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

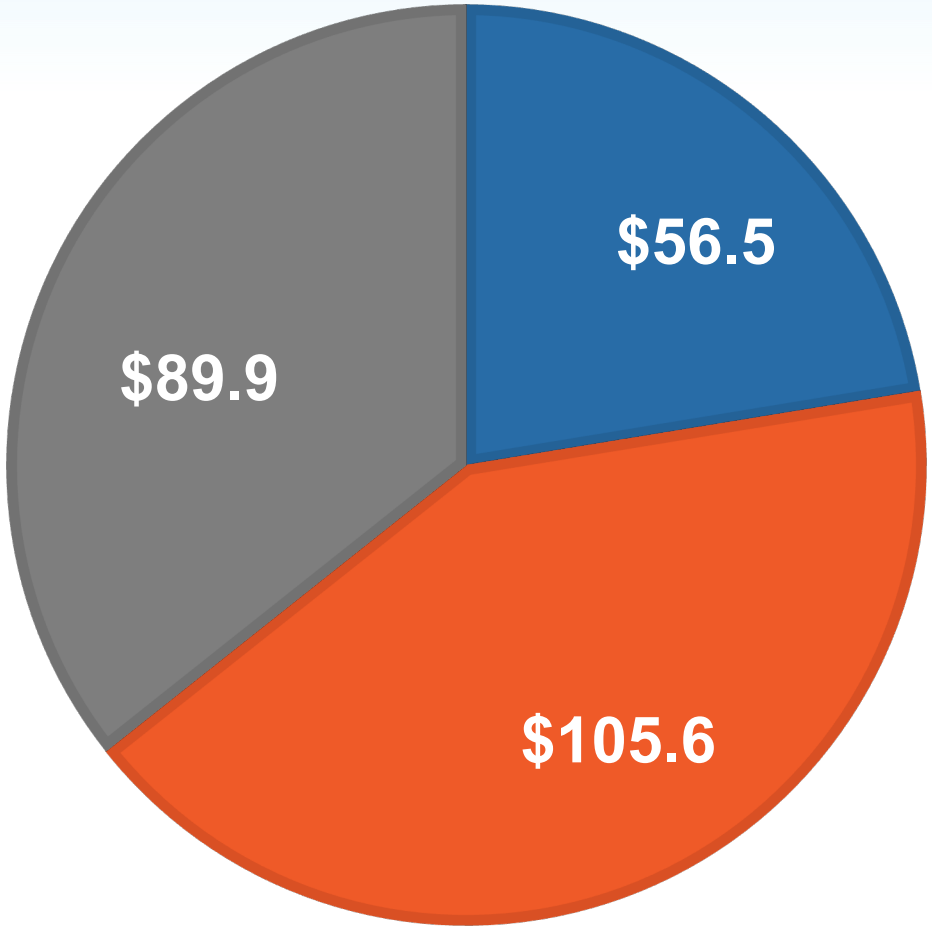
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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 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

CLIN2-14801

Title	Stem-Derived IL13Ra2 Chimeric Antigen Receptor T cells for Patients with Melanoma and Advanced Solid Tumors
Therapy	Engineered CAR T cells targeting IL13Ra2
Indication	Advanced cancers that express IL13Ra2, including melanoma
Goal	Complete first in human clinical trial
Funds Requested	$10,211,085 Co-funding: $0 (None required)

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

CLIN2-14801: Background Information

Clinical Background: Many solid tumors express the IL13Ra2 molecule such as gliomas, melanoma and breast cancer. Melanoma, in particular, is the deadliest form of skin cancer with over 100,000 estimated cases in the US alone in 2020 and 6,850 deaths.

Value Proposition of Proposed Therapy: The proposed T cell therapy targets tumor cells expressing IL13Ra2 and the applicants intend to initially test safety and efficacy in patients with melanoma. The therapy offers a potentially more practical, cost-effective, and innovative option for patients with tumors expressing IL13Ra2.

Why a stem cell or gene therapy project: The therapy is composed of T memory stem cells and involves genetic manipulation of the cells.

CLIN2-14801: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1	Pre-IND meeting	Dec 2024	Melanoma	T cell immunotherapy	T cells genetically modified to detect and kill melanoma cells that express a specific protein
CLIN1	IND enabling	Dec 2024	Melanoma, breast cancer, head/neck carcinomas	Mesenchymal stem cells loaded with oncolytic virus	Modifies tumor environment to support effective viral amplification and killing of cancer cells.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN2	Malignant glioma	Phase 1 clinical trial	3 years	$12,753,854	Five milestones proposed, all were achieved on time.
CLIN2	Malignant brain tumors	Phase 1 clinical trial	4 years	$8,401,309	Award currently launching.
TRAN	Malignant glioma	Translational activities	3 years	$5,215,447	Six aims proposed, all completed.

CLIN2-14801: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	14
2	0
3	0

DEI Score: 7 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $10,211,085*

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

CLIN1-14845

Title	Neural stem cell delivered oncolytic viro-immunotherapy for ovarian cancer
Therapy	Neural stem cells loaded with oncolytic virus
Indication	Chemo-resistant, metastatic ovarian cancer
Goal	Complete IND-enabling studies
Funds Requested	$5,314,547 Co-funding: $0 (none required)

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

CLIN1-14845: Background Information

Clinical Background: Approximately 22,000 women are diagnosed with ovarian cancer each year in the US. The 5-year survival rate is about 50%, and for most who experience recurrence, survival is typically less than 3 years. The standard of care includes aggressive chemotherapy, which results in toxic side effects. The tumor environment also becomes immunosuppressed making it difficult to treat.

Value Proposition of Proposed Therapy: If successful, the proposed therapy would provide a potentially safer and more effective therapeutic option for patients with ovarian cancer where other approaches been less successful.

Why a stem cell or gene therapy project: The therapy involves neural stem cells.

CLIN1-14845: Similar CIRM Portfolio Projects

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

CLIN2-14845: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	May 2025	Solid tumors	Cytokine-induced killer cells with oncolytic virus	CIK cells loaded with oncolytic virus target and kill tumor cells

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN1	Ovarian cancer	Pre-IND meeting	3 years	$2,873,262	Five milestones were proposed, and all milestones completed resulting in a pre-IND meeting.
Disease Team	Glioblastoma	IND enabling	5 years	$17,890,623	Twenty-four milestones (pre-CIRM 2.0) were set. All achieved, some with delay.

CLIN1-14845: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI Score: 8.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $5,314,547*

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

CLIN1-15337

Title	Chimeric TGFB Signaling Receptor (CTSR) Enabled Anti-B7H3 CAR T-cell Therapy in Children and AYA with Recurrent Solid Tumors
Therapy	Engineered CAR T cells
Indication	Children, adolescent, young adults with solid tumors
Goal	Complete IND-enabling activities and file an IND
Funds Requested	$6,000,000 Co-funding: $0 (none required)

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

CLIN1-15337: Background Information

Clinical Background: Recurrent solid tumors such as metastatic sarcomas in children and young adults represents an unmet medical need given the less than 30% overall survival and complications from the standard chemotherapy and radiation treatments.

Value Proposition of Proposed Therapy: CAR T cell therapies have demonstrated promise in treating blood cancers but has proven more challenging in solid tumors. The applicants propose the development of a CAR T cell therapy that addresses several key factors that have limited effectiveness of this approach such as T cell suppression in the tumor microenvironment. The therapy offers the possibility of a new approach that would provide an effective option for patients.

Why a stem cell project: The therapeutic candidate is a genetic therapy

CLIN1-15337: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing metastatic sarcomas in children and young adults.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-15337: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	11
2	4
3	0

DEI Score: 10 (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.

CLIN2-15547

Title	Phase 1/2a Dose Escalation Study of Autologous Neuron Replacement in Sporadic Parkinson Disease
Therapy	Autologous stem cell-derived dopaminergic (DA) neurons
Indication	Parkinson's disease
Goal	Complete first in human clinical trial
Funds Requested	$8,000,000 Co-funding: $3,641,502 (30% required)

Maximum funds allowable for this category: $8,000,000

CLIN2-15547: Background Information

Clinical Background: Parkinson's disease (PD) is a progressive neurological disorder affecting almost 1 million Americans. PD is caused by dopaminergic neuronal cell death in regions of the brain, especially the substantia nigra. Patients experience motor symptoms such as tremors, limb stiffness and impaired balance and non-motor symptoms affecting cognition and behavior.

Value Proposition of Proposed Therapy: There is no cure for PD. Levodopa medication controls motor symptoms but loses efficacy as the disease progresses. Deep brain stimulation surgery controls motor symptoms in patients non-responsive to medication. The proposed cell therapy has the potential to replace lost dopaminergic neurons and improve disease outcomes.

Why a stem cell or gene therapy project: The therapy is derived from induced pluripotent stem cells.

CLIN2-15547: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1	Pre-IND meeting	Jan 2026	Parkinson's Disease	Autologous iPSC-derived dopaminergic progenitor cells	The iPSC derived cells replace cells lost in Parkinson's Disease
CLIN1	IND enabling	April 2024	Parkinson's Disease	Allogeneic iPSC-derived dopaminergic progenitor cells	The iPSC derived cells replace cells lost in Parkinson's Disease
CLIN2	Phase 1 clinical trial	Jan 2024	Parkinson's Disease	Gene therapy for GDNF	The gene therapy stimulates production of a growth factor expected to stimulate neurons and lead to improved neuron function

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
DISC2	Parkinson's Disease	Translational Tool	1 year	$ 177,579	All milestones completed except for a late time point, which was found to be not helpful/relevant.

CLIN2-15547: GWG Review

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: $8,000,000*

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

CLIN2-15562

Title	Phase 1 Study of Autologous E-SYNC T Cells in Adult Participants with EGFRvIII+ Glioblastoma
Therapy	Engineered CAR T cells targeting EGFRvIII
Indication	Glioblastoma
Goal	Complete first-in-human trial
Funds Requested	$10,927,618 Co-funding: $311,890 (None required)

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

CLIN2-15562: Background Information

Clinical Background: Glioblastoma is a critical unmet need as it is the most common malignant primary brain tumor in adults, and each year about 12,000 Americans are diagnosed. Because of the diffuse nature of GBM, treatment is challenging, and recurrence is high. The 5-year survival rate is less than 10%.

Value Proposition of Proposed Therapy: The current standard of care involves resection of the tumor followed by radiation and chemotherapy. Despite these treatments, survival remains low. The proposed therapy has the potential to improve survival and quality of life for patients with glioblastoma via a CAR T cell approach that might only require a one-time treatment.

Why a stem cell or gene therapy project: The therapy involves genetic manipulation of the autologous T cells.

CLIN2-15562: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	Jul 2024	Brain metastasis from breast cancer	Autologous CAR-T cells	Chimeric antigen receptor T cells engineered to target HER-2 positive tumor cells that have metastasized to the brain
CLIN2	Phase 1 clinical trial	Mar 2025	Pediatric malignant brain tumors	Autologous CAR-T cells	Chimeric antigen receptor T cells engineered to target tumor cells via IL13R alpha2
CLIN2	Phase 1 clinical trial	Dec 2025	Gliomas	Autologous CAR-T cells	Chimeric antigen receptor T cells engineered to target tumor cells via GD2
CLIN2	Phase 1 clinical trial	Oct 2027	Glioblastoma	Autologous CAR-T cells	Chimeric antigen receptor T cells engineered to target B7-H3

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN1	Glioblastoma	Pre-IND meeting	2 years	$4,556,536	The team has completed all milestones and finished the award ahead of schedule.
DISC2	Pediatric gliomas	Candidate discovery	3 years	$900,000	Candidates were tested but were not effective in animal models.

CLIN2-15562: GWG Review

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 Award Amount: $10,927,618*

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

CLIN2-16063

Title	A phase 1/2 study to evaluate a bispecific CD19/CD20-directed CAR T cell, in refractory lupus nephritis and systemic lupus erythematosus
Therapy	Engineered CAR T cells
Indication	Lupus nephritis and systemic lupus erythematosus
Goal	Complete first in human clinical trial
Funds Requested	$8,000,000 Co-funding: $10,005,801 (30% required)

Maximum funds allowable for this category: $8,000,000

CLIN2-16063: Background Information

Clinical Background: Systemic lupus erythrematosus (SLE) is an autoimmune disorder that affects multiple organ systems and causes widespread chronic inflammation that leads to end-organ damage and death. SLE affects all people but is most prevalent among African American and Hispanic women. The standard of care is largely focused on immunosuppression including use of corticosteroids.

Value Proposition of Proposed Therapy: B cells that generate auto-antibodies are a key contributor to the disease, and a depletion of these B cells could significantly affect outcomes. The proposed therapy uses CAR T cells to target and deplete B cells in patients with SLE.

Why a stem cell or gene therapy project: The therapy involves genetic manipulation of cells to create autologous CAR T cells.

CLIN2-16063: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing systemic lupus erythematosus.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-16063: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	9
2	2
3	1

DEI Score: 9 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $8,000,000*

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

CLIN2-16303

Title	A Phase 1 Study of CAR T cells in Participants with Moderate to Severe Active Systemic Lupus Erythematosus
Therapy	iPSC-derived CAR T cells
Indication	Systemic lupus erythematosus
Goal	Complete first in human clinical trial
Funds Requested	$7,934,448 Co-funding: $3,400,478 (30% required)

Maximum funds allowable for this category: $8,000,000

CLIN2-16303: Background Information

Clinical Background: Systemic lupus erythrematosus (SLE) is an autoimmune disorder that affects multiple organ systems, and causes widespread chronic inflammation that leads to end-organ damage and death. SLE affects all people but is most prevalent among African American and Hispanic women. The standard of care is largely focused on immunosuppression including use of corticosteroids.

Value Proposition of Proposed Therapy: B cells that generate auto-antibodies are a key contributor to the disease, and a depletion of these B cells could significantly affect outcomes. The proposed therapy uses CAR T cells to target and deplete B cells in patients with SLE.

Why a stem cell or gene therapy project: The therapy is derived from induced pluripotent stem cells.

CLIN2-16303: Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing systemic lupus erythematosus.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN1	Cancer	IND filing	2 years	$4,000,000	Four milestones proposed, all completed on time.

CLIN2-16303: GWG Review

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 Award Amount: $7,934,448*

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