gene therapy.

CIRM does not currently have any active TRAN or CLIN awards addressing SPG50.

# Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN1	CMT4J	IND filing	Jan 2024 – Dec 2025	\$3,930,964	Six milestones proposed. Project just launching.



**GWG Recommendation:** Sufficiently flawed that it does not warrant funding and the same project should not be resubmitted for at least 6 months

Scientific Score	GWG Votes
1	0
2	4
3	10

**DEI Score: 7 (scale 1-10)**

**CIRM Team Recommendation:** Do not fund (concur with GWG recommendation)

**Amount Requested:** \$15,000,000