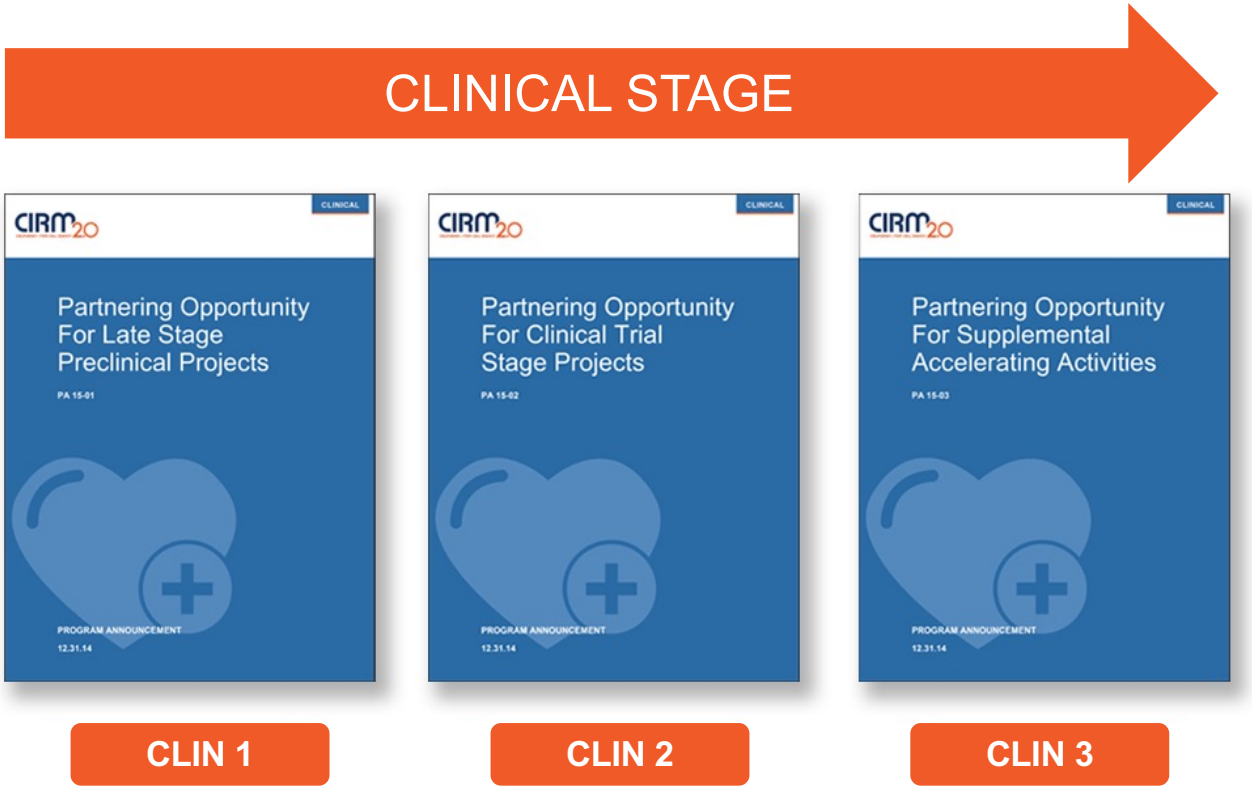
GWG Recommendations for Applications Submitted to the CLIN Program

Gil Sambrano
Vice President
Portfolio Development and Review

July 20, 2021

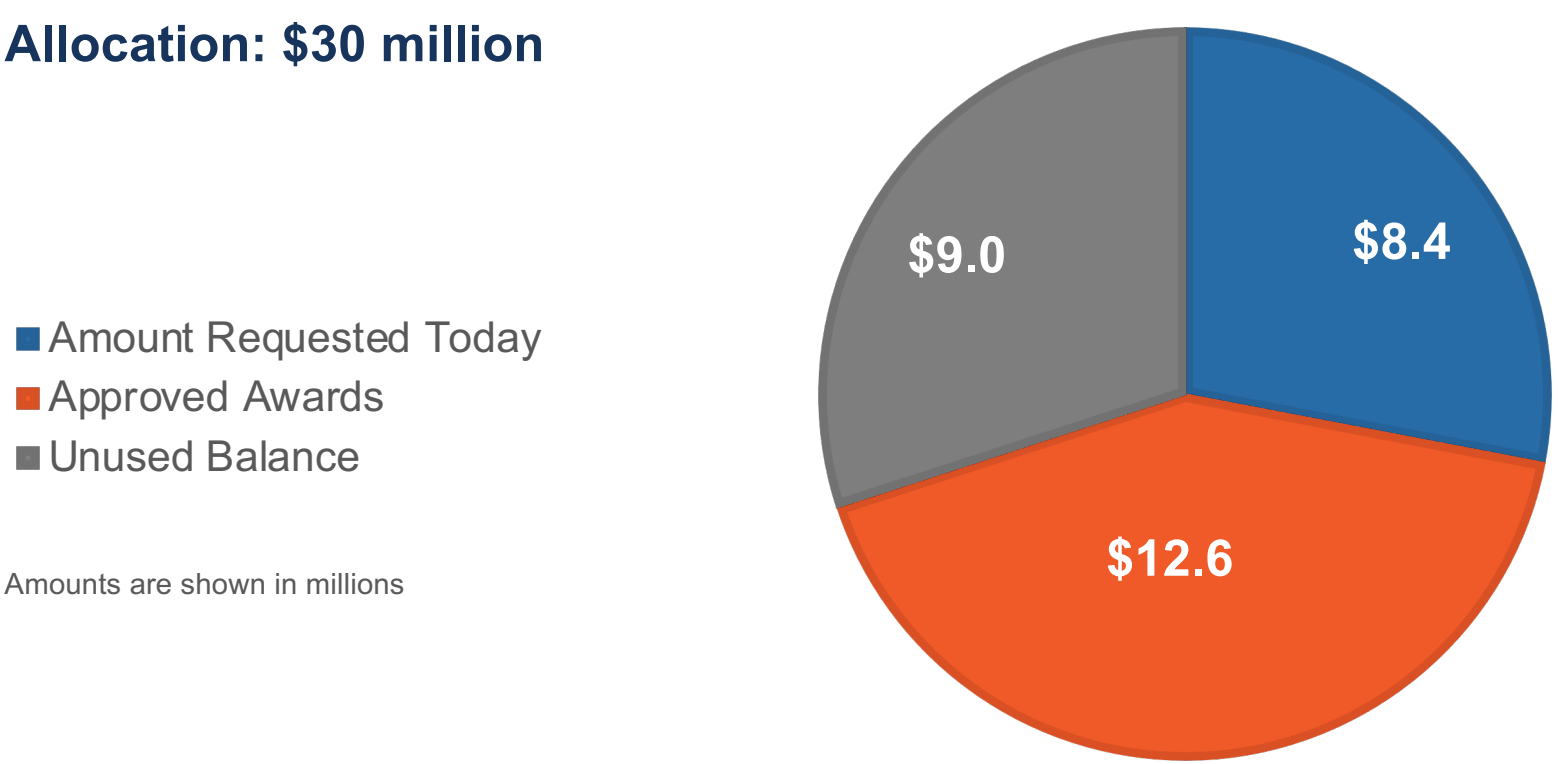
CIRM
CALIFORNIA'S STEM CELL AGENCY

Clinical Stage Programs



Sickle Cell Disease Clinical Budget Status

Allocation: $30 million



Amounts are shown in millions

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?

Scientific Scoring System for Clinical Applications

- **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.

Elements in CIRM Application Review

- **Addressing the Needs of Underserved Communities**
  - **This section describes the applicant's plan for outreach and enrollment of a diverse patient cohort that accounts for racial, ethnic and gender diversity**
  - **The section is evaluated as part of the overall project and incorporated into the scientific merit score (1,2 or 3)**
- **Diversity, Equity and Inclusion**
  - **This section describes how the applicant team incorporates diverse perspectives and experiences to improve the project through the composition of the team and/or any other approaches**
  - **This section is evaluated and scored by patient advocate/nurse members of the Board (appointed to the GWG) and shown in the DEI score (0-10)**

CLIN2SCD-11722: Cell and Gene Therapy for Sickle Cell Disease

Therapy	CD34+ hematopoietic stem cells genetically modified to correct the sickle mutation
Indication	Individuals with severe sickle cell disease
Goal	Complete a phase 1 trial to assess safety and initial efficacy
Funds Requested (CIRM + NHLBI)	$16,778,814 Total cost of project is shared equally by CIRM and NHLBI, each contributing $8,389,407 (NHLBI contribution pending approval)

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

CLIN2SCD-11722 : Background Information

Clinical Background: SCD affects approximately 100,000 Americans. SCD is particularly common in those with sub-Saharan African ancestry affecting 1 in 365 African-American births. Globally, over 300,000 babies are born with SCD every year.

Value Proposition of Proposed Therapy: The only current cure is allogeneic HSC transplantation, but donor availability is very limited with high risk of complications such a GVHD. The proposed autologous therapy would avoid the medical risks of allogeneic transplant and need for donors while providing a potential cure.

Why a stem cell project: The therapeutic candidate includes hematopoietic stem cells.

CLIN2SCD-11722: Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1 (NHLBI)	IND	11/30/2020	Sickle Cell Disease	Autologous CRISPR-edited hematopoietic stem cells	Virus-free CRISPR editing to correct the pathogenic hemoglobin S allele mutation in HSC
CLIN2	Phase 1	12/31/21	Sickle Cell Disease	Autologous lentiviral gene-modified hematopoietic stem cells	Expression of lentiviral transferred anti-sickling hemoglobin gene
CLIN2	Phase 1	10/31/23	Sickle Cell Disease	Allogeneic cord blood hematopoietic stem cells	Hematopoietic stem cell transplantation to replace patient sickle red blood cells
CLIN2	Phase 1	04/30/22	Sickle Cell Disease	CD4 T Cell depleted haploidentical HSC transplant	Achieving immune tolerance by inducing mixed chimerism
CLIN2 (NHLBI)	Phase 2	12/31/24	Sickle Cell Disease	Autologous gene-modified CD34+ cells	Expression of a gene to induce anti-sickling fetal hemoglobin and silence beta-sickle globin

CLIN2SCD-11722: Previous CIRM Funding to Applicant

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones*
IND-enabling (Active)	Sickle Cell Disease	Preclinical studies, IND filing	Jun 2019 – Nov 2020	$2,217,805	**M1-M3**: Preclinical safety/toxicity, manufacturing filing (Achieved on time) **M4**: File IND (Achieved on time)
Translational (Closed)	Sickle Cell Disease	Pre-IND meeting	Feb 2017 – Aug 2019	$4,438,435	**M1-M3:** Reagent optimization, off-targe assessments, GMP-compliant manufacturing, Pre-IND meeting (Achieved with minor delays)

CLIN2SCD-11722 : GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	12
2	3
3	0

DEI Score: 8

CIRM Team Recommendation: Fund (concur with GWG recommendation)

CIRM Award Amount: $8,389,407* (NHLBI contribution of $8,389,407 pending approval)

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

CIRM will not launch the award until NHLBI's co-funding decision is confirmed. If NHBLI does not meet its co-funding contribution, CIRM will require the applicant to secure co-funding for the project costs over the CIRM award limit prior to returning to the ICOC for approval of a revised award amount of $12,000,000.