Accelerating the Development of Stem Cell Treatments: Clinical Stage Programs

The mission of CIRM is to accelerate stem cell treatments to patients with unmet medical needs. To better serve this mission, CIRM has overhauled the manner in which it does business, referred to as "CIRM 2.0." Under CIRM 2.0, CIRM has implemented a streamlined process for awarding and administering grants that allows frequent and predictable submission opportunities followed by rapid review, quick funding decisions, streamlined contracting and the prompt initiation of research. Post-award, CIRM has been an active partner with its recipients to further increase the probability of timely success.

Through the CIRM Clinical Stage Program, which was launched as the first CIRM 2.0 program, CIRM has expedited support for clinical stage candidate stem cell treatments that demonstrate scientific excellence. Under this initiative, CIRM has established an open call for proposals and accepts applications on a monthly basis for three complementary award types. CIRM offers funding for eligible projects that are completing late stage preclinical development through any stage of clinical trial activity.

CIRM 2.0 has resulted in timely and efficient funding high quality research projects and has significantly improved outcomes and milestone achievement of CIRM-funded projects. Given the urgency of CIRM's mission, CIRM is committed to constantly improving our programs to better serve and advance the mission. This concept plan further describes the three proposed Program Announcements listed below.

- **CLIN 1:** Funding Opportunity for Late Stage Preclinical Projects
- **CLIN 2:** Funding Opportunity for Clinical Trial Stage Projects
- **CLIN 3:** Partnering Opportunity for a Stem Cell Therapy Registration Clinical Trials

Given the open opportunity to apply and amend rejected applications, requests to appeal the outcome of a GWG review will be limited to demonstrable conflicts of interest as defined in the CIRM Grants Administration Policy.

FUNDING ALLOCATION

CIRM will request funding for this program from the Board on an annual basis as part of the Board's consideration of CIRM's annual research budget.

The Indirect Cost rate will be set at 20% for not-for-profit institutions. For-profit applicants are not eligible for indirect costs. Each application will undergo a thorough independent budget review prior to review by the GWG.

ELIGIBILITY REVIEW

CIRM has the sole discretion to determine whether an applicant has satisfied the eligibility criteria for a program. With the exception of those criteria that are subjective and are subject to appeal to the Grants Working Group (identified with an asterisk in the CLIN program announcements) CIRM may exercise its authority at any time before an award is executed. To the extent that CIRM exercises this authority after the Application Review Subcommittee has approved an award, CIRM will notify the Application Review Subcommittee and the public of its action by including an action item regarding the decision on the agenda for the next meeting of the Application Review Subcommittee.

CLIN 1: FUNDING OPPORTUNITY for LATE STAGE PRECLINICAL PROJECTS

OBJECTIVE

The objective of this funding opportunity is to complete late stage preclinical studies necessary to attain an active IND/IDE with the FDA and initiate start-up activities to prepare for a clinical trial for a stem cell-based therapy or gene therapy.

AWARD INFORMATION

What activities will CIRM fund?

CIRM funds will support the following activities under this opportunity:

- All activities necessary for the conduct and completion of ~~preclinical studies~~IND-enabling activities necessary for ~~that will enable~~ the filing of a single~~well-supported~~ IND/IDE with the FDA ~~for~~to initiate a clinical trial with a single therapeutic candidate
- ~~Assay development~~
- ~~Process development~~
- ~~IND/IDE-enabling preclinical safety, efficacy, and toxicology studies~~
- ~~Manufacturing to support IND/IDE-enabling studies~~
- ~~cGMP manufacturing to supply the intended clinical trial(s)~~
- Product development activities appropriate to support the IND/IDE filing and the resulting clinical trial
- Manufacturing of the therapeutic candidate to support IND/IDE-enabling studies or to support the intended clinical trial(s)
- Clinical trial start-up activities

CIRM funds cannot be used to support the following activities under this opportunity:

- The conduct of a clinical trial beyond start-up activities
- Patient recruitment, screening, or enrollment
- Studies for therapeutic candidate discovery including lead optimization or lead candidate selection

What is the term of the award?

The term of the award will be set forth in the Program Announcement.

Data Sharing Plan

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating treatments to patients. CIRM requires its awardees to develop and execute a Data Sharing Plan that includes management and preservation of data and making applicable data available to the broader scientific community. CIRM strongly encourages sharing of data in accordance with FAIR data principles through established repositories including, but not limited to, specialized NIH-supported repositories, generalist repositories, cloud platforms and institutional repositories. The Data Sharing Plan must be included in the application and the plan is subject to evaluation by the Grants Working Group. Applicants are encouraged to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project. The repository selected and summary of the data shared must be reported to CIRM during and after the project period. To promote the generation of knowledge CIRM may publicly share where CIRM-funded data are deposited.

How will funds be awarded?

Funds will be disbursed pursuant to a CIRM Notice of Award (including projects funded under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative). Awardees may elect, upon completion of their award, to treat their award as a loan pursuant to CIRM's award conversion policy. (See CLIN Grants Administration Policy, Ch. IV(C).) Except for the first payment issued upon initiation of an award, payments will be disbursed upon completion of specific operational milestones. CIRM expects projects to advance rapidly and will not accept applications under this PA that propose more than 18 months to the planned filing of an IND or IDE.

What is the CIRM project funding?

- CIRM will fund total project costs of up to
  - $6,000,000 per award to a non-profit awardee; and
  - $4,000,000 per award to for-profit awardee

ELIGIBILITY

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) Must be ready to initiate work on the funded project within 45 days of approval

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 45 days of approval and authorization for funding by the Application Review Subcommittee of the Independent Citizens' Oversight Committee.

Because of the open and ongoing nature of this Program Announcement, investigators should only apply when their program has reached the stage where all eligibility criteria are met.

(2) Must propose studies to support the filing of a single IND or IDE with a single stem cell-based therapeutic candidate

CIRM will support preclinical studies that enable a well-supported IND for a therapeutic candidate that is either:

- A cell therapy where stem or progenitor cells[1] (collectively, "stem cells") either compose the therapy or are used to manufacture the cell therapy. Minimally manipulated bone marrow, minimally manipulated cord blood or unmodified hematopoietic stem cells (HSCs) or mesenchymal stem cells (MSCs), are eligible **only if** being developed as a novel method of addressing a rare or unmet need unlikely to receive funding from other sources.
- A gene therapy[2] approach (**i**) that targets a stem cell for its therapeutic effect, OR any other somatic cell ~~if deemed a "vital research opportunity" by the CIRM Grants Working Group~~; AND (**ii**) is intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs; AND (**iii**) is being developed for a rare or unmet medical need unlikely to receive funding from other sources.
- A small molecule or biologic (**i**) that acts on or is dependent on endogenous stem cells for its therapeutic effect, that is dependent on targeting cancer stem cells for its therapeutic effect, that modifies a stem cell therapy, OR where a stem cell is necessary to manufacture the therapy; (**ii**) is being developed for a rare or unmet need unlikely to receive funding from other sources; AND **(iii)** is a therapeutic candidate previously funded by CIRM, OR proposes a therapeutic candidate to treat sickle cell disease.

CIRM will support preclinical studies that enable an IDE filing for a medical device candidate previously funded by CIRM (including a diagnostic device) that is:

[1] Under Proposition ~~71~~14, progenitor cells are "multipotent or precursor cells that are partially differentiated but retain the ability to divide and give rise to differentiated cells."

[2] For the scope of this solicitation, CIRM considers gene therapy to mean a human therapeutic intervention intended to: 1) alter the genomic sequence of cells or 2) alter the cellular lineage via gene delivery (i.e., direct lineage reprogramming). The intervention may include strategies to repair a disease-causing gene sequence, remove or inactivate a disease-causing gene, introduce new or modified genes that augment the therapeutic potential of the target cells.

- A device where human stem or progenitor cells are a necessary component of the device or are used to manufacture the device.
- A device intended for clinical use with human stem or progenitor cells where the stem or progenitor cell contributes to the therapeutic MOA of the combination product.
- A device intended to address a critical bottleneck to clinical development or use of a stem cell treatment AND where testing with a human stem or progenitor cell confirms the clinical safety and efficacy of the device.
- A device where the therapeutic MOA requires the recruitment or incorporation of an endogenous stem or progenitor cell.

(3) Must demonstrate appropriate stage of readiness

All projects developing a cell-based therapy, a combination product including a cell therapy component, or an eligible biologic product regulated through CBER must have completed a pre-IND meeting or equivalent with the FDA.

All projects developing a medical device (including a diagnostic) must have completed a pre-IDE submission meeting or equivalent with the FDA.

All projects developing an eligible small molecule or biologic candidate regulated through CDER must have selected a lead molecule and have already performed proof of concept studies and have pharmacokinetic/pharmacodynamic (PK/PD) data with that lead.

The proposed IND/IDE filing must be no more than 18 months from the project start date.

(4) Must include a project manager

The project team must include a Project Manager with experience in managing development programs and able to devote at least 75 percent effort to the project. This requirement may be satisfied through a contract with CIRM's Stem Cell Center to provide project management services.

(5) Co-funding requirements

CIRM will require for-profit applicants to co-fund at least 20% of the total costs of the project. Non-profit applicants may provide co-funding but it is not required. The co-funding may come from any funding source arranged by the applicant. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided by the application deadline (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

(6) Must provide a plan for outreach and inclusion of underserved and disproportionately affected populations.

All proposals developing and preparing a clinical trial study must include a written plan in the application for outreach and study participation by underserved and disproportionately affected populations. Applicants should also address how the research team has or will incorporate diverse and inclusive perspectives and experience in the implementation of the research project.

The GWG and CIRM's governing board will evaluate these plans as a review criterion in making funding recommendations. Priority will be given to projects with the highest quality plans in this regard.

(~~6~~7) For-profit organizations must demonstrate solvency

For-profit organizations must provide documentation that shows 180 days cash on hand from date of application submission and the financial ability to meet the co-funding requirements for the term of the project. The determination of solvency will be made at CIRM's sole discretion.

(~~7~~8) CIRM applicant must be the IND/IDE sponsor

The intended IND/IDE sponsor (i.e., the entity to be named as the sponsor on the IND or IDE application to the FDA) must be the CIRM applicant organization if an organization-sponsored IND/IDE or the CIRM PI if an investigator-sponsored IND/IDE.

(~~8~~9) Application must be accurate and complete

All required components of the application must be completed and may not contain false or inaccurate information.

(~~9~~10) Applicant must be in "good standing"

In order to be eligible to apply for CIRM funding, an applicant must certify that it is in good standing, as follows:

a. For-Profit and Non-Profit (in existence for less than five years):
   (i) The applicant's Chief Executive Officer, Chief Financial Officer, and Principal Investigator must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation; and
   (ii) The applicant must have accounting systems in place that are capable of tracking CIRM funds.

b. All Applicants:

The Principal Investigator or key personnel must not be currently under investigation for research misconduct by the applicant institution or a funding agency, and must not be currently debarred by HHS Office of Research Integrity.

(11~~0~~) CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative

All applications proposing a therapeutic candidate or medical device for the treatment of sickle cell disease will be considered for funding under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative and all application materials will be shared with appropriate NHLBI staff. Under this program, successful applicants are awarded funds from both CIRM and NHLBI. Co-funded projects must adhere to the NHLBI Data Sharing policies and are required to share aggregate data with the Cure Sickle Cell initiative's designated Data Coordinating Center.

Who can apply?

California Research Organizations

California Organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the state of California, and must direct and control the award activities from the California location.

Non-California Research Organizations

Non-California organizations may also apply; however, CIRM funding can be used only for allowable expenditures incurred within California, including the costs of a contract with CIRM's Stem Cell Center. The applicant must demonstrate by the application deadline a commitment of funds from other sources for project activities outside of California. Non-California applicants submitting under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative opportunity may concurrently seek funds from NHLBI to cover CIRM unallowable activities outside of California.

Who can serve as the Principal Investigator (PI)?

To be eligible, the PI must satisfy the following requirements:

- Must be an employee of the applicant organization or be accountable for the conduct of the proposed project to the applicant organization through a formal contract
- Must propose a level of effort on the project consistent with achieving the project's aims and not less than 15% on average over the project period (note: "project" includes both the CIRM-funded and applicant co-funded components). Any effort for which salary from CIRM is claimed must be expended in California

- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI
- Must not currently have another application pending review or approval under this funding opportunity
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

SCHEDULE AND DEADLINES

Applications Due	~~5~~2:00 pm (PDT/PST) on the last business day of each month
Grants Working Group (GWG) Review	Approximately 60 days post submission
ICOC Review and Approval	Approximately 90 days post submission
Award Start	Must start within 45 days of award approval (i.e., approximately 130 days post submission)

CLIN 2: FUNDING OPPORTUNITY for CLINICAL TRIAL STAGE PROJECTS

OBJECTIVE

The objective of this funding opportunity is to complete a clinical trial for a stem cell-based therapy that addresses an unmet medical need.

AWARD INFORMATION

What activities will CIRM fund?

CIRM funds will support the following activities under this opportunity:

- All activities necessary for the conduct and completion of a Phase 1, Phase 2 (limited to cell and gene therapies), or Phase 3 (limited to cell and gene therapies, with a preference for pediatric or rare indications, e.g., FDA orphan drug designation) clinical trial with a single therapeutic candidate
- Manufacturing of product to supply the proposed clinical trial, including a follow on clinical trial, where ~~practical~~ appropriately justified
- Commercial development activities including pharmacoeconomic analysis
- Product development activities to support the clinical trial or clinical development
- Comparability studies
- ~~Exploratory biomarker testing of samples from the clinical trial~~
- ~~In vivo or in vitro assays (e.g. assay development/ parallel in vivo product characterization or potency assays) to support the clinical trial or ongoing product development (as long as it is a component of the trial)~~
- ~~Commercial development activities~~

CIRM funds cannot be used to support the following activities under this opportunity:

- Studies for therapeutic candidate discovery including lead optimization or lead candidate selection
- Preclinical IND-enabling activities
- ~~Early research and translation for candidate discovery/selection~~
- Studies to remove a clinical hold by the FDA

What is the term of the award?

The proposed Project Period must not exceed ~~36~~48 months from the award start date, approximately ~~30~~45 days after the date of ICOC approval. ~~All awards (regardless of start date) must be closed out by November 2023~~. During the Project Period, CIRM funds shall only be used for allowable project costs and activities. ~~Projects under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative may propose a Project Period of 48 months and may exceed the November 2023 close out date.~~

Data Sharing Plan

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating treatments to patients. CIRM requires its awardees to develop and execute a Data Sharing Plan that includes management and preservation of data and making applicable data available to the broader scientific community. CIRM strongly encourages sharing of data in accordance with FAIR data principles through established repositories including, but not limited to, specialized NIH-supported repositories, generalist repositories, cloud platforms and institutional repositories. The Data Sharing Plan must be included in the application and the plan is subject to evaluation by the Grants Working Group. Applicants are encouraged to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project. The repository selected and summary of the data shared must be reported to CIRM during and after the project period. To promote the generation of knowledge CIRM may publicly share where CIRM-funded data are deposited.

How will funds be awarded?

Funds will be disbursed pursuant to a CIRM Notice of Award. Awardees may elect, upon completion of their award, to treat their award as a loan pursuant to CIRM's award conversion policy. (See CLIN Grants Administration Policy, Ch. IV(C).) Except for the first payment issued upon initiation of an award, payments will be disbursed upon completion of specific operational milestones.

What is the CIRM project funding?

- CIRM will fund total project costs of *up to*:
    - For Phase 1 or 1/2:
        - ~~$9,000,000 (or~~ $12,000,000 ~~for sickle cell disease projects)~~ per award to a non-profit awardee; and

- ~~$6,000,000 (or~~ $8,000,000 ~~for sickle cell disease projects)~~ per award to a for-profit awardee

- For Phase 2:
  - ~~$11.25,000,000 (or~~ $15,000,000 ~~for sickle cell disease projects)~~ per award for either a non-profit or for-profit awardee

- For Phase 3:
  - ~~$7.5,000,000 (or~~ $10,000,000 ~~for sickle cell disease projects)~~ per award for either a non-profit or for-profit awardee

ELIGIBILITY

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) Must be ready to initiate work on the funded project within ~~30~~45 days of approval

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within ~~30~~45 days of approval and authorization for funding by the Application Review Subcommittee of the Independent Citizens' Oversight Committee. ~~Projects under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative may initiate work on the funded project within 45 days of approval.~~

Because of the open and ongoing nature of this Program Announcement, investigators should only apply when their program has reached the stage where all eligibility criteria are met.

(2) Must propose a single clinical trial using a stem cell-based therapy

CIRM will support the completion of a single clinical trial per award to test the safety and/or efficacy of a therapeutic candidate, as follows:

Phase 1 trial:

- A cell therapy where stem or progenitor cells either compose the therapy or are used to manufacture the cell therapy. Minimally manipulated bone marrow, minimally manipulated cord blood or unmodified hematopoietic stem cells (HSCs), are eligible **only if** being developed as a novel method of addressing a rare or unmet need unlikely to receive funding from other sources.

- A gene therapy[3] approach (**i**) that targets a stem cell for its therapeutic effect, OR any other somatic cell ~~if deemed a "vital research opportunity" by the CIRM Grants Working Group~~; AND (**ii**) is intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs; AND (**iii**) is being developed for a rare or unmet medical need unlikely to receive funding from other sources.
- A small molecule or biologic (**i**) that acts on or is dependent on endogenous stem cells for its therapeutic effect, that is dependent on targeting cancer stem cells for its therapeutic effect, that modifies a stem cell product, OR where a stem cell is necessary to manufacture the therapy, AND (**ii**) is being developed for a rare or unmet need unlikely to receive funding from other sources.

Phase 2 trial:

- A cell therapy where stem or progenitor cells either compose the therapy or are used to manufacture the cell therapy. Minimally manipulated bone marrow, minimally manipulated cord blood or unmodified hematopoietic stem cells (HSCs), are eligible **only if** being developed as a novel method of addressing a rare or unmet need unlikely to receive funding from other sources.
- A gene therapy[3] approach (**i**) that targets a stem cell for its therapeutic effect, OR any other somatic cell ~~if deemed a "vital research opportunity" by the CIRM Grants Working Group~~; AND (**ii**) is intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs; AND (**iii**) is being developed for a rare or unmet medical need unlikely to receive funding from other sources.

Phase 3 trial:

- A cell therapy where stem or progenitor cells either compose the therapy or are used to manufacture the cell therapy, with a preference for pediatric or rare indications (e.g., FDA orphan drug designation). Minimally manipulated bone marrow, minimally manipulated cord blood or unmodified hematopoietic stem cells (HSCs), are eligible **only if** being developed as a novel method of addressing a rare or unmet need unlikely to receive funding from other sources.
- A gene therapy[3] approach (**i**) that targets a stem cell for its therapeutic effect, OR any other somatic cell ~~if deemed a "vital research opportunity" by the CIRM Grants Working Group~~; AND (**ii**) is intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs; AND (**iii**) is

[3] For the scope of this solicitation, CIRM considers gene therapy to mean a human therapeutic intervention intended to: 1) alter the genomic sequence of cells or 2) alter the cellular lineage via gene delivery (i.e., direct lineage reprogramming). The intervention may include strategies to repair a disease-causing gene sequence, remove or inactivate a disease-causing gene, introduce new or modified genes that augment the therapeutic potential of the target cells.

being developed for a rare or unmet medical need unlikely to receive funding from other sources.

Device Trial:

Under an IDE, CIRM will support a feasibility trial of a medical device (including a diagnostic device), as follows:

- A device where human stem or progenitor cells are a necessary component of the device or are used to manufacture the device.
- A device intended for clinical use with human stem or progenitor cells where the stem or progenitor cell contributes to the therapeutic MOA of the combination product.
- A device intended to address a critical bottleneck to clinical development or use of a stem cell treatment AND where testing with a human stem or progenitor cell confirms the clinical safety and efficacy of the device.
- A device where the therapeutic MOA requires the recruitment or incorporation of an endogenous stem or progenitor cell.

(3) Must have regulatory approval to proceed with proposed trial

- ***All applicants*** must have an active IND/IDE for the proposed candidate in the proposed indication before applying (i.e. the IND/IDE has been filed with FDA for >30 days and has approval to proceed with the proposed clinical protocol) .
- ***Phase 2 trial applicants*** must have Phase 1 safety data, obtained with the proposed candidate in an appropriate indication.
- ***Phase 3 trial applicants*** must have Phase 2 data for the proposed indication(s).

(4) Must include a project manager

The project team must include a Project Manager with experience in managing clinical development programs and able to devote at least ~~75~~50 percent effort to the project. This requirement may be satisfied through a contract with CIRM's Stem Cell Center to provide project management services.

(5) Co-funding requirements

CIRM will require co-funding from the applicant as indicated below. The co-funding may come from any funding source arranged by the applicant. Applicants must commit at least the percentage of total project costs indicated below. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must

be provided by the application deadline (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

Minimum Percentage of Total Allowable Project Costs the Applicant Must Provide

Applicant Type	Phase 1	Phase 2	Phase 3
Non-profit	None	40%	50% with CIRM contribution not to exceed $10M
For-profit	30%	40%	50% with CIRM contribution not to exceed $10M

(6) Must adhere to requirements for clinical trial sites in California

Applicant organizations located outside of California must have at least one clinical site in California.

California applicant organizations are expected to have clinical trial sites in California and must provide justification for inclusion of any sites located outside the State.

(7) Must provide a plan for outreach and inclusion of underserved and disproportionately affected populations.

All clinical trial proposals must include a written plan in the application for outreach and study participation by underserved and disproportionately affected populations. Applicants should also address how the research team has or will incorporate diverse and inclusive perspectives and experience in the implementation of the research project.

The GWG and CIRM's governing board will evaluate these plans as a review criterion in making funding recommendations. Priority will be given to projects with the highest quality plans in this regard.

(8) For-profit organizations must demonstrate solvency

For-profit organizations must provide documentation that shows 180 days cash on hand from date of application submission and the financial ability to meet the co-funding requirements for the term of the project. The determination of solvency will be made at CIRM's sole discretion.

(9) CIRM applicant must be the IND/IDE sponsor

The IND/IDE sponsor (i.e., the entity named as the sponsor on the IND or IDE application to the FDA) for the proposed therapeutic or device must be the CIRM applicant organization if an organization-sponsored IND/IDE or the CIRM PI if an investigator-sponsored IND/IDE.

(10) Application must be accurate and complete

All required components of the application must be completed and may not contain false or inaccurate information.

(11) Applicant must be in "good standing"

In order to be eligible to apply for CIRM funding, an applicant must certify that it is in good standing, as follows:

a. For-Profit and Non-Profit (in existence for less than five years):

(i) The applicant's Chief Executive Officer, Chief Financial Officer, and Principal Investigator must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation; and

(ii) The applicant must have accounting systems in place that are capable of tracking CIRM funds.

b. All Applicants:

The Principal Investigator must not be currently under investigation for research misconduct by the applicant institution or a funding agency, and must not be currently debarred by NIH Office of Research Integrity.

(12) CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative

All applications proposing a therapeutic candidate or medical device for the treatment of sickle cell disease will be considered for funding under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative and all application materials will be shared with appropriate NHLBI staff. Under this program, successful applicants are awarded funds from both CIRM and NHLBI. Co-funded projects must adhere to the NHLBI Data and Safety Monitoring and NHLBI Data Sharing policies and are required to share aggregate clinical trial data with the Cure Sickle Cell initiative's designated Data Coordinating Center.

Who can apply?

California Research Organizations

California Organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the

state of California, and must direct and control the award activities from the California location.

Non-California Research Organizations

Non-California organizations may also apply; however, CIRM funding can be used only for allowable expenditures incurred within California, including the pro rata share of costs incurred out-of-state to treat California clinical trial subjects. The applicant is expected to demonstrate by the application deadline a commitment of funds from other sources for project activities outside of California. Non-California applicants submitting under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative opportunity may concurrently seek funds from NHLBI to cover CIRM unallowable activities outside of California.

Who can serve as the Principal Investigator (PI)?

To be eligible, the PI must satisfy the following requirements:

- Must be an employee of the applicant organization or be accountable for the conduct of the proposed project to the applicant organization through a formal contract
- Must propose a percent effort consistent with achieving the project's aims and not less than 15% on average over the project period (note: "project" includes both the CIRM-funded and applicant co-funded components). Any effort for which salary from CIRM is claimed must be expended in California
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI
- Must not currently have another application pending review or approval under this funding opportunity
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

SCHEDULE AND DEADLINES

Applications Due	~~5~~2:00 pm (PDT/PST) on the last business day of each month
Grants Working Group (GWG) Review	Approximately 60 days post submission

ICOC Review and Approval	Approximately 90 days post submission
Award Start	Must start within 45 days of award approval (i.e., approximately 130 days post submission)

CLIN 3: PARTNERING OPPORTUNITY FOR A STEM CELL THERAPY REGISTRATION CLINICAL TRIAL

OBJECTIVE

The objective of this funding opportunity is to support new activities on active CIRM-funded projects that will, if successful, enable a sponsor to attain marketing approval of the proposed stem cell treatment with the Food and Drug Administration (FDA).

AWARD INFORMATION

What activities will CIRM fund?

CIRM funds will support the following activities under this opportunity:

- New activities not being funded under a parent award (see below) that would enable the sponsor to conduct clinical activities that are necessary for registration.

CIRM funds cannot be used to support the following activities under this opportunity:

- Studies for therapeutic candidate discovery
- Specific activities already funded under the parent award
- Activities not necessary to obtain FDA marketing approval
- Activities occurring after attaining marketing approval

What is the term of the award?

The proposed Project Period must not exceed 48 months from the award start date, approximately 45 days after the date of ICOC approval. During the Project Period, CIRM funds shall only be used for allowable project costs and activities.

Data Sharing Plan

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating treatments to patients. CIRM requires its awardees to develop and execute a Data Sharing Plan that includes management and preservation of data and making applicable data available to the broader scientific community. CIRM strongly encourages sharing of data in accordance with FAIR data principles through established repositories including, but not limited to, specialized NIH-supported repositories, generalist repositories, cloud platforms and institutional repositories. The Data Sharing Plan must be included in the application and the plan is

subject to evaluation by the Grants Working Group. Applicants are encouraged to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project. The repository selected and summary of the data shared must be reported to CIRM during and after the project period. To promote the generation of knowledge CIRM may publicly share where CIRM-funded data are deposited.

How will funds be awarded?

Funds will be disbursed pursuant to a Notice of Award. Awardees may elect to treat their award as a loan pursuant to CIRM's award conversion policy. (See CLIN Grants Administration Policy, Ch. IV(C).) Except for the first payment issued upon initiation of an award, payments will be disbursed upon completion of specific operational milestones.

Award Cap

CLIN3 awards are capped at a maximum amount of $10 million total per award.

ELIGIBILITY

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) Must be ready to initiate work on the new activities within 45 days of approval

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded new activities within 45 days of approval and authorization for funding by Application Review Subcommittee of the Independent Citizens' Oversight Committee.

Because of the open and ongoing nature of this Program Announcement, investigators should only apply when their program has reached the stage where all eligibility criteria are met.

(2) Must supplement an active, development, CIRM-funded project

The applicant must currently have an active CIRM-funded clinical trial award (such as a Disease Team Award, Strategic Partnership Award, or Clinical Trial Stage Award [CLIN2]).

(3) Must use the same therapeutic candidate as the parent CIRM-funded project

The new activities proposed must use the same stem cell therapeutic candidate as in the parent award and any process development or product improvements must be under the same IND.

(4) Co-funding requirements

CIRM will require all applicants to co-fund at the same level required for a Phase 3 trial. The co-funding may come from any funding source arranged by the applicant. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided by the application deadline (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

(5) CIRM applicant must be the IND sponsor

The IND sponsor (i.e., the entity named as the sponsor on the IND application to the FDA) must be the CIRM applicant organization if an organization-sponsored IND or the CIRM PI if an investigator-sponsored IND.

(6) Must provide a plan for outreach and inclusion of underserved and disproportionately affected populations.

All clinical trial proposals must include a written plan in the application for outreach and study participation by underserved and disproportionately affected populations. Applicants should also address how the research team has or will incorporate diverse and inclusive perspectives and experience in the implementation of the research project.

The GWG and CIRM's governing board will evaluate these plans as a review criterion in making funding recommendations. Priority will be given to projects with the highest quality plans in this regard.

(~~6~~7) Application must be accurate and complete

All required components of the application must be completed and may not contain false or inaccurate information.

(~~7~~8) Limit to One CLIN3 Award Per Parent Award

An applicant is only eligible for a single CLIN3 award per parent award.

(~~8~~9) FDA Concurrence

The applicant must present correspondence with the Food and Drug Administration confirming that the activities would support registration.

(~~9~~10) Applicant must be in "good standing"

In order to be eligible to apply for CIRM funding, an applicant must certify that it is in good standing, as follows:

a. For-Profit and Non-Profit (in existence for less than five years):

(i) The applicant's Chief Executive Officer, Chief Financial Officer, and Principal Investigator must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation; and

(ii) The applicant must have accounting systems in place that are capable of tracking CIRM funds.

b. All Applicants:

The Principal Investigator must not be currently under investigation for research misconduct by the applicant institution or a funding agency, and must not be currently debarred by NIH Office of Research Integrity.

(1~~0~~1) CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative

All applications proposing a therapeutic candidate or medical device for the treatment of sickle cell disease will be considered for funding under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative and all application materials will be shared with appropriate NHLBI staff. Under this program, successful applicants are awarded funds from both CIRM and NHLBI. Co-funded projects must adhere to the NHLBI Data and Safety Monitoring and NHLBI Data Sharing policies and are required to share aggregate clinical trial data with the Cure Sickle Cell initiative's designated Data Coordinating Center.

Who can apply?

Only CIRM grantees with an active CIRM-funded clinical trial award (such as a Disease Team Award, Strategic Partnership Award, or Clinical Trial Stage Award [CLIN2]) can apply.

California Research Organizations

California Organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the state of California, and conduct the award activities from the California location.

Non-California Research Organizations

For non-California organizations, CIRM funding can be used only for allowable expenditures incurred within California, including the pro rata share of costs incurred out-of-state to treat California clinical trial subjects. The applicant is expected to demonstrate by the application deadline a commitment of funds from other sources for project activities outside of California. Non-California applicants submitting under the CIRM/NHLBI Cure Sickle Cell Disease Joint Initiative opportunity may concurrently seek funds from NHLBI to cover CIRM unallowable activities outside of California.

Who can serve as the Principal Investigator (PI)?

To be eligible, the PI must satisfy the following requirements:

- Must be the same PI as the parent award
- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Applications Due	~~5~~2:00 pm (PDT/PST) on the last business day of each month
Grants Working Group (GWG) Review	Approximately 60 days post submission
ICOC Review and Approval	Approximately 90 days post submission
Award Start	Must start within 45 days of award approval (i.e., approximately 130 days post submission)