Real Life™

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Grants Working Group Recommendations CLIN

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CIRM
CALIFORNIA'S STEM CELL AGENCY

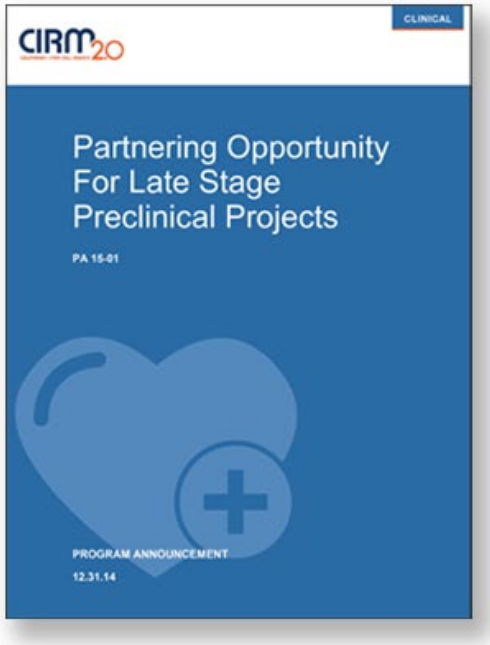
Mission Statement

OUR MISSION

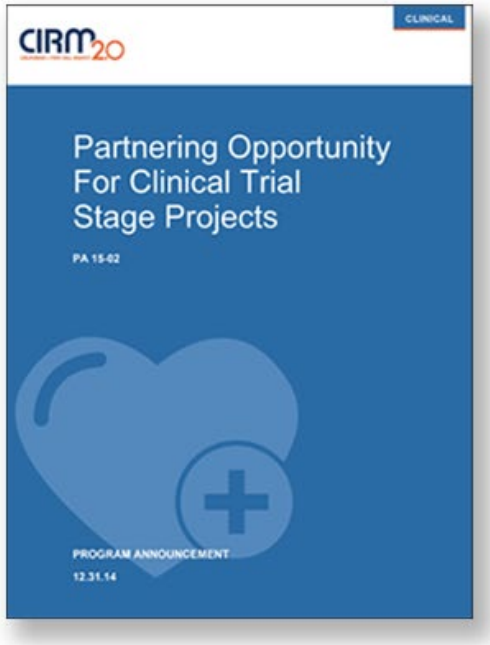
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

Clinical Stage Programs

CLINICAL STAGE



CLIN 1



CLIN 2

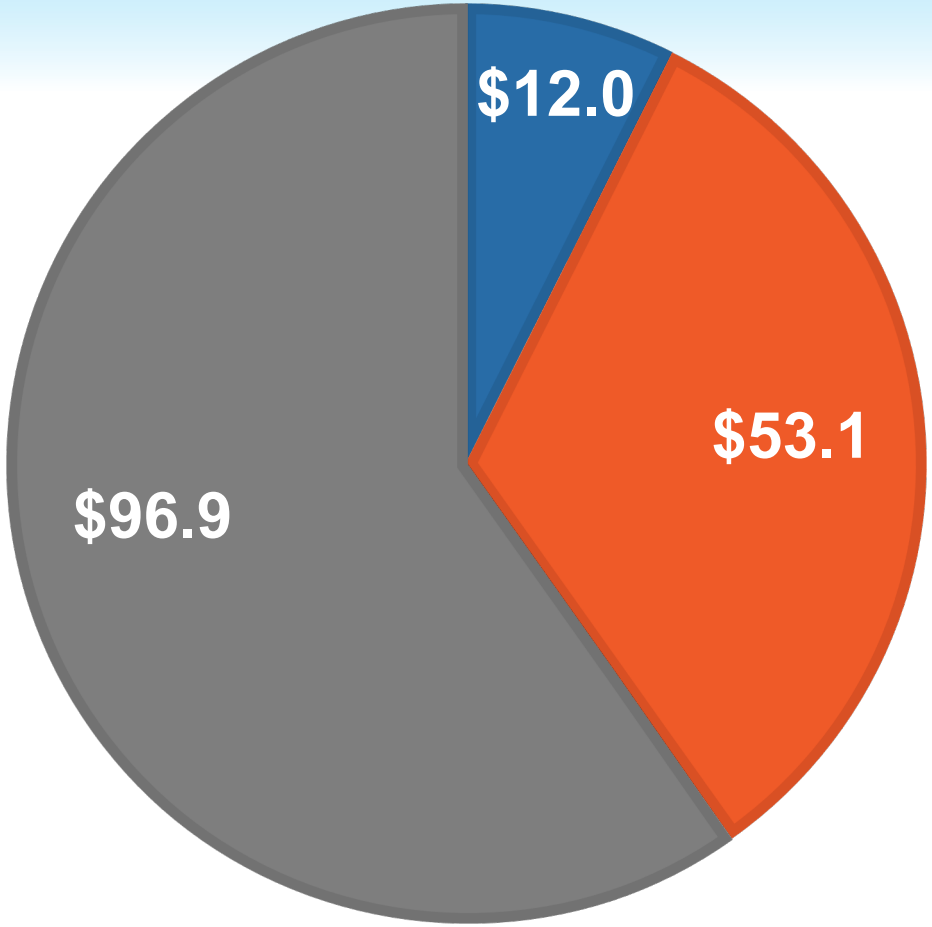
CLIN 3

2021/22 Clinical Budget Status

Annual Allocation: $162 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

CLIN2-13259

Title	Phase 1 Study of Autologous CD4LVFOXP3 in Participants with IPEX Syndrome
Therapy	Gene-corrected CD4+ T cells
Indication	IPEX syndrome (monogenic autoimmune disease)
Goal	Completion of phase 1 clinical trial
Funds Requested	$11,999,179 (co-funding: $0)

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

CLIN2-13259: Background Information

Clinical Background: Immune Dysregulation Polyendocrinopathy Enteropathy X-linked (IPEX) syndrome is a rare autoimmune inflammatory disease caused by a FOXP3 gene mutation that leads to a lack of regulatory T cells and is fatal if untreated.

Value Proposition of Proposed Therapy: The current standard of care options are either chronic immunosuppression or allogeneic hematopoietic stem cell transplant (HSCT). Immunosuppression is not curative and has significant side effects. HSCT is curative but there are insufficient matched donors. Other future curative autologous gene editing therapies are a longer-term goal, and the proposed therapy offers a bridging opportunity for IPEX treatment.

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

CLIN2-13259: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
TRAN1	Translational	Jan 2024	IPEX Syndrome	Gene-corrected HSCs (FoxP3)	Hematopoietic stem cells (HSCs) with defective Foxp3 expression are modified with a lentiviral vector which restores a normal copy of the defective gene. Transplantation of gene-modified HSCs, produce all blood lineages, including regulatory T cells with restored FoxP3 expression that can control the severe autoimmunity present in IPEX Syndrome.

Previous CIRM Funding to Applicant Team

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones/Aims
CLIN1	IPEX Syndrome	Complete IND-enabling activities	Dec 2019 – Feb 2022	$4,952,496	**M1-M5**: Manufacture of product, in vivo/in vitro studies of safety and efficacy, comparability studies (Achieved on time) **M5**: Submit IND to the FDA (Achieved on time) **M6**: Complete clinical readiness activities (Achieved on time)
DISC2	IPEX Syndrome	Develop therapeutic candidate (*Different from study above*)	Apr 2017 – Oct 2019	$984,228	**M1-M3**: Demonstrate reproducibility of gene insertion in HSC and disease modifying activity in a mouse model (Achieved on time) **M4-M5**: Not completed due to unsuccessful outcomes of M1-M3

CLIN2-13259: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	13
2	1
3	0

DEI Score: 9.5

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $ 11,999,179*

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