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

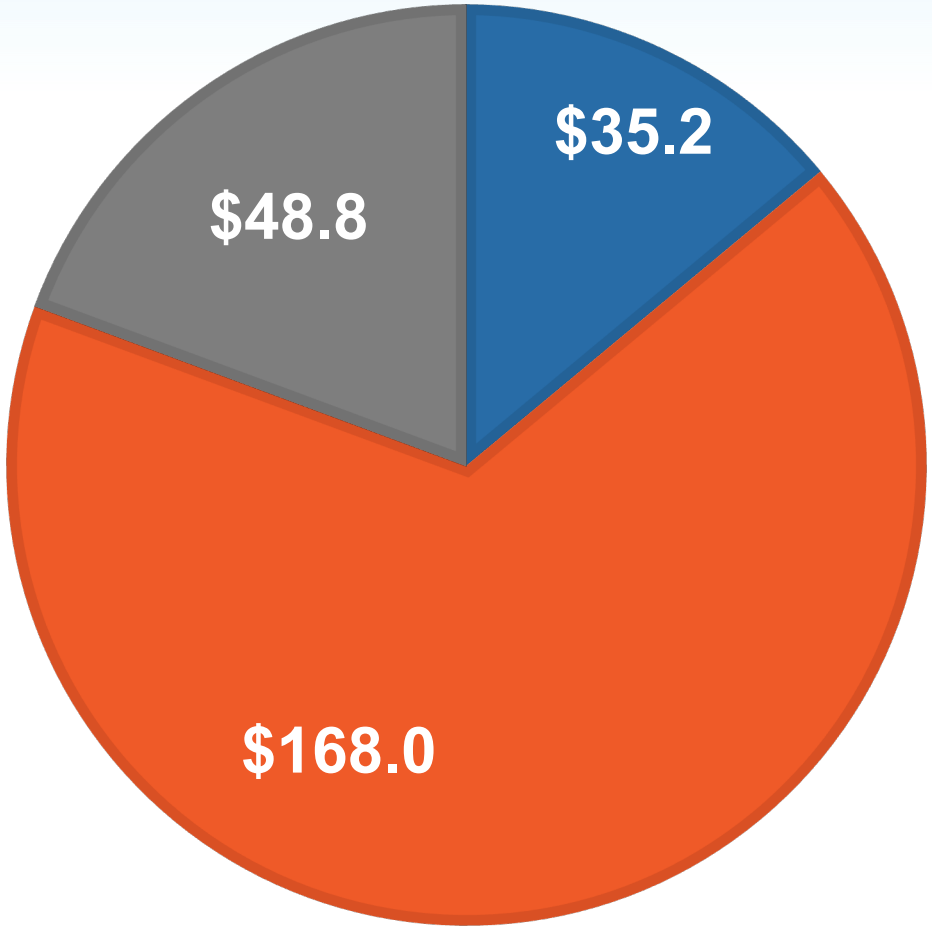
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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

Board Members with Conflicts of Interest for Application CLIN-15343

Maria Bonneville

CLIN2-15343

Title	A Phase 1b study evaluating the safety and efficacy of an allogeneic cell therapy in subjects with clear cell renal cell carcinoma (ccRCC)
Therapy	Allogeneic anti-CD70 CAR-T cells
Indication	Advanced or metastatic clear cell renal cell carcinoma
Goal	Phase 1b trial completion
Funds Requested	$15,000,000 Co-funding: $42,615,970

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

CLIN2-15343: Background Information

Clinical Background: Clear cell renal cell carcinoma (ccRCC) is the most common type of kidney cancer in adults. Standard of care includes surgery and immunotherapy. However, options are limited for patients in whom the cancer reoccurs.

Value Proposition of Proposed Therapy: The proposed therapy has several modifications that aim to improve tumor killing by patient T cells, and, if successful, may enable similar approaches in other cancers. In addition, the therapy is off-the-shelf, which would shorten timelines to treatment improve patient access as compared to autologous CAR-T treatments.

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

CLIN2-15343: Similar CIRM Portfolio Projects

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

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-15343: 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: $ 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.

Board Members with Conflicts of Interest for Application CLIN2-15282

Ysabel Duron

CLIN2-15282

Title	RPESC-RPE Therapy for dry Age-related Macular Degeneration
Therapy	Retina pigment epithelial stem cell (RPESC)-derived RPE progeny
Indication	Dry age-related macular degeneration (dry AMD)
Goal	Phase 1/2a trial completed
Funds Requested	$4,009,675 Co-funding: $3,317,347

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

CLIN2-15282: Background Information

Clinical Background: People with dry age-related macular degeneration (AMD) experience progressive vision loss due to the loss of the retinal pigment epithelial (RPE) cells. There are a few standard of care treatments available. However, they slow progression but do not improve and restore vision.

Value Proposition of Proposed Therapy: The aim of the proposed cell product is to replace the RPE cells that have been lost due to disease. This therapy has the potential to improve vision in patients with dry AMD.

Why a stem cell or gene therapy project: The therapy is composed of cells derived from retinal pigment epithelial stem cells.

CLIN2-15282: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1	Preclinical	Q4 2024	Dry age-related macular degeneration	Allogeneic cryopreserved neural stem cell therapy product	Implanted cells exert protective effects over target areas and could potentially restore areas of geographic atrophy.
TRAN1	Preclinical	Q1 2025	Geographic atrophy age-related macular degeneration	Optogenetic gene therapy for patients with geographic atrophy age related macular degeneration	Gene therapy to deliver optogenetic protein to the targeted cells of the retina to restore vision.
CLIN1	IND enabling	Q2 2025	Maculopathies related to RPE atrophy	Patient specific (autologous) induced pluripotent stem cell derived retinal pigment epithelium	A cell replacement to the endogenous RPE layer in patients with advanced RPE atrophy.
CLIN2	Phase 2 Clinical Trial	Q3 2027	Geographic atrophy	hESC derived RPE cells on a paralene membrane	Replace dying RPE cells in the eye to promote survival of the cells of the adjacent retina.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-15282: 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: $ 4,009,675*

*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

Board Members with Conflicts of Interest for Application CLIN2-15311
Dan Bernal
Ysabel Duron
Elena Flowers
Chris Miaskowski

CLIN2-15311

Title	A Phase I/IIa Study to Evaluate the Efficacy of a Gene Therapy with Standard of Care Therapy in Newly Diagnosed High Grade Glioma
Therapy	A retroviral replicating vector expressing yeast cytosine deaminase, which converts an antifungal prodrug to an anticancer drug
Indication	Newly diagnosed high-grade glioma
Goal	Complete Phase 1/2a trial
Funds Requested	$11,807,220 Co-funding: $0 (None required)

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

CLIN2-15311: Background Information

Clinical Background: High-grade gliomas are the most common primary brain tumor in adults. People with high grade gliomas have a poor prognosis. The current standard of care is surgery to remove the tumor followed by radiation and chemotherapy. The median overall survival with standard of care treatment is less than 15 months.

Value Proposition of Proposed Therapy: The gene therapy aims to activate an anti-cancer drug in only cancer cells, in combination with standard of care treatments. The proposed therapy may provide localized killing of cancer cells, and ultimately could increase survival for patients.

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

CLIN2-15311: 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
CLIN2	Phase 1 clinical trial	Mar 2028	Glioblastoma	Autologous CAR-T cells	Chimeric antigen receptor T cells engineered to target EGFRvIII

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TR2 Preclinical research	Glioblastoma	Preclinical	3 years	$3,340,625	11 of 14 milestones were met. The current application involves the same virus.
RS1 Basic research	n/a	Basic research	2 years	$399,239	Two publications and one patent were reported as outcomes for this award.

CLIN2-15311: 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: $ 11,807,220*

*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 Application CLIN1-14852

Ysabel Duron

CLIN1-14852

Title	IND-enabling studies for a 2nd Generation Vaccine Targeting Glioblastoma
Therapy	A vaccine that is designed to enhance the immune response against tumors expressing EGFRvIII
Indication	Glioblastoma
Goal	Approval of IND to initiate Phase 1 trial
Funds Requested	$4,367,348 Co-funding: $0 (None required)

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

CLIN1-14852: 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 may improve survival for patients with glioblastoma that express EGFRvIII.

Why a stem cell or gene therapy project: The therapy is a vaccine that targets cancer stem cells.

CLIN1-14852: 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
CLIN2	Phase 1 clinical trial	Mar 2028	Glioblastoma	Autologous CAR-T cells	Chimeric antigen receptor T cells engineered to target EGFRvIII

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN1	Glioblastoma	Pre-IND meeting	3 years	$2,929,889	The team completed all three milestones for the award, two of which were completed with delay.
DISC2	SARS-CoV-2	Candidate discovery	1 year	$249,999	Five milestones were proposed, two were achieved. Work on the remaining milestones were to be continued after the award period.

CLIN1-14852: GWG Review

GWG Recommendation: Sufficiently flawed that it does not warrant funding, and the same project should not be submitted for at least 6 months after the GWG review

Scientific Score	GWG Votes
1	0
2	0
3	15

DEI Score: 8 (scale 1-10)

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

CIRM Award Amount: $4,367,348*

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