Real Life™

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Grants Working Group Recommendations CLIN

October 27, 2022

CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

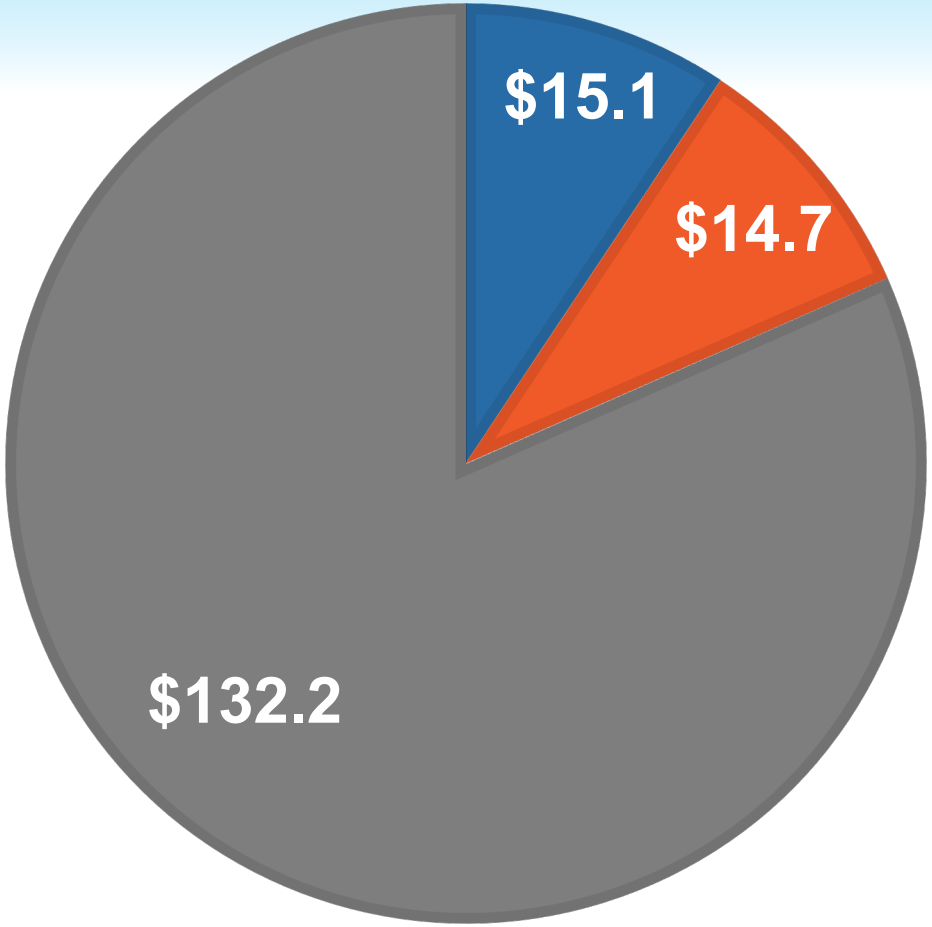
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

2022/23 Clinical Budget Status

Annual Allocation: $169 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.

Review Criteria

1. Does the project hold the necessary significance and potential for impact? (i.e., what value does it offer; is it worth doing?)
2. Is the rationale sound? (i.e., does it make sense?)
3. Is the project well planned and designed?
4. Is the project feasible? (i.e., can they do it?)
5. Does the project uphold the principles of diversity, equity, and inclusion (DEI)?

GWG Composition and Roles

Scientific GWG Member	Scientific evaluation (disease area expert, regulatory, CMC, product development) Provides scientific score on all applications
Patient Advocate or Nurse GWG Member	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 CLIN 1 application	Board members with Conflicts of Interest for CLIN 2 application
Linda Malkas	Linda Boxer
	Ysabel Duron
	Linda Malkas

CLIN2-13162

Title	A Phase I Study of Multiple doses of NSC-Based Oncolytic Virotherapy Administered Intracerebrally to Patients with Recurrent High-Grade Gliomas
Therapy	Genetically engineered neural stem cells expressing a cancer-killing virus that target brain tumor cells
Indication	Adult Gliomas and Glioblastoma
Goal	Completion of phase 1 clinical trial to assess safety
Funds Requested	$11,999,984 (co-funding: $0)

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

CLIN2-13162: 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. The 5-year survival rate is only about 10%.

Value Proposition of Proposed Therapy: The current standard of care involves resection of the tumor followed by radiation, chemotherapy, and alternating electric field therapy. Despite these treatments, survival remains low. The proposed therapy has the potential to improve survival and quality of life for patients with glioblastoma.

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

CLIN2-13162: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1 clinical trial	Dec 2023	Malignant glioma	CAR-T cell therapy with lymphodepletion	Chimeric antigen receptor T cells engineered to target tumor cells combined with lymphodepletion of patients to enhance effectiveness
CLIN2	Phase 1 clinical trial	Jul 2023	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	Jun 2024	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

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN	Ovarian cancer	Pre-IND meeting	Oct 2019 – Dec 2022	$2,873,262	**M1-M3**: Manufacturing process development and dosing studies (Completed on time) **M4-M5**: Preliminary safety studies and pre-IND meeting (In progress)

CLIN2-13162: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	11
2	4
3	0

DEI Score: 8.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 11,999,984*

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

CLIN1-14080

Title	Allogeneic mesenchymal stem cells loaded with oncolytic virus for cancer treatment
Therapy	Allogeneic MSCs loaded with virus that targets cancer
Indication	Solid tumors: melanoma, breast cancer, head and neck cancer
Goal	Completion of IND-enabling studies and filing of an IND
Funds Requested	$3,111,467 (co-funding: $777,867)

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

CLIN1-14080: Background Information

Clinical Background: Solid tumor cancers such as melanoma, breast cancer, and head & neck cancer are associated with significant morbidity, few treatment options, and poor survival rates.

Value Proposition of Proposed Therapy: The standard of care varies by tumor type but may involve chemotherapy, radiation, resection, and/or available drugs. If successful, the proposed therapy would provide a potentially safer and more effective therapeutic option for patients with solid tumors where approaches such as novel CAR-T have been less successful.

Why a stem cell or gene therapy project: The therapeutic candidate is composed of mesenchymal stem cells.

CLIN1-14080: 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 containing oncolytic virus	Cytokine Induced Killer cells target tumor cells to deliver oncolytic virus

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14080: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	12
2	2
3	0

DEI Score: 7.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 3,111,467*

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