Real Life™

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Grants Working Group Recommendations CLIN

July 28, 2022

CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

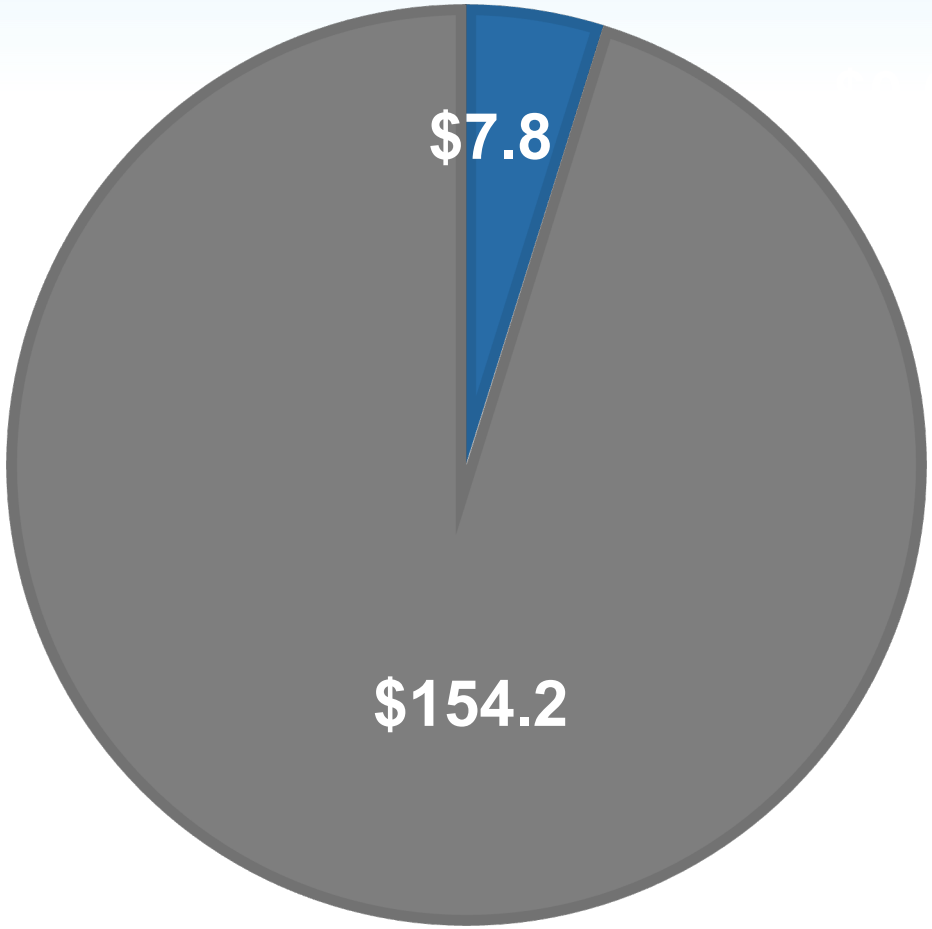
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

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 address the needs of underserved communities?

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 applications	
CLIN2-13267	**CLIN1-13315 #2**
Haifaa Abdulhaq	Judy Gasson
Loren Alving	Leon Fine
Ysabel Duron	Art Torres
Elena Flowers	Karol Watson
Christine Miaskowski	
Art Torres	
Barry Selick	
Keith Yamamoto	

CLIN2-13267

Title	Phase 1 Treatment of Urethral Strictures in Humans
Therapy	An engineered urethral segment comprising autologous urothelial, smooth muscle, and progenitor cells within a tubular scaffold.
Indication	Patients with urethral strictures that are too long for treatment by current methods
Goal	Completion of phase 1 clinical trial to assess safety and feasibility
Funds Requested	$3,841,593 (co-funding: $0)

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

CLIN2-13267: Background Information

Clinical Background: Stricture disease can have a profound impact on quality of life, resulting in infection, bladder stones, fistulas, sepsis, and ultimately renal failure.

Value Proposition of Proposed Therapy: Standard of care for long segment urethral strictures may include internal urethrotomy, urethroplasty, and reconstruction using grafts or vascularized flaps. Stricture recurrence along with infections and other complications are very common with these techniques. The proposed therapy offers the potential for a life-long cure for urethral strictures that eliminates complications associated with existing therapies.

Why a stem cell or gene therapy project: Urothelial and muscle progenitor cells are used to manufacture the therapy.

CLIN2-13267: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN	Pre-IND	Aug 2022	Urinary incontinence	iPSC-derive smooth muscle cell progenitors	Transplantation of smooth muscle cell progenitors into urethral muscle to regenerate weak urethra.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN2-13267: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI Score: 7 (scale 1-10)

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 3,841,593*

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

CLIN1-13315

Title	Hematopoietic Stem Cell Gene Therapy for X-linked Chronic Granulomatous Disease (XCGD)
Therapy	Autologous gene-corrected hematopoietic stem cells
Indication	X-linked Chronic Granulomatous Disease (XCGD)
Goal	Completion of IND-enabling studies and IND submission
Funds Requested	$3,999,959 (co-funding: $999,990)

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

CLIN1-13315: Background Information

Clinical Background: X-linked Chronic Granulomatous Disease (X-CGD) is a rare immune disorder that prevents white blood cells from killing foreign invaders. This results in severe, recurrent infections that can impact quality and length of a patient's life. X-CGD is usually diagnosed before age 5, but without treatment, children die before age 10.

Value Proposition of Proposed Therapy: The current standard of care involves ongoing antibacterial and antifungal prophylaxis and allogeneic hematopoietic stem cell transplant. If successful, the therapy offers patients the potential for immune restoration and cure.

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

CLIN1-13315: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2	Phase 1/2 clinical trial	Dec 2022	XCGD	Autologous gene-corrected CD34+ cells	Lentiviral vector correction of gene defect in patient CD34+ cells.

Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award.

CLIN1-13315: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes	Previous GWG Votes
1	15	8
2	0	7
3	0	0

DEI Score: 7.0 (scale 1-10) **Previous DEI Score: 5.5**

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 3,999,959*

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