CIRM
CALIFORNIA'S STEM CELL AGENCY

Clinical Program
GWG Recommendations

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TRANSFORMING medicine lives futures

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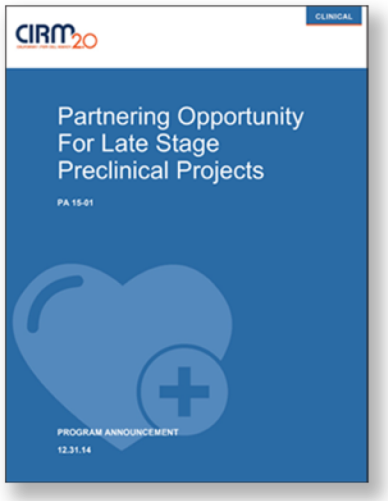
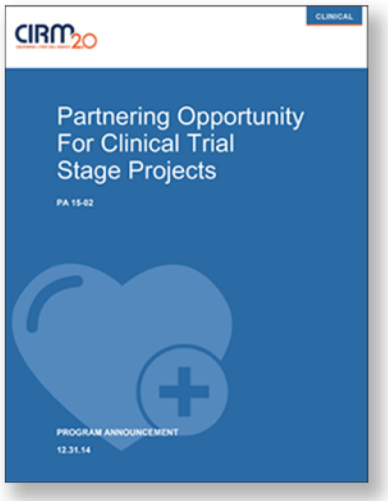
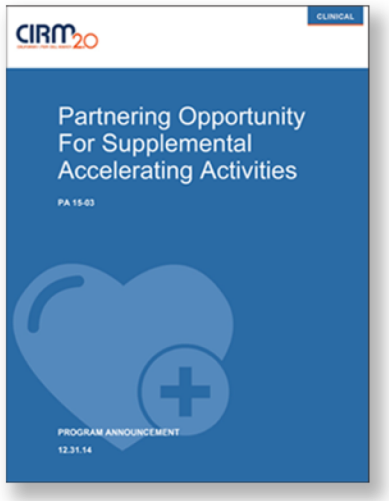
Clinical Stage Programs

CLINICAL STAGE







CLIN 1 **CLIN 2** **CLIN 3**

Scoring System for Clinical Applications

- **Score of "1"**

  Exceptional merit and warrants funding.

- **Score of "2"**

  Needs improvement and does not warrant funding at this time but could be resubmitted to address areas for improvement.

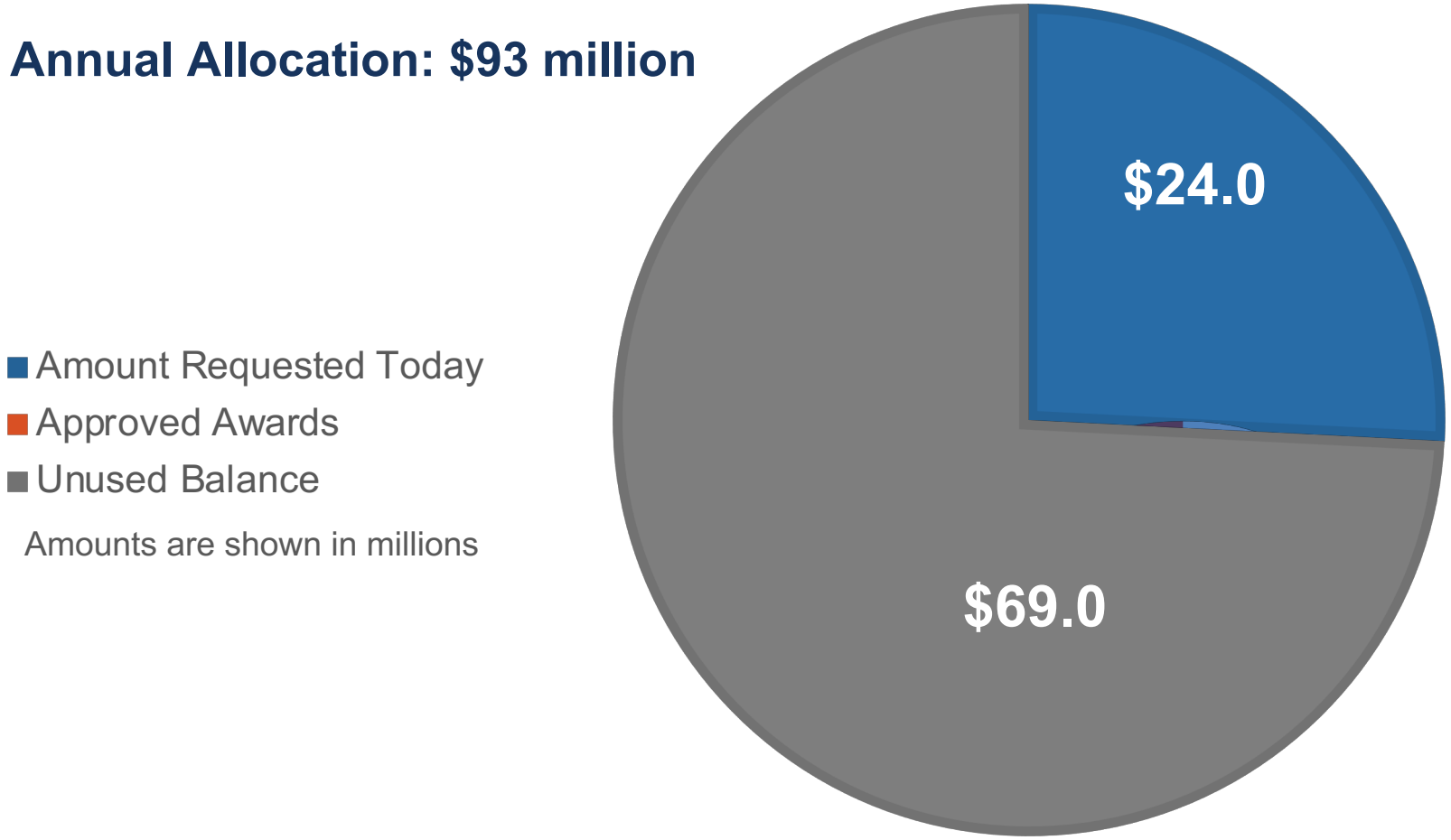
- **Score of "3"**

  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.

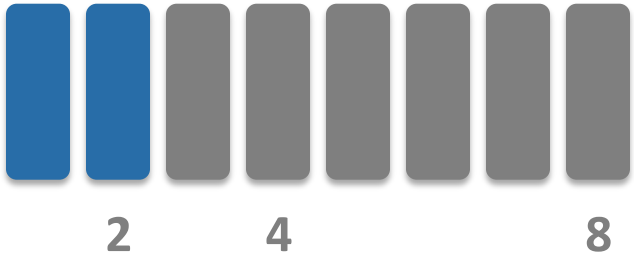
2019 Clinical Budget Status

Annual Allocation: $93 million



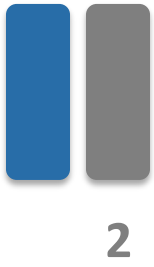
2019 Clinical Award Targets

CLIN2
Clinical Trials



GOAL

CLIN1
Late Stage Preclinical



GOAL

Approved Award

Awaiting Today's Approval

CLIN1-10953: Preclinical Study of Therapy for Huntington's Disease

Project Summary

Therapy	Human embryonic stem cell-derived neural stem cells
Indication	Huntington's Disease
Goal	Manufacturing optimization, IND enabling preclinical studies, IND filing
Funds Requested	$6,000,000 ($0 Co-funding)

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

CLIN1-10953: Preclinical Study of Therapy for Huntington's Disease

Potential impact: HD is an inherited disease that affects 30,000 patients in the US. Adult-onset HD is more common than juvenile HD with adult patients developing symptoms between ages of 30-50. HD patients typically live for 15-20 years after onset of symptoms.

Value Proposition: HD is a progressive neurodegenerative disease caused by a defect in the huntingtin gene that leads to death of neurons in certain regions of the brain. There are currently no cures or disease modifying therapies for HD. The proposed neural stem cell therapy has the potential to delay progression of the disease.

Why a stem cell project: The therapy involves neural stem cells derived from embryonic stem cells.

Related CIRM Portfolio Projects

There are currently no CLIN stage projects targeting Huntington's Disease in CIRM's active projects portfolio.

Previous CIRM Funding

Applicant has received previous funding from CIRM for a related candidate and indication.

Project Stage	Project Outcome	Project End Date
Translational	Pre-IND Meeting	12/31/2018
Candidate Discovery	Single Candidate	08/31/2015

CLIN1-10953: Preclinical Study of Therapy for Huntington's Disease

GWG Recommendation: Exceptional merit and warrants funding

Score	GWG Votes
1	8
2	1
3	5

CIRM Team Recommendation: Fund (concur with GWG recommendation)

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.

CLIN2-11400: Clinical Study of Therapy for Renal Failure

Project Summary

Therapy	Donor hematopoietic stem cell graft, donor T cells and recipient T regulatory cells
Indication	Kidney disease requiring kidney transplantation
Goal	Complete phase 1 study
Funds Requested	$11,969,435 ($0 Co-funding)

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

CLIN2-11400: Clinical Study of Therapy for Renal Failure

Potential impact: Over 100,000 new cases of kidney failure are reported and over 17,000 kidney transplants are performed annually in the US. An estimated 100,000 patients are on the transplant waitlist.

Value Proposition: Even with improvements in immunosuppression regimens 50% of HLA-mismatched transplants are lost to chronic rejection. Lifelong immunosuppression also increases the risk of infection, cardiovascular disease and diabetes. The proposed therapy aims to achieve mixed hematopoietic chimerism to induce transplant tolerance and to eliminate the need for immunosuppression.

Why a stem cell project: The therapy includes hematopoietic stem cells.

Related CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
Current Application	Phase 1	N/A	Renal Failure	Donor hematopoietic stem cell graft, donor T cells and recipient T regulatory cells	Treg aid donor HSC in inducing mixed chimerism in HLA-mismatched recipients.
CLIN2	Phase 1	01/31/21	Renal Failure	Donor hematopoietic stem cell graft and donor T cells	Donor HSC induce mixed chimerism in HLA-mismatched recipients.
CLIN2	Phase 3	12/31/22	Renal Failure	Donor hematopoietic stem cell graft and donor T cells	Donor HSC induce mixed chimerism in HLA-matched recipients.

Previous CIRM Funding

Applicant has received previous funding from CIRM for a related candidate and indication.

Project Stage	Project Outcome	Project End Date
Phase 1	Ongoing	01/31/21

CLIN2-11400: Clinical Study of Therapy for Renal Failure

GWG Recommendation: Exceptional merit and warrants funding

Score	GWG Votes
1	14
2	0
3	0

CIRM Team Recommendation: Fund (concur with GWG recommendation)

Award Amount: $11,969,435*

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

CLIN2-11431: Clinical Study of Therapy for Severe Combined Immunodeficiency

Project Summary

Therapy	Anti-CD117 antibody followed by allogeneic $CD34^+$ $CD90^+$ cell transplantation
Indication	Severe Combined Immunodeficiency (SCID)
Goal	Complete phase 1 trial
Funds Requested	$5,999,984 ($0 Co-funding)

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

CLIN2-11431: Clinical Study of Therapy for Severe Combined Immunodeficiency

Potential impact: SCID is a rare disease affecting an estimated 1/58,000 infants born in the US each year. SCID has a significantly higher incidence of 1/2000 births in the Navajo population. If untreated, SCID patients will likely die before age 2. Allogeneic HSC transplantation is curative in 94% of infants screened and treated within 3 months of birth.

Value Proposition: SCID infants are vulnerable to toxicity from the conditioning regimen and GvHD from the allogeneic HSCT. The proposed treatment seeks to address both limitations with a novel targeted conditioning agent and purified HSC graft. In addition, the conditioning agent may be broadly applicable in treatments involving hematopoietic transplants for blood diseases.

Why a stem cell project: The proposed treatment involves both targeting of endogenous HSC and transplantation of allogeneic HSC.

Related CIRM Portfolio Projects

The proposed project initially seeks to improve curative treatment of SCID. Related CIRM portfolio projects developing SCID cures are listed below.

The novel conditioning agent may be broadly applicable in blood diseases. CIRM is not currently funding similar projects developing novel conditioning agents.

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
Current Application	Phase 1	N/A	SCID	Anti-CD117 antibody followed by allogeneic $CD34^+$ $CD90^+$ cell transplantation	Selective elimination of native HSC and improved engraftment of allogeneic HSC
CLIN2	Phase 1/2	03/31/22	X-SCID	Gene-modified autologous HSC	Immune reconstitution by gene-modified cells
CLIN2	Phase 2	01/31/21	ADA-SCID	Gene-modified autologous HSC	Immune reconstitution by gene-modified cells
CLIN2	Phase 1	06/30/23	ART-SCID	Gene-modified autologous HSC	Immune reconstitution by gene-modified cells

Previous CIRM Funding

Applicant has received previous funding from CIRM for a related candidate and indication.

Project Stage	Project Outcome	Project End Date
Phase 1	Ongoing	10/31/20

CLIN2-11431: Clinical Study of Therapy for Severe Combined Immunodeficiency

GWG Recommendation: Exceptional merit and warrants funding

Score	GWG Votes
1	9
2	6
3	0

CIRM Team Recommendation: Fund (concur with GWG recommendation)

Award Amount: $5,999,984*

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