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

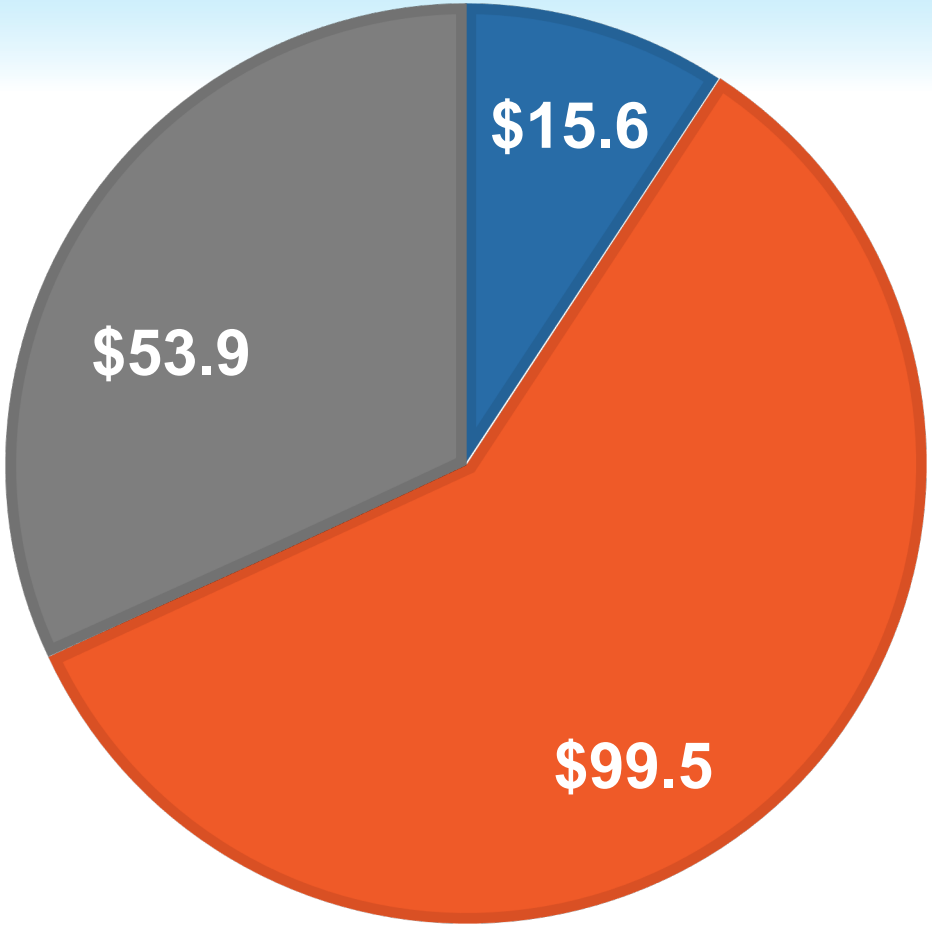
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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 CLIN2-14265 application
Ysabel Duron

CLIN2-14265

Title	A Phase 1b, Randomized, Blinded, Placebo-Controlled Dose-Ranging Study Evaluating [Product] Safety, Pharmacodynamics, and Biomarkers in Knee Osteoarthritis
Therapy	Gene therapy
Indication	Osteoarthritis of the knee
Goal	Completion of phase 1b clinical trial
Funds Requested	$11,637,194 Co-funding: $7,758,130 (40% required)

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

CLIN2-14265: Background Information

Clinical Background: Osteoarthritis (OA) affects over 27 million people in the US and is the leading cause of disability. Knee OA accounts for more than 80% of the disease burden. The disease results in a breakdown of joint tissue and inflammation accompanied by pain, the predominant symptom of OA.

Value Proposition of Proposed Therapy: The current standard of care depends on severity and ranges from life-style changes to use of pain relieving/anti-inflammatory medication and surgical procedures including joint replacement. The proposed therapy offers the potential for a one-time treatment that could significantly reduce the inflammatory process and facilitate repair and regeneration of cartilage tissue.

Why a stem cell or gene therapy project: The therapeutic candidate is a gene therapy targeting chondrocytes in articular cartilage.

CLIN2-14265: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1 $5,999,782	IND-enabling studies	Dec 2023	Knee OA	Pluripotent stem cell-derived chondrocytes seeded on matrix	Surgical implantation in the knee joint to replace and repair damaged cartilage

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-14265: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	14
2	0
3	1

DEI Score: 8.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 11,637,194*

*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 CLIN1-14299 application
Karol Watson

CLIN1-14299

Title	Ex vivo Engineering of Autologous Hematopoietic Stem Cells for the Treatment of Hypophosphatasia
Therapy	Genetically modified hematopoietic (blood) stem cells
Indication	Hypophosphatasia (HPP)
Goal	Completion of preclinical studies to file an IND
Funds Requested	$3,999,980 (co-funding: $999,995 – 20% required)

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

CLIN1-14299: Background Information

Clinical Background: Hypophosphatasia (HPP) is a rare systemic metabolic disease (~1:100,000 in North America) caused by a mutation in a gene that regulates bone mineralization. The severe form of HPP can result in a variety of symptoms including respiratory failure, seizures, bone deformities, & motor development delays. Perinatal/infantile HPP forms have 58% to 100% mortality rates during the first year of life.

Value Proposition of Proposed Therapy: The current standard of care includes enzyme replacement therapy, which requires weekly injections and is extremely costly. The proposed therapy involves gene modified blood stem cell transplant with the potential to deliver the missing enzyme indefinitely for a permanent and more affordable therapeutic option.

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

CLIN1-14299: Similar CIRM Portfolio Projects

CIRM does not currently have any active awards addressing hypophosphatasia.

CIRM does have projects addressing other unrelated metabolic disorders such as cystinosis, Type 1 diabetes, and mucopolysaccharidosis type 1

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-14299: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	13
2	1
3	0

DEI Score: 9.0 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 3,999,980*

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