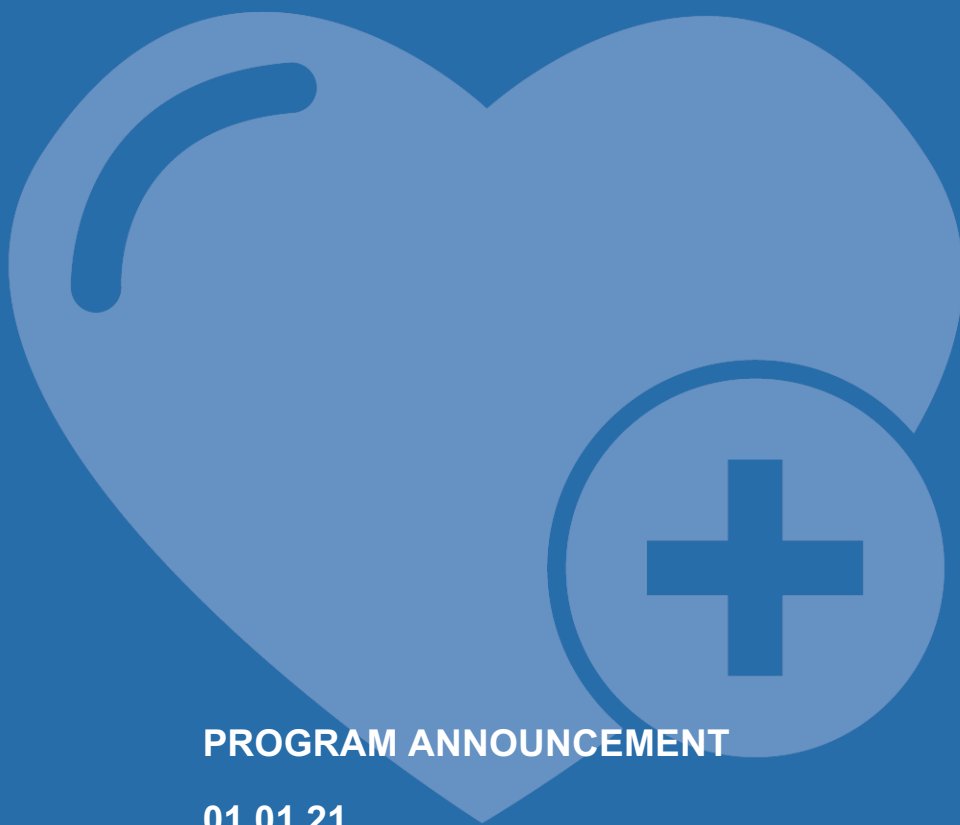


# Partnering Opportunity for Clinical Trial Stage Projects

CLIN2



PROGRAM ANNOUNCEMENT

01.01.21



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# Partnering Opportunity for Clinical Trial Stage Projects

(CLIN2)

## Objective

The mission of California Institute for Regenerative Medicine (CIRM) is to accelerate stem cell treatments to patients with unmet medical needs.

The objective of this program announcement is to create a highly competitive partnering opportunity to accelerate the completion of a clinical trial for a promising stem or progenitor cell-based or gene therapy treatment that addresses an unmet medical need.

Under this program, CIRM will act not only as a funding agency, but will also devote significant internal resources and leverage its external team of world-class subject matter experts to actively advance the project. The result of a successful application will be the formation of a true partnership that both accelerates the program and gives it the greatest opportunity for success.



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## Award Information

### What activities will CIRM support?

CIRM resources will support the following activities under this opportunity:

- ✓ All activities necessary for the conduct and completion of a Phase 1, Phase 2, or Phase 3 clinical trial with a single therapeutic candidate or medical device
- ✓ Manufacturing of product to supply the proposed clinical trial, including a follow on clinical trial, where appropriately justified
- ✓ Commercial development activities including pharmacoeconomic analysis
- ✓ Product development activities to support the clinical trial or clinical development
- ✓ Comparability studies

CIRM resources 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
- ✗ Studies to remove a clinical hold by the FDA

### How will funds be awarded?

CIRM will disburse funds pursuant to a 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 Grants Administration Policy for Clinical Stage Projects, Ch. IV(C)

[https://www.cirm.ca.gov/sites/default/files/files/funding\\_page/CIRM\\_Grants\\_Administration\\_Policy\\_for\\_Clinical\\_Stage\\_Projects.pdf](https://www.cirm.ca.gov/sites/default/files/files/funding_page/CIRM_Grants_Administration_Policy_for_Clinical_Stage_Projects.pdf). If an awardee does not make this election, the award will be treated as a grant. Except for the first payment issued upon initiation of an award, payments will be disbursed upon completion of specific Operational Milestones. **Costs resulting from a delay or failure to meet an Operational Milestone will be the sole responsibility of the recipient.** Successful applicants will have thoughtfully accounted for foreseeable project risks and developed contingency plans that **do not** involve additional funding from CIRM (see "Contingency Plan" under application components). CIRM expects projects under this program to advance rapidly through clinical development; hence, CIRM does not allow applicants to propose more than 48 months of CIRM funding. The proposal must aim to enroll and dose all patients in the trial and to complete initial analysis of the trial's primary endpoint(s) within the maximum 48 month timespan.



**Award Caps**

Applicant Type	Phase 1, Phase 1/2, Feasibility Award Cap*	Phase 2 Award Cap*	Phase 3 Award Cap*
Non-profit	\$12M	\$15M	\$10M
For-profit	\$8M	\$15M	\$10M

\*Total funds requested from CIRM.

**Eligibility**

**What types of projects are eligible for partnering?**

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 CIRM’s governing board, the Independent Citizens’ Oversight Committee (“ICOC”).

Because of the open and ongoing nature of this Program Announcement, investigators should only apply when their project has reached the stage where all eligibility criteria are met. **CIRM reserves the right to refuse to consider an application that is submitted prior to the completion of all necessary prerequisites.**

**(2) Must propose a single clinical trial using a stem<sup>1</sup> or progenitor<sup>2</sup> (collectively “stem cells”) cell-based treatment, gene therapy, or a device for use with stem cell-based treatment**

CIRM will support the completion (as defined in the Award Information section on page 3) 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 (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), are eligible **only if** being developed as a novel method of addressing a rare or unmet need unlikely to receive funding from other sources.\*

<sup>1</sup> Under Proposition 14, stem cells are “nonspecialized cells that have the capacity to divide in culture and to differentiate into more mature cells with specialized function.”

<sup>2</sup> Under Proposition 14, progenitor cells are “multipotent or precursor cells that are partially differentiated, but retain the ability to divide and give rise to differentiated cells.”



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- A gene therapy<sup>3</sup> approach (i) that targets a stem cell for its therapeutic effect, OR any other somatic cell; 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 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<sup>3</sup> approach (i) that targets a stem cell for its therapeutic effect, OR any other somatic cell; 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 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.\*Review preference will be given to projects where the proposed therapy is for pediatric or rare indications (i.e., FDA orphan drug designation<sup>4</sup>).
- A gene therapy<sup>3</sup> approach (i) that targets a stem cell for its therapeutic effect, OR any other somatic cell; 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.

Device trial

Under an IDE CIRM will support a phase 1 or feasibility trial of a medical device (including a diagnostic device) as follows:

- A medical 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 mechanism of action (MOA) of the combination product.

<sup>3</sup> 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.

<sup>4</sup> See FDA orphan designation for definition.



- 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 or 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). The applicant must provide communication from FDA indicating it is safe to proceed with the proposed clinical protocol if proposing a new trial under an open IND/IDE
- **Phase 2 trial applicants** must have Phase 1 safety data obtained with the proposed treatment in an appropriate indication unless agreement to proceed with the Phase 2 protocol is otherwise indicated by the FDA.\*
- **Phase 3 trial applicants** must have Phase 2 data for the proposed indication(s)\* and have completed the End-of-Phase 2 meeting or equivalent.

### (4) Must include a project manager

The project team must include a project manager who has experience managing clinical development programs and is able to devote at least 50 percent effort to the project. This requirement may be satisfied through a contract with CIRM's Cell and Gene Therapy Center to provide project management services.

### (5) Co-funding requirements

CIRM will require applicants to co-fund at least the percentage of the total "Allowable Project Costs" indicated in the table below. Allowable Project Costs are those costs that: (1) are permitted under CIRM policies and regulations and (2) are for allowable project activities (see below). Allowable Project Costs include both direct, facilities, and indirect costs. The sum of CIRM funds requested plus the co-funding contribution by the applicant make up the total Allowable Project Costs. The co-funding may come from any funding source arranged by the applicant, but may not include "in-kind" or similar types of support. Applicants must commit at least the percentage of total Allowable Project Costs indicated below. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission (e.g., copy of executed term sheet showing amount of co-funding) and by the project start date the awardee must have cash-on-hand to co-fund the first operational milestone disbursement. Only funds that will be spent concurrently with CIRM funds (i.e., no sooner than ICOC approval and no later than completion of the final Operational Milestone) will qualify toward this co-funding requirement.



**Minimum Percentage of the Total Allowable Project Costs the Applicant Must Provide**

Applicant Type	Phase 1, Phase1/2, Feasibility	Phase 2	Phase 3
Non-profit	None	40%	50%
For-profit	30%	40%	50%

**(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, including, for example, the inclusion of team members from different socio-economic backgrounds and team members who are the first in their family to attend college.

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 and contingency 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 sponsor**

The IND/IDE sponsor (i.e., the entity named as the sponsor on the IND or IDE) 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.\*



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## (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.

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

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

All Applicants:

- The Principal Investigator and key personnel named in the application 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.

## (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 and on what activities can funds be spent?

#### California Organizations

A California Organization is a for-profit or non-profit organization that employs and pays more than 50% of its employees in California, and that directs and controls the award activities from the California location.

For a California Organization, Allowable Project Costs include:

- The per subject share of the costs of clinical and non-clinical research activities that are directly attributable to the treatment of subjects enrolled in the proposed clinical trial; and
- Costs of manufacturing activities for a subsequent clinical trial when applicant adequately justifies conducting such activities during the proposed clinical trial

#### Non-California Organization

A Non-California Organization is a for-profit or non-profit organization that employs and pays 50% or less of its employees in California.

For a Non-California Organization, Allowable Project Costs include:





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- The per subject share of the costs of clinical and non-clinical research activities, whether conducted in California or outside of California, that are directly attributable to the treatment of California subjects enrolled in the proposed clinical trial; and
- Costs of manufacturing conducted in California for the proposed clinical trial for subjects enrolled, provided such costs are deducted before calculating the per subject share of costs; and
- Costs of manufacturing conducted in California for a subsequent clinical trial when the applicant adequately justifies conducting such activities during the proposed clinical trial

### **Unallowable Costs**

For both California Organizations and Non-California Organizations, Allowable Project Costs do NOT include the costs of activities performed by a separate out-of-state organization that retains intellectual property or independent publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM funded project. Unallowable costs also include project costs incurred before the date the ICOC approves the application for funding, which can be as early as 90 days post application submission.

### **CIRM Discretion**

CIRM may determine, in its sole discretion, whether an applicant is a California organization and whether the project activities are allowable. If an applicant is a non-California organization at the time of application, but intends to become a California organization by the time this project would need to execute a CIRM award contract (~115 days from time of application), then the applicant may submit a budget that includes the Allowable Project Costs for California organizations and must describe their intentions and the timing of becoming a California organization in this application.

### **Funding of Non-Allowable Project Activities**

The applicant must demonstrate by the application deadline a commitment of funds from other sources for non-allowable project activities that are necessary to achieve the goals of the application.

### **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 partnering 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

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

## Application Review Information

### What is the process for evaluating an application?

#### **Pre-submission Consultation**

In accordance with CIRM's mission, the Agency is committed to helping develop promising stem cell treatments by partnering with world-class investigators. Therefore, prospective applicants are encouraged to contact CIRM before applying with questions or to discuss their project's eligibility, scientific, or budget considerations.

#### **Eligibility Review**

CIRM will assess whether the proposed project meets eligibility requirements sought under this program. If CIRM determines, in its sole discretion, that an application does not meet the eligibility requirements of the program, CIRM will notify the applicant of its decision, if CIRM deems it appropriate allow an opportunity to remedy. If CIRM deems it inappropriate, or if the applicant does not timely remedy the deficiency, CIRM will terminate all further action on the application. In the event CIRM determines that the application does not meet the eligibility requirements of the program based on a subjective criterion (designated in the ELIGIBILITY section with an asterisk "\*\*"), the applicant may request that the CIRM Grants Working Group (GWG) review the decision. This request must be submitted to CIRM no later than 14 days after the date of CIRM's notification that the application is ineligible. If the working group affirms CIRM's decision, the applicant will be notified and no further



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action will be taken on the application. If the GWG determines the application meets the eligibility requirements, the application will be accepted into the next available review cycle.

CIRM may exercise its authority to make eligibility determinations at any time before an award is executed.

### **Budget Review**

CIRM will review the proposed budget to assess how the proposed costs compare with established market rates for similar activities, how well the costs are justified when market rates are not established and to confirm that costs designated as Allowable Project Costs comply with CIRM policies. When a proposed budget differs significantly from market rates, is not well justified or does not comply with Allowable Project Cost policy, adjustments to the budget will be required by CIRM prior to further review of the application. Applicants will be notified of the specific discrepancies and applications will not be forwarded for scientific review until an amended budget has been submitted and approved by CIRM. Additionally, project budgets may be subject to further adjustments prior to issuance of an award based upon assessments of the GWG, the CIRM team, or by the Application Review Subcommittee of the ICOC.

### **Scientific Review**

The scientific merit of each application will be assessed by the GWG, which is composed of fifteen subject matter experts from outside California, seven patient advocate members of the ICOC, and the Chair of the ICOC. The list of scientific members who may participate in the GWG review can be found at [http://www.cirm.ca.gov/WorkingGroup\\_GrantsReview](http://www.cirm.ca.gov/WorkingGroup_GrantsReview). The composition of the ICOC can be viewed at <http://www.cirm.ca.gov/GoverningBoard>.

The fifteen participating scientists on the GWG will evaluate the applications and score them according to scientific and technical merit, applying the review criteria described below. The GWG will score each application and make one of the following specific recommendations to the ICOC's Application Review Subcommittee: 1) fund the project based on its exceptional merit; 2) do not fund the project but allow for resubmission to address areas for improvement; or 3) do not fund the project and do not allow resubmission for 6 months. In the event the GWG recommends amendment and resubmission, the applicant may elect, prior to the ICOC's final funding decision, to amend and resubmit the application for reevaluation by the GWG.

The ICOC's Application Review Subcommittee will make final funding decisions giving consideration to the GWG recommendations and any CIRM team recommendations.

### **Consideration of Related CIRM Award Information (If Applicable)**

The GWG may consider information from a previously funded and related CIRM award as part of its review. CIRM will provide the GWG with objective information regarding a related award that CIRM, in its sole discretion, deems relevant, including but not limited to achievement of specific milestones, data, and outcomes for a related CIRM award or awards.

A "related CIRM award" includes: (1) an award for which the applicant PI served as the PI, a co-PI, a co-investigator, or otherwise substantially participated in the



conduct of the award; (2) an award involving the same research project or product; or (3) an award that includes overlapping team members.

### 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 expects 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.

### Confidentiality

CIRM's confidentiality and conflict screening rules apply to everyone who will have access to applications or who will attend any review meeting in which confidential information is discussed, including but not limited to CIRM team members, reviewers and members of the ICOC. (Per Gov. Code §6254.5(e) non-public records may be disclosed to government agencies under confidentiality agreements).

### How will the scientific merit of an application be evaluated?

Scientific members of the GWG will evaluate and score applications based on the following key questions:

#### 1. Does the project hold the necessary significance and potential for impact?

Does the proposed treatment address an unmet medical need? Is the approach likely to provide an improvement over the standard of care for the intended patient population? Does the proposed treatment offer a sufficient value proposition such that the value created by the treatment supports its adoption by patients and/or health care providers? If a Phase 3 trial is proposed, is the therapy for a pediatric or rare indication (i.e. FDA orphan drug designation) or, if not, is the project unlikely to receive funding from other sources?

#### 2. Is the rationale sound?

Is the proposed project based on a sound scientific and/or clinical rationale? Is the project plan supported by the body of available data? Do the data support the continued development of the treatment?



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### 3. Is the project well planned and designed?

Is the project appropriately planned and designed to meet the objective of the program announcement and achieve meaningful outcomes to support further development of the therapeutic candidate? Do the project plan and timeline demonstrate an urgency that is commensurate with CIRM's mission (i.e. Are the proposed experiments essential and do they create value that advances CIRM's mission? Is the timeline appropriate to complete the essential work without unnecessarily extending it for non-essential activities)?

### 4. Is the project feasible?

Are the intended objectives likely to be achieved within the proposed timeline? Is the proposed team appropriately qualified and staffed and have access to all the necessary resources to conduct the proposed activities? Does the team have a viable contingency plan to manage risks and delay?

### 5. Does the project serve the needs of underserved communities?

Does the proposal provide a clear and robust plan for outreach and study participation by underserved and disproportionately affected populations? Does the proposal adequately address the planned distribution of subjects by sex/gender, race and ethnicity? Does the proposal provide an appropriate rationale for the study population selection criteria? Does the application provide adequate justification for the proposed exclusion of a group(s) at risk for the disease/condition under study?

## Application Components and Submission

### How does one apply?

Applications must be completed and submitted online using the CIRM Grants Management Portal at <https://grants.cirm.ca.gov>. Any prospective PI must create a login in the system to access application materials and apply. Applications are available in the system only to the PI and his or her designee. A PI may submit only a single application in a given review cycle.

**Applications are due by 2:00pm (Pacific Time) on the last business day of each month.** Applications received after the deadline will be deferred to the next monthly review cycle.

### What components does an application include?

The Grants Management Portal provides instructions for completing all the necessary components and submitting a final application. The application is designed to collect information necessary to appropriately evaluate the proposal and for CIRM to rapidly initiate an award if approved for funding. Applicants are required to indicate key personnel involved in the project, describe how the proposal addresses the objective of the partnering opportunity, provide a detailed plan of proposed activities, complete a detailed activity-based budget, and provide reference materials, such as FDA



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correspondence that confirms the status of the project. Applicants will also be required to provide a financial contingency plan that addresses how the applicant will cover possible funding shortfalls.

The main body of the proposal contains the following sections:

1. **Project Summary:** Description of the project for which partnering is sought. If a phase 3 clinical trial is proposed, description of how the therapy qualifies as a pediatric or orphan indication or, if it does not, why the project is unlikely to receive funding from other sources.
2. **Target Product Profile:** Description of the aspirational goals of the commercialized product that outlines the base case and optimal product profile that describes a medical and commercial value proposition that supports adoption by patients and health care providers.
3. **Value Proposition & Risk/Benefit Profile:** Description of the indication and unmet medical need that will be addressed with the product. Description of the current standard of care and how the proposed product will improve patient outcomes and/or quality of life. Description of the value created by this product that supports its adoption by patients and healthcare providers. Description of next steps in clinical development of the proposed product.
4. **Outreach & Inclusion of Underserved Populations:** Description of plans for outreach and study participation by underserved and disproportionately affected populations in the proposed clinical trial.
5. **Rationale:** Discussion of the scientific rationale and data, including with the therapeutic candidate, that supports its use in the target disease or injury and for the patient population in which testing will occur and the intended treatment population.
6. **Completed IND-Enabling Studies Summary:** Tabular summary of completed IND-enabling studies and description of study outcomes.
7. **Previous Clinical Experience Summary:** Tabular summary of completed or ongoing clinical studies with the proposed or related product (if applicable).
8. **Timeline in Gantt-Like Format:** Timeline of all activities required to achieve the project/PA objective.
9. **Project Plan to Achieve the Program Announcement Objective:** Description of planned activities to achieve the project and PA objective (this should annotate the Gantt chart).
10. **FDA Correspondence:** Summary of relevant FDA comments, plan for addressing FDA comments, and official FDA meeting minutes and/or FDA correspondence relevant to the proposed project.
11. **Manufacturing Summary:** Manufacturing plan synopsis.
12. **Clinical Protocol:** Clinical protocol synopsis. Provide full FDA approved clinical protocol in Uploads section.
13. **Operational Plan:** Clinical operations plan for the proposed clinical trial.
14. **Commercial Development Plan:** Describe any planned commercial development activities.
15. **Data Sharing Plan:** A description of the proposed plan to make available data generated from the project. The description should include the type(s) of data expected to be produced, how the data will be managed, what data will be





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shared and how (i.e., repository), justification for not sharing certain data, timeline for data sharing and expected costs.

- 16. Risk Mitigation and Financial Contingency Plan:** Potential risks, mitigation strategies, and associated costs, including a description of a viable source to cover these costs (other than CIRM and not including co-funding).
- 17. Team Organization:** Team qualifications, structure, leadership and communications plan.
- 18. Resources and Environment:** Resources available to the project and environment.
- 19. Diversity, Equity and Inclusion in Research:** A statement on how the research team has or will incorporate diverse and inclusive perspectives and experience in the implementation of the research project, including, for example, the inclusion of team members from different socio-economic backgrounds and team members who are the first in their family to attend college.
- 20. References**

#### **Who are Key Personnel?**

In the application, we ask you to identify by name pertinent Key Personnel and their specific roles on the project. Key Personnel are defined as (1) the principal investigator or program director; or (2) any other person, including an independent consultant or an employee of a Subcontractor or Partner, who is expected to contribute to the scientific development or execution of the project in a substantive, measurable way *and* who is expected to: (a) receive or has been promised income, or anything else of value, of \$10,000 or more per year for his or her contribution to the project or (b) contribute one percent (1%) or more effort to the proposed project. "Key Personnel" does not include a person who is expected to be involved in the proposed project but who does not satisfy conditions (1) or (2).

Individuals who do not meet the definition of Key Personnel may be supported with CIRM funds, but should not be identified by name in the application. Such unnamed personnel may be referenced indirectly by their role on the project (e.g., technician). The budget includes a line item for requesting support for unnamed personnel.

#### **What should one know before preparing the budget?**

A specific and well-justified activities-based budget must be provided that clearly outlines the total costs of the project, including those costs not proposed to be funded by CIRM. The corresponding budget justification should provide enough detail to allow budget professionals to determine the appropriateness of the costs in relation to the activities being performed. Allowable Project Costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy for Clinical Stage Projects

[https://www.cirm.ca.gov/sites/default/files/files/funding\\_page/CIRM\\_Grants\\_Administration\\_Policy\\_for\\_Clinical\\_Stage\\_Projects.pdf](https://www.cirm.ca.gov/sites/default/files/files/funding_page/CIRM_Grants_Administration_Policy_for_Clinical_Stage_Projects.pdf). Generally, project costs for



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personnel, supplies, travel, equipment, and subcontracts may be claimed. Limits for specific cost categories must be observed.

### **What are Direct Facilities Costs and how much can an applicant claim?**

Direct Facilities Costs are the general operating costs of the Awardee's facilities attributable to housing all elements of the CIRM-funded project or activity. Facilities costs for non-profit applicant organizations are limited to the current applicable, federally negotiated rates for the organization as defined by the Office of Management and Budget (OMB) Circular A-21 or A-122. Facilities rates for for-profit applicant organizations are limited to 35% of the direct project costs. Facilities rates are applied to direct project costs exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of \$25,000. The facilities cost rates approved and in place at the time of the application are to be applied to the entire award project period.

### **How much can an applicant claim for indirect costs?**

For-profit organizations cannot claim indirect (administrative) overhead costs. For non-profit organizations, indirect costs will be limited to 20% of allowable direct research funding costs awarded by CIRM (i.e., direct project costs and facilities costs), exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of \$25,000. The indirect cost rate budgeted at the time of application is to be applied to the entire award project period.

### **How does one utilize CIRM Infrastructure Programs?**

CIRM has established Infrastructure Programs to help CIRM applicants and Awardees prepare competitive applications and to accelerate the conduct of high quality stem cell clinical trials and research.

The CIRM Alpha Stem Cell Clinics are a statewide Network composed of 6 leading California Medical Centers (<https://www.cirm.ca.gov/patients/alpha-clinics-network>). The Network has performed over 40 stem cell clinical trials for academic and commercial partners (<https://www.cirm.ca.gov/patients/alpha-clinics-network/alpha-clinics-trials>). Applicants and awardees can partner with the Alpha Stem Cell Clinics Network to identify California trial sites, evaluate patient cohorts and accelerate trial initiation and completion.





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## Award Administration

### Issuance of Award

A CIRM award is issued via a Notice of Award Agreement, which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM.

### Operational Milestones and Payment

CIRM funds under the award will be disbursed based on achievement of specific Operational Milestones established by CIRM. An “Operational Milestone” is an objective event that is indicative of project progress occurring as proposed in the application. CIRM establishes Operational Milestones for inclusion in the Grant or Loan Agreement based upon information provided in the Application. Upon issuance of the award, funds budgeted to achieve the initial Operational Milestone will be disbursed. Upon the successful completion of the initial Operational Milestone and each successive milestone, additional funds will be disbursed. If funds allocated to a specific Operational Milestone (including both CIRM funds and the required applicant co-funds) are exhausted prior to achievement of that milestone, the Awardee will be responsible for covering any remaining costs. CIRM expects that the applicant’s contingency plan will identify project timeline and budget risks and will provide details for covering such costs, including the source of funding. CIRM reserves the right to make adjustments to the timeline for inclusion in the Notice of Award to ensure that funds are appropriately dispersed across Operational Milestones.

If CIRM determines, in its sole discretion, that an awardee has failed to satisfy an Operational Milestone within four months of the date that the Operational Milestone was scheduled to have been completed, or if the delay is not addressed to CIRM’s satisfaction, CIRM may permanently cease disbursements and terminate the award.

### Suspension Events

CIRM reserves the right to hold or terminate disbursements if CIRM determines, in its sole discretion, that a Suspension Event has occurred. A “Suspension Event” means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable. Following a Suspension Event, the Awardee is expected to provide CIRM with a plan to resolve the issue that triggered the Suspension Event. CIRM establishes Suspension Events for inclusion in the Notice of Award based on information provided in the Application.

### Reporting

Awardees will be required to provide periodic written progress and financial reports to CIRM.

Upon approval of an award, CIRM will appoint a Clinical Advisory Panel (CAP) to partner with the Awardee. The CAP will be composed of at least one CIRM science officer, one external advisor, and a patient representative and will provide guidance and advice to foster success of the project. CAPs have the ability to enlist the help of CIRM’s external subject matter experts when needed. Awardees will have ongoing communication with the CAP throughout the duration of the award, typically meeting by teleconference on a quarterly basis and in person once a year.



### **Other Requirements**

#### **CIRM Regulations**

Grant or Loan awards made through this program announcement will be subject to all applicable CIRM regulations. These regulations can be found on CIRM's website at <http://www.cirm.ca.gov/reg/default.asp>.

#### **Clinical Trials**

Clinical trials funded by CIRM must be listed on <http://www.clinicaltrials.gov/> and awardees must submit the administrative and scientific results of the trial to the clinicaltrials.gov results database within one year of completion of the studies (in compliance with FDAAA801), for the benefit of the field.

#### **Change in Status**

Applicants are required to notify CIRM of any material change in status while the application is pending review, e.g., the applicant has commenced the trial that is the subject of the award, the applicant no longer qualifies as a California Organization, etc.

A list of frequently asked questions regarding managing a CIRM award can be found at <https://www.cirm.ca.gov/researchers/managing-your-grant>



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## Contacts

For information about this program announcement:

Send email correspondence to [Clinical@cirm.ca.gov](mailto:Clinical@cirm.ca.gov)

or

Call our main line at 510-340-9101 and select "Funding Opportunities" then "Clinical"



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## Definitions

“California organization” means: An entity, regardless of profit status, that has >50% of its employees located in, and paid in, the state of California, and that directs and controls the award activities from the California location.

“For-profit organization” means: a sole-proprietorship, partnership, limited liability company, corporation, or other legal entity that is organized or operated for the profit or financial benefit of its shareholders or other owners. Such organizations also are referred to as “commercial organizations”.

“Non-profit organization” means: (1) a governmental entity of the state of California; or (2) a legal entity that is tax exempt under Internal Revenue Code section 501(c)(3) and California Revenue and Taxation Code section 23701d.

“Operational Milestone” means an objective event that is indicative of project progress occurring as proposed in the application.

“Partner” means an organization that, in exchange for the right to the opportunity for a future financial return, has (1) agreed to provide matching funds for the proposed project or (2) entered into an agreement with the applicant organization relating to the commercialization of the proposed project.

“Subcontractor” means an organization (other than the applicant organization) that is expected to: (a) contribute to the scientific development or execution of the project in a substantive, measurable way *and* (b) receive \$25,000 or more through the proposed project. “Subcontractor” does not include suppliers of widely available goods.

“Suspension Event” means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable.



## Revisions

Revision Date	List of Changes
4/19/19	<ul style="list-style-type: none"> <li>Clarified definition for completion of a clinical trial as:                             <ul style="list-style-type: none"> <li>enrolling and dosing all patients</li> <li>completion of initial analysis of primary endpoint(s)</li> </ul> </li> </ul>
11/28/18	<ul style="list-style-type: none"> <li>Revised candidate eligibility:                             <ul style="list-style-type: none"> <li>Gene therapy approaches for non-stem cells are eligible if a 'vital research opportunity'</li> </ul> </li> <li>Revised PI eligibility:                             <ul style="list-style-type: none"> <li>PI cannot have substantially similar applications currently pending review or approval.</li> </ul> </li> <li>Updated hyperlinks</li> <li>Name change of "Stem Cell Center" to "Cell and Gene Therapy Center"</li> </ul>
07/22/20	<ul style="list-style-type: none"> <li>Adjusted maximum award amount and duration:                             <ul style="list-style-type: none"> <li>Total project cost limits were reduced.</li> <li>Project duration cannot exceed 36 months and awards must close out by November 2023.</li> </ul> </li> <li>Revised project start time:                             <ul style="list-style-type: none"> <li>Projects must be ready to start 30 days after approval.</li> </ul> </li> <li>Added requirement for statement on addressing the underserved:                             <ul style="list-style-type: none"> <li>Applicants must include a written plan in the application for outreach and study participation by underserved and disproportionately affected populations.</li> </ul> </li> <li>Application components were updated.</li> </ul>
01/01/21	<ul style="list-style-type: none"> <li>Adjusted maximum award amount and duration:                             <ul style="list-style-type: none"> <li>Total project cost limits were restored to amounts prior to 07/22/20 revision.</li> <li>Project duration cannot exceed 48 months.</li> </ul> </li> <li>Revised project start time:                             <ul style="list-style-type: none"> <li>Projects must be ready to start 45 days after approval.</li> </ul> </li> <li>Revised percent effort requirement for project manager:                             <ul style="list-style-type: none"> <li>Project manager must devote at least 50% effort to the project.</li> </ul> </li> <li>Clarified therapeutic candidate eligibility:                             <ul style="list-style-type: none"> <li>Gene therapy projects do not require a "vital research opportunity" vote by GWG under Prop 14.</li> <li>Clarified that minimally manipulated bone marrow and HSC are eligible for phase 2 and 3 proposals.</li> </ul> </li> <li>Added Data Sharing Plan Requirement.</li> <li>Added review criterion for serving the needs of underserved communities.</li> <li>Added requirement to address diversity, equity and inclusion in research.</li> <li>Updated Prop 14 definitions.</li> <li>Added paragraph regarding CIRM/NHLBI Sickle Cell Initiative requirements.</li> </ul>



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