

GWG Recommendations: Clinical Program (CLIN1, CLIN2, CLIN4)

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Review

ICOC/ARS Meeting

January 30, 2025



Our Mission

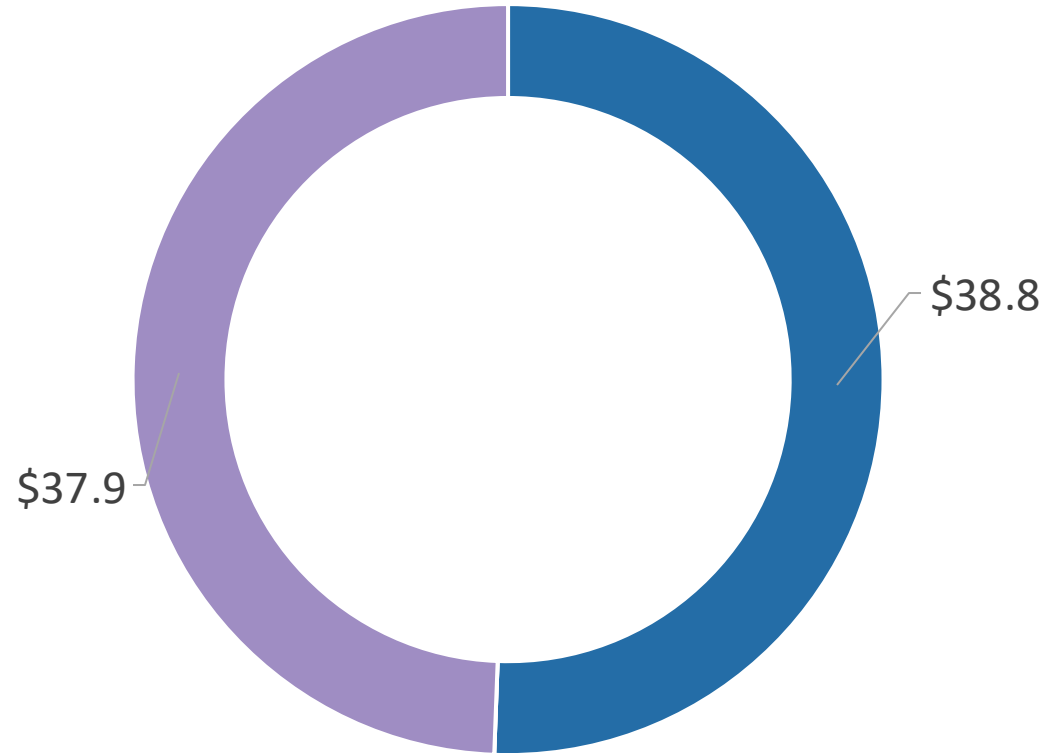
Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world.



Clinical Budget Status

Budget Allocation: \$76.7 million
(Jan to June 2025)

- Amount Requested Today
- Approved Awards
- Unused Balance



Clinical



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.

Clinical



Scientific Review Criteria

1. Does the project hold the necessary significance and potential for impact? (*what value does it offer; is it worth doing?*)
2. Is the rationale sound? (*does it make sense?*)
3. Is the project well planned and designed?
4. Is the project feasible? (*can they do it?*)
5. Does the project uphold principles of diversity, equity, and inclusion (DEI)? (*e.g., does it consider patient diversity?*)

Clinical



Diversity, Equity and Inclusion Scoring System

- DEI Score of 9-10: *Outstanding Response*
- DEI Score of 6-8: *Responsive*
- DEI Score of 3-5: *Not Fully Responsive*
- DEI Score of 0-2: *Not Responsive*

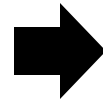
Applications are scored for adherence to principles of DEI by all GWG Board Members with no conflict.

The criteria used to measure adherence fall under overarching categories of: Commitment to DEI, Project Plans and Cultural Sensitivity.

Clinical



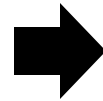
Scientific GWG
Members



Scientific evaluation (disease area expert, regulatory, CMC, product development)

Provides scientific score on all applications

GWG Board
Member
(Patient Advocate/Nurse)

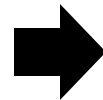


DEI evaluation, patient perspective on significance and potential impact, oversight on process

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

CLIN1-16103

Targeted DOK7 gene therapy
for Congenital Myasthenic
Syndromes

FUNDS REQUESTED

\$2,894,305

Co-funding: \$723,577 (20%
required)

California organization



THERAPY

A gene therapy product for the treatment of
DOK7 Congenital Myasthenic Syndrome



INDICATION

DOK7 Congenital Myasthenic Syndrome



GOAL

IND filing for the therapeutic candidate

CLIN1-16103 Background Information

Clinical background

Congenital Myasthenic Syndromes (CMS) are a group of rare genetic neuromuscular disorders that cause muscle weakness. Patients with DOK7 CMS have decreased quality of life. The severity of the disease ranges from using breathing aids to a complete inability to move with life-threatening complications.

Value proposition of proposed therapy

The current standard of care treats symptoms only, requires chronic administration, and the effectiveness can decrease over time. The proposed gene therapy would potentially be a one-time curative treatment.

Why a stem cell or gene therapy project

The therapy is a gene therapy product.

CLIN1-16103 Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing congenital myasthenic syndrome.

CLIN1-16103 Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award

CLIN1-16103

GWG Review

Targeted DOK7 gene
therapy for Congenital
Myasthenic Syndromes

CIRM Award Amount:
\$2,894,305*

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

GWG RECOMMENDATION

Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI SCORE

8 (scale 1-10)

CIRM TEAM RECOMMENDATION

Fund (concur with GWG recommendation)

CLIN1-17165

Advancing a novel antisense oligonucleotide for the treatment of SCA3, a devastating neurodegenerative disease

FUNDS REQUESTED

\$5,692,538

Co-funding: \$0 (none required)

California organization



THERAPY

An antisense oligonucleotide of the ATXN3 (Ataxin-3) gene



INDICATION

Spinocerebellar Ataxia Type 3 (SCA3)



GOAL

IND submission

CLIN1-17165 Background Information

Clinical background

Spinocerebellar Ataxia Type 3 (SCA3) is a neurodegenerative disease caused by a toxic mutation in the Ataxin-3 gene. Disease symptoms appear around midlife and usually impacts patient gait, speech, balance/spatial awareness and eye movement. SCA3 progresses over time and is eventually fatal.

Value proposition of proposed therapy

There are currently no effective treatments that target the underlying disease. Current standard of care is treatment for pain relief and anti-spasticity drugs. The proposed antisense oligonucleotide treatment skips the mutated part of the gene to produce a functional protein. Ideally, this reduces the accumulation of toxic protein, reduces symptoms, and slows progression of the disease.

Why a stem cell or gene therapy project

The therapy is a genetic therapy.

CLIN1-17165 Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing SCA3.

CLIN1-17165 Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award

CLIN1-17165 GWG Review

Advancing a novel antisense oligonucleotide for the treatment of SCA3, a devastating neurodegenerative disease

CIRM Award Amount:
\$5,692,538*

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

GWG RECOMMENDATION

Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	14
2	0
3	0

DEI SCORE

7 (scale 1-10)

CIRM TEAM RECOMMENDATION

Fund (concur with GWG recommendation)

CLIN2-14796

The [redacted] Delayed
Immunological Tolerance after
Kidney Transplantation Program

FUNDS REQUESTED

\$7,343,925

Co-funding: \$0 (none required)

California organization



THERAPY

CD34+ hematopoietic stem/progenitor cells
(HSPC) and CD3+ cells



INDICATION

Recipients with HLA-identical kidney transplant



GOAL

Complete Phase 1 study

CLIN2-14796 Background Information

Clinical background

Kidney disease, where the organs cannot filter and clean the blood as they should, can ultimately lead to kidney failure and the need for dialysis or a kidney transplant. Current kidney transplant recipients need life long immunosuppressive drugs to prevent transplant rejection. Immunosuppressive drugs increase the risk of infection, cancer, diabetes, and heart disease.

Value proposition of proposed therapy

The potential to withdraw these drugs from transplant recipients could extend the functionality of the transplanted kidney and positively impact patient quality of life. The ability to induce tolerance after the kidney transplant could benefit groups that are not able to undergo both procedures at the same time.

Why a stem cell or gene therapy project

The therapy is made from stem/progenitor cells.

CLIN2-14796 Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN2 \$11,217,155	Phase 3 clinical trial	Q4 2024	HLA matched kidney transplant recipients	Kidney transplant donor- derived CD34+HSCs and CD3+ T cells	Combine kidney transplant with donor stem cells to create immune tolerance to the donor kidney
CLIN2 \$11,955,585	Phase 1 clinical trial	Q4 2024	HLA-mismatched kidney transplant recipients	Kidney transplant donor stem cells and expanded recipient Treg cells	Combine kidney transplant with donor stem cells and recipient Treg cells to create immune tolerance to the donor kidney
CLIN2 \$6,653,266	Phase 1 clinical trial	Q2 2025	HLA-mismatched kidney transplant recipients	Kidney transplant donor stem cells and T cells	Combine kidney transplant with donor stem cells to create immune tolerance to the donor kidney
CLIN2 \$11,998,188	Phase 1b/2a clinical trial	Q1 2027	HLA-mismatched pediatric kidney transplant recipients	Kidney transplant donor peripheral blood stem cells	Donor stem cell transplant followed by kidney transplant to create immune tolerance to the donor kidney

CLIN1-14796 Previous CIRM Funding to Applicant Team

Applicant has not previously received a CIRM award

CLIN1-14796

GWG Review

The [redacted] Delayed
Immunological Tolerance
after Kidney
Transplantation Program

CIRM Award Amount:
\$7,343,925*

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

GWG RECOMMENDATION

Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI SCORE

8 (scale 1-10)

CIRM TEAM RECOMMENDATION

Fund (concur with GWG recommendation)

CLIN2-17083

Phase 1b Study of [redacted] in Adults with PKP2 Mutation-associated Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

FUNDS REQUESTED

\$8,000,000

Co-funding: \$15,936,236 (40% required)

California organization



THERAPY

AAV gene therapy to deliver a functional PKP2 gene



INDICATION

Arrhythmogenic right ventricular cardiomyopathy (ARVC)



GOAL

Phase 1b study completed

CLIN2-17083 Background Information

Clinical background

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited heart condition that causes progressive heart muscle loss and typically manifests in young adults. This condition results in a high risk of life-threatening ventricular arrhythmias, sudden cardiac death, and progression to heart failure.

Value proposition of proposed therapy

The current standard of care does not address the underlying disease. The proposed product would deliver a functional version of the Plakophilin-2 (PKP2) gene, restoring lost function in heart cells, which can potentially slow or reverse disease progression.

Why a stem cell or gene therapy project

The therapy is a gene therapy product.

CLIN2-17083 Similar CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1 \$4,000,000	IND enabling	Q2 2026	Desmoplakin- Associated Arrhythmogenic Cardiomyopathy	Adeno-associated virus vector-based gene therapy that drives over expression of FGF21	Targets liver specific expression of FGF21 to restore heart cell function in patients at high risk of life- threatening arrhythmias and sudden cardiac death.

CLIN2-17083 Previous CIRM Funding to Applicant Team

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
DISC2 \$1,017,000	Candidate discovery	Aug 2024	Heart Failure	A gene therapy to deliver cardiac reprogramming factors	Deliver reprogramming factors to convert resident cardiac fibroblasts into functioning cardiac muscle

CLIN2-17083 GWG Review

Phase 1b Study of [redacted] in
Adults with PKP2 Mutation-
associated Arrhythmogenic
Right Ventricular
Cardiomyopathy (ARVC)

CIRM Award Amount:
\$8,000,000*

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

GWG RECOMMENDATION

Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	15
2	0
3	0

DEI SCORE

8 (scale 1-10)

CIRM TEAM RECOMMENDATION

Fund (concur with GWG recommendation)

CLIN2-17091

Phase 3 (Pivotal) Clinical Trial
for SPG50

FUNDS REQUESTED

\$14,908,859

Co-funding: \$9,939,239 (40%
required)

California organization



THERAPY

AAV9 gene therapy encoding human AP4M1 transgene



INDICATION

Spastic Paraplegia Type 50 caused by the AP4M1 gene



GOAL

Complete Phase 3 trial with BLA approval

CLIN2-17091 Background Information

Clinical background

Spastic paraplegia type 50 (SPG50) is a rare genetic neurodegenerative disease caused by a mutation in the adapter protein complex 4 (AP-4). The disease is characterized by the gradual onset of spastic paraplegia during the initial decade of life, which escalates to quadriplegia during adolescence or early adulthood. About 16 individuals in North America are affected by this specific disorder.

Value proposition of proposed therapy

The proposed therapy offers the potential to correct the gene mutation in SPG50 patients and to develop a framework for applying this approach to other ultra-rare monogenic diseases.

Why a stem cell or gene therapy project

The therapy is a gene therapy product.

CLIN2-17091 Similar CIRM Portfolio Projects

CIRM does not currently have any active TRAN or CLIN awards addressing SPG50.

CLIN2-17091 Previous CIRM Funding to Applicant Team

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Mechanism of Action
CLIN1 \$3,930,964	IND enabling	Dec 2025	Charcot-Marie- Tooth disease type 4J (CMT4J)	AAV9-mediated gene therapy for CMT4J, a rare neurodevelopmental disease	Targets affected neurons to provide a functional version of the FIG4 gene to slow or halt disease progression

CLIN2-17091

GWG Review

Phase 3 (Pivotal) Clinical
Trial for SPG50

CIRM Award Amount:
\$14,908,859*

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

GWG RECOMMENDATION

Sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for at least 6 months

Scientific Score	GWG Votes
1	0
2	0
3	14

DEI SCORE

8 (scale 1-10)

CIRM TEAM RECOMMENDATION

Do not fund (concur with GWG recommendation)

C I R M

CALIFORNIA INSTITUTE FOR
REGENERATIVE MEDICINE

Thank You



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