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

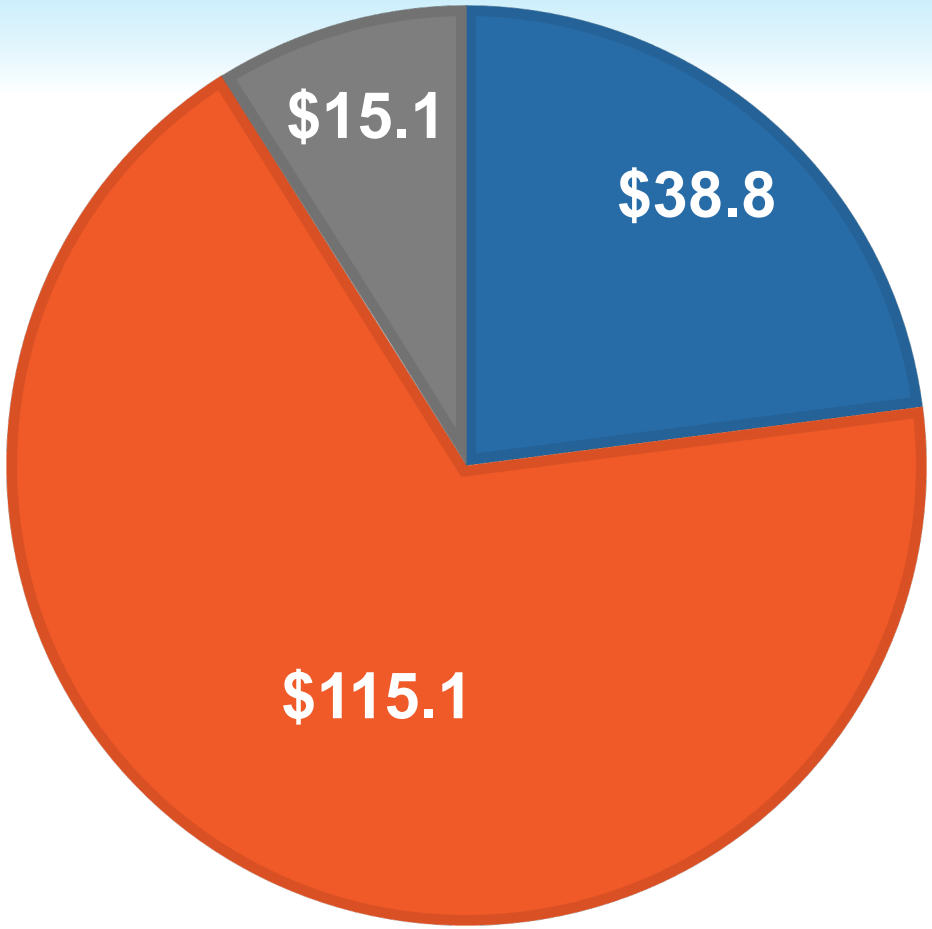
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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
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

Board members with Conflicts of Interest for CLIN applications
Mark Fischer-Colbrie
Ysabel Duron
Karol Watson

CLIN2-14315

Title	Reduced intensity conditioning with [candidate product] prior to TCRαβ+ T-cell/CD19+ B-cell depleted hematopoietic stem cell transplant for Fanconi Anemia patients
Therapy	Antibody targeting HSC for conditioning followed by alpha, beta depleted HSC transplant
Indication	Fanconi anemia
Goal	Completion of phase 1 clinical trial
Funds Requested	$11,813,964 Co-funding: $0 (none required)

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

CLIN2-14315: Background Information

Clinical Background: Conditioning regimens, which are necessary to remove existing diseased blood stem cells prior to transplant of new healthy stem cells, requires the use of toxic agents that are especially dangerous to individuals with Fanconi anemia (FA). Individuals with FA have a significant propensity of developing leukemias and other solid organ cancers that may be exacerbated.

Value Proposition of Proposed Therapy: The proposed therapy utilizes a conditioning regimen made up of an antibody that is not genotoxic and holds the potential for a safer and more effective blood stem cell transplants in patients with FA.

Why a stem cell or gene therapy project: The therapeutic candidate is a biologic that acts on blood stem cells and is followed by a blood stem cell transplant.

CLIN2-14315: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $2,313,398	Phase 1 clinical trial	Dec 2024	X-linked SCID	Monoclonal antibody to deplete blood stem cells	Conditioning regimen using antibody followed by HSC transplant.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
INFR	N/A	Alpha Clinic	Feb 2023 – Jan 2028	$7,997,246	6 milestones proposed to establish and manage new Alpha Clinics site.
CLIN1	Sickle cell disease	File IND	Nov 2017 – Sep 2020	$4,849,363	3 milestones proposed to conduct manufacturing and preclinical studies. All milestones achieved with slight delay.
DISC2	Cystic fibrosis	Candidate discovery	May 2017 – Oct 2019	$1,968,456	5 milestones proposed and all completed on time.
TRAN	Severe combined immunodeficiency (SCID)	Pre-IND	Oct 2015 – Mar 2018	$874,877	6 milestones proposed. 3 milestones completed on time, 1 completed after award, and 2 not completed

CLIN2-14315: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	10
2	3
3	2

DEI Score: 9.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 11,813,964*

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

CLIN2-14516

Title	Phase 2b Clinical Study of a Topical Ophthalmic Human Mesenchymal Stem Cell Secretome for the Treatment of Persistent Corneal Epithelial Defect
Therapy	Topical therapy produced from mesenchymal stem cells
Indication	Persistent Corneal Epithelial Defect
Goal	Completion of phase 2b clinical trial
Funds Requested	$15,000,000 Co-funding: $14,287,645 (40% required)

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

CLIN2-14516: Background Information

Clinical Background: Persistent corneal epithelial defect (PCED) results in a delay of corneal healing due to trauma, disease or other factors. This delay initially results in severe pain and redness but can progress to infection, corneal ulcers, stromal scarring, opacification, among other complications. PCED is a significant burden on patients and caregivers.

Value Proposition of Proposed Therapy: The current standard of care involves treatment of damaged tissue and prevention of further damage where possible. Oxervate is the only approved drug available to treat a subset (~1/3) of PCED cases and no effective treatments are available for remaining fraction. The proposed therapy would offer a treatment aimed at repairing and healing corneal tissue regardless of etiology.

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

CLIN2-14516: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 $10,301,486	Phase 1 clinical trial	Nov 2023	Limbal stem cell deficiency	Autologous limbal stem cells	Transplantation of patient specific limbal stem cells following expansion in culture

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-14516: GWG Review

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.

CLIN1-14602

Title	Clinical Translation of Autologous Regenerative Pluripotent Stem Cell Therapy for Blindness
Therapy	Autologous iPSC-derived retinal pigment epithelial cells
Indication	Retinal pigment epithelial atrophy
Goal	Completion of preclinical studies to file an IND
Funds Requested	$6,000,000 Co-funding: $1,729,181 (none required)

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

CLIN1-14602: Background Information

Clinical Background: Maculopathies, such as macular degeneration and Stargardt disease, represent an unmet medical need as there are no approved treatments that directly address the problem of retinal pigment epithelial (RPE) atrophy. Collectively, maculopathies are the leading cause of blindness in the developed world.

Value Proposition of Proposed Therapy: The proposed cell therapy offers the potential for a safe and effective treatment that may preserve and possibly restore vision for some maculopathies.

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

CLIN1-14602: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1 $4,235,758	PreIND	Dec 2023	Age-related macular degeneration	Allogeneic neural stem cells	Transplantation of neural stem cells to provide trophic factors and preserve vision

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN	Maculopathies	Pre-IND meeting	Jan 2019 – May 2021	$5,068,026	5 milestones proposed to conduct CMC studies and prepare for pre-IND. 3 milestones achieved on time and 2 achieved with delays related to pandemic.

CLIN1-14602: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	13
2	2
3	0

DEI Score: 8.0 (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.

CLIN1-14764

Title	Treatment of the temporomandibular joint (TMJ) disc complex
Therapy	Tissue implant engineered using expanded, allogeneic chondroprogenitor cells
Indication	Defects of the temporomandibular joint disc (TMJ) complex
Goal	Completion of preclinical studies to file an IND
Funds Requested	$6,000,000 Co-funding: $0 (none required)

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

CLIN1-14764: Background Information

Clinical Background: The temporomandibular joints (TMJ) connect the lower jaw to the skull and allows for basic actions such as chewing, talking, yawning and speaking. Pathologies of the TMJ occur in 5-25% of the general population and are debilitating. About 70% of TMJ pathologies involve disc (fibrocartilage component) replacement.

Value Proposition of Proposed Therapy: The current standard of care includes steroid injections and removal of the TMJ disc complex which results in further joint degeneration. For end-stage cases, only total joint replacements are available. The proposed therapy would provide for the possibility of TMJ disc complex healing and restoration of function.

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

CLIN1-14764: Similar CIRM Portfolio Projects

CIRM does not currently have any active awards addressing temporomandibular joints (TMJ) pathologies.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
TRAN	Cartilage injury repair	Preclinical studies	Mar 2013 – Nov 2016	$1,735,703	4 milestones proposed to conduct preclinical safety and efficacy studies. All milestones achieved.

CLIN1-14764: 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: $ 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.